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The worker with diabetes mellitus and the legacy between health care professionals

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Diabetes mellitus is a complex, degenerative, chronic disease that is paradigmatic of the degree of complexity related to numerous factors, making the patients with diabetes different one from another. For this reason, it constitues a formidable challenge for the clinicians and for the occupational health professional.

At a pathophysiological level, it is recognized that beyond the most frequent clinical form of the disease (type 2 diabetes), less frequent clinical forms of diabetes (type 1 diabetes, gestational diabetes, MODY and LADA) are all characterized by different pathophysiological mechanisms. However, also in patients with type 2 diabetes at least five different clinical clusters of individuals may be identified.

At a therapeutic level it is simple to think about the obvious consequences of the complexity of an insulin-based therapeutic regimen and the associated risk of hypoglycemia. At the same time, in the last few years formidable improvements in the way patients may perform self-blood glucose monitoring and nowadays continuous interstitial glucose monitoring reduced this risk even if this monitoring and also the use of pumps for the continuous subcutaneous administration of insulin may require different conditions in the work environment to be performed properly.

Also, in the last few years novel oral and non-insulin injectable drugs became available with a better safety profile in terms of the risk of hypoglycemia, but with different pattern of potential, and practical, side effects that need to be taken into account.

In addition, patients with diabetes are often undergoing a complex combination of therapeutic regimens involving many drugs with potential interactions to be considered, as well as consequent important adverse events.

Furthermore, in organ transplantation with additional pharmacologic therapeutic regimens, and in bariatric surgery with its potential metabolic complications and life-style modification, therapeutic tools are increasingly used and they may change profoundly and require a different skills profile to be acquired by the patients at work-places.

At the prognostic level, micro- and macro-vascular complications of diabetes mellitus with potential impact on cardiovascular disease risk, chronic kidney disease, eye impairment, sensitive-motor neuropathy along with autonomic neuropathy are to be carefully considered when we have a patient with diabetes in his work environment. The combination of sensitive-motor neuropathy and peripheral vascular disease may determine foot abnormalities with important consequences for these patients at work, in terms of performance but also in terms of appropriate protection of the extremities.

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Similarly, patients with diabetes may often have co-morbidity with a relevant fallout about the work environment; respiratory failure, cardiac failure and hepatic failure are not infrequent, as well as osteoporosis and arthropathy.

Also, patients with diabetes are at higher risk of experiencing acute intercurrent illnesses, especially infections.

Finally, it is difficult to say whether the high frequency of mood disorders is to be considered a co-morbidity or rather a consequence of the metabolic disease, but it is certainly a component in the everyday life of patients with diabetes with relevance related to their career progression as well as safety and responsibility at the work-place.

The high number of variables to be taken into consideration from clinical and practical stand-points is further complicated by the fact that many health care professionals are involved with the treatment of the disease and prevention of diabetes complications: the diabetologist, the dietitian, the nurse, the psychologist, the podologist, within the restricted diabetes-team, but most often, the cardiologist, nephrologist, ophthalmologist, gastroenterologist, vascular surgeon, bariatric surgeon, psychiatrist may be all involved in handling the many different aspects of the disease.

Last but not least, the environment in which the patient with diabetes works and lives is of paramount importance in terms of infrastructures, including shift- and night-time work, working activities at high risk of accidents, work at heights, working tasks requiring high-energy expenditure, working activities at extreme temperatures. The working and living environment is also important in terms of the relationships with colleagues and family members.

So, although diabetes, generally, does not prevent a person from properly performing the working tasks, all the above described conditions and disease complications may compromise a person's ability to work. This Editorial aimed to demonstrate the thesis initially stated that the patient with diabetes may be a very difficult task for the occupational physician. The Italian Society of Occupational Medicine (SIML), the Italian Diabetes Society (SID) and the Association of Diabetologists (AMD) joined a working group to improve the understanding of the available evidence regarding the interplay between specific working conditions. The objectives of the efforts of this working group are to ensure diabetic workers the possibility to safely and effectively undertake their jobs but also to adequately manage and treat their disease to guarantee their well-being, also in the workplace. In this perspective concerted action of all the workplace preventive figures, the occupational physician and the diabetologist should be strongly encouraged. The event entitled "*Approccio multi-disciplinare al lavoratore con diabete: dialogo tra medici del lavoro, diabetologi e specialisti*" which was held in Milano in March 2019, represents an effort in this direction.

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Diabetes mellitus: up-to-date on antidiabetic drugs and hypoglycemic risk for the occupational physician

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Keywords: Diabetes mellitus; hypoglycaemia; chronic complications; treatment

Parole chiave: Diabete mellito; ipoglicemia; complicanze croniche; trattamento

Summary
Diabetes Mellitus (DM) is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control. Diabetes and hyperglycemia cause chronic complications: cardiovascular disease, blindness, kidney failure and lower-limb amputation, that can lead to the exclusion of some work tasks. Diabetes drugs, as insulin or sulphonylureas, can cause hypoglycemia and the worker may be at risk of accidents. In recent years, numerous innovative drugs have become available and it is very important that the occupational physician knows their mechanism of action and their side effects since they could influence the worker's job. Finally, the occupational physician could play a role in the prevention of type 2 diabetes: this is why it is important to know the disease, how to diagnose it and how to change the lifestyle in workers at risk.

Riassunto
«Diabete mellito: aggiornamento su farmaci antidiabete e rischio ipoglicemico per il Medico del lavoro». *Il diabete mellito (DM) è una malattia cronica complessa che richiede cure mediche continue con strategie multifattoriali, per ottenere una riduzione del rischio di complicanze, oltre al controllo glicemico. Il diabete e l'iperglicemia causano complicazioni croniche: malattie cardiovascolari, cecità, insufficienza renale e amputazione degli arti inferiori, che possono portare all'esclusione da alcune attività lavorative. I farmaci per il diabete, come l'insulina o le sulfoniluree, possono causare ipoglicemia e mettere a rischio di incidenti il lavoratore. Negli ultimi anni si sono resi disponibili farmaci innovativi per la cura del diabete ed è molto importante che il medico del lavoro conosca il loro meccanismo d'azione e i loro effetti collaterali, poiché potrebbero influenzare l'attività lavorativa. Infine, il medico del lavoro potrebbe svolgere un ruolo nella prevenzione del diabete di tipo 2: ecco perché è importante conoscere la malattia, come diagnosticarla e le strategie per cambiare lo stile di vita dei lavoratori a rischio.*

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Epidemiology

Recent data estimated that 438 million people aged between 20-64 years will suffer from DM by the year 2045 (4). Type 1 Diabetes Mellitus (T1DM) is more prevalent in children, especially those who range from birth to 14 years old, but individuals of any age can be diagnosed with it, with an excess of male seen among young adults. On the other hand, adults or obese individuals are mostly affected by Type 2 Diabetes Mellitus (T2DM), but it can occur in children too according to recent reports. Also, T2DM is the most common type of diabetes, accounting for around 90% of all cases of diabetes. Globally, the prevalence of T2DM is high and is rising across all world regions. This rise is due to the aging of population, economic development and increasing urbanization leading to more sedentary lifestyles and greater consumption of unhealthy foods linked with obesity. Patients with T2DM have a higher risk of death from cardiovascular causes compared with their nondiabetic counterparts, and the mortality rate of DM-associated cardiovascular disease varies among different ethnic and sex groups (8). In 1984 the American Diabetes Association adopted the following position on employment "Any person with diabetes whether insulin or non-insulin treated should be eligible for any employment for which he/she is otherwise qualified (1). Previous research has found that people who left the labor force early due to diabetes had an income five times lower than those who did not have a chronic illness (13). Men and women with T2DM were 7.1% and 4.4%, respectively, less likely to be working compared to their non-diabetic counterparts (15). The same study also found that people with diabetes had more work-loss days per year than those without the disease.

Physiopathology

DM is a metabolic disease commonly characterized by an increase of the blood glucose levels that warrant frequent monitoring and proper control. Pancreatic beta cells produce the hormone insulin which facilitates the absorption of glucose into the cells in order to provide energy and is also involved in a variety of other functions. T1DM is typically associated with failure in insulin production resulting from the destruction of pancreatic β-cells by T-cell-mediated autoimmunity. T2DM occurs due to lack of insulin production and insulin sensitivity. It is mainly classified into many types, however the most common is T2 DM. A few susceptible genes were identified to be risk factors for T1DM. These include some of the human leukocyte antigen (HLA) types. Studies shows that identical twins have a higher likelihood to develop T1DM than fraternal twins, showing a strong familial genetic predisposition. T1DM can also be triggered by environmental factors such as viral infections, low levels of vitamin D and several dietary and lifestyle factors such as childhood obesity, rapid growth in infancy, older maternal age and short duration of breastfeeding. In summary, the onset of T1DM appears to be related with a complex interplay of genetic, immune and environmental factors that destruct the pancreatic β-cell function. Insulin resistance is the most powerful predictor of future development of T2DM and cardiovascular disease (CVD) and represents a therapeutic target once hyperglycemia is present (14). Insulin resistance is responsible for the physio-pathologic process where cells fail to respond normally to insulin. Liver, skeletal muscle and adipocytes are mainly involved. Dysregulation of fatty acid metabolism plays a pivotal role in the pathogenesis of insulin resistance in skeletal muscle, with decreasing insulin-stimulated glucose uptake due to impaired insulin signaling and multiple post-receptor intracellular defects including impaired glucose transport and glucose phosphorylation, and reduced glucose oxidation and glycogen synthesis (3).

Suppression of glucose production in the liver is decreased and activation of GLUT-4-mediated glucose uptake does not take place, particularly in skeletal muscles and adipocytes. This overall failure typically is not due to low insulin levels. Instead, insulin-stimulated signal transduction pathways for peripheral glucose uptake and for hepatic glucose production are reduced, including insulin receptors and downstream mediators. Hyperglycemia is then driven by excessive hepatic glucose production and reduced uptake of glucose by peripheral tissues (3). To counteract glycemic elevations, β cells of the

pancreas boost insulin production, further contributing to hyperinsulinemia. The risk factors for T2DM are a sedentary lifestyle, an incorrect diet that involves the consumption of foods rich in carbohydrates, fats, and sugary drinks but low in fiber and which can also be linked to genetics. Obesity and a previous gestational diabetes are also correlated with incidence of T2DM (1, 2)

Classification and diagnostic criteria

Diabetes can be classified into the following general categories:

1. T1DM, due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency
2. T2DM, due to a progressive loss of –β cell insulin secretion frequently on the background of insulin resistance
3. Gestational diabetes mellitus (GDM), diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation
4. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes, such as neonatal diabetes and maturity-onset diabetes of the young (MODY), diseases of the exocrine pancreas, such as cystic fibrosis and pancreatitis, and drug- or chemical-induced diabetes, such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation (1). In Table 1 Pre-diabetes and Diabetes diagnostic criteria are described (1). The onset of T2DM is usually slow and its usual presentation without the acute metabolic disturbance seen in T1DM means that the exact time of onset is difficult to determine. As a result, there is often a long pre-detection period and as many as one-third to one-half of T2DM cases in the population may be undiagnosed because they may remain without symptoms for many years. When unrecognized for a prolonged time period, the complications of chronic hyperglycemia may develop.

Glycemic target and hypoglycaemia

Table 2 describes glycemic targets for a good metabolic control in diabetic patients, according to national and international Scientific Societies. It is important to underline that these goals must be achieved without hypoglycemia. Hypoglycemia is the most important predictor of cardiovascular mortality, as shown in large studies on diabetics at

Table 1 - Pre-diabetes and Diabetes mellitus diagnostic criteria

Impaired fasting glucose (Ifg)	Impaired glucose Torelance (igt)	Diabetes
Fasting plasma glucose 6.1-6.9 mmol/L (110 to 125 mg/ dL) and Two-hour plasma glucose <7.8mmol/L (140mg/dL) following a 75g oral glucose load	Fasting plasma glucose <7.0 mmol/L (126 mg/dL) and Two-hour plasma glucose ≥7.8 <11.1mmol/L (≥140 to <200 mg/dL) following a 75g oral glucose load	Fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) or Two-hour plasma glucose ≥11.1 mmol/L (200 mg/dL) following a 75g oral glucose load or A random glucose > 11.1 mmol/L (200 mg/ dL) or HbA1c ≥ 48 mmol/mol (equivalent to 6.5%)

Table 2 - Glycaemic target

	ADA	IDF	ACE/AACE	Consensus (SID)
HbA_{1c} (%)	<7,0	< 6,5	< 6,5	<7 (<6.5)
Fasting glucose/preprandial glycemia (mg/dl)	90–130	<110	<110	70-130
Postprandial glycemia (mg/dl)	<180 (peak)	<145 (1–2 hrs)	<140	<180 (<140)

risk or already with cardiovascular disease (7). Insulin therapy can cause hypoglycemia, and it is essential to titrate the dosage based on the characteristics of the patient, such as age, diabetes duration, life expectancy, etc. The possible consequences of hypoglycemia are described in Fig. 1. New drugs for T2DM are now available that do not cause hypoglycemia and can achieve glucose values as in non-diabetic people. For diabetic workers this aspect is very important, especially for those employed in shift work, at night or for special tasks, due to the risk of accidents and worsening of glycometabolic control.

Treatment

Due to destruction of pancreatic β-cells by T-cell-mediated autoimmunity, insulin therapy is the only choice in the treatment of T1DM. The main objective is to reproduce the physiological kinetics of the hormone, without hypoglycemia. Insulin preparations now available are shown in Table 3.

The cornerstone of T2DM treatment is a healthy lifestyle which includes the adoption of a healthy diet, increased physical activity, smoking cessation plan and maintenance of a healthy body weight. If attempts to change lifestyle are not adequate to control blood glucose levels, oral medication is usually initiated for treatment of hyperglycemia with metformin being the most commonly used initial treatment worldwide. Recent studies have shown that in patients with type 2 diabetes and an elevated risk of cardiovascular and kidney disease, the rate of cardiovascular events and kidney failure was lower among patients receiving SGLT2 inhibitors and GLP1 RA than in the placebo group (12, 11, 9, 17, 16). These consistent results have contributed to modify the algorithm of treatment in T2DM in recent Guidelines (5). So, if glycometabolic control with metformin is not adequate, a range of combination therapy options are now available, including thiazolidinediones (TZD), Dipeptidyl Peptidase 4 inhibitors (DPP-4 i), Sodium-glucose transporter 2 inhibitors (SGLT2 i), Glucagon Like Peptide-1 receptor agonists (GLP1 RA), according to the risk of chronic complications. Combination therapy is started for faster, more effective control on blood glucose and dose reductions in individual medications. When oral hypoglycemic medications are unable to control hyperglycemia to recommended targets, insulin injections may be prescribed. Exogenous insulin can be combined with various oral antidiabetic drugs or GLP-1RA to allow insulin dosage lowering and reduction in weight (5).

Table 3 - Insulin preparations

Insulin	Onset (min)	Peak(h)	Duration (h)
Lyspro, aspart, glulisine	15 to 30	1 to 2	3 to 6
Detemir	60-120	No peak	19-24
Glargine 100	240 to 3600	No peak	24
Glargine 300	360	No peak	36
Degludec	600 to 720	No peak	42
Human Rapid action	30 to 60	2 to 4	3 to 6
NPH intemediate action	120 to 240	8 to 10	10 to 18

Chronic complications and occupational rules

Beyond the control of raised glucose levels, it is mandatory to regularly screen and manage the risk for development of micro and macrovascular complications: nephropathy, retinopathy, neuropathy and cardiovascular disease. For some individuals it is also necessary to seek modifications for long-term diabetes-related complications. The key message in accommodating an employee with diabetes is to ensure that accommodations are tailored to the individual and effective in helping the individual perform his or her job (6). Specific job requirements-individual's health status interactions must be assessed. Work at heights is contraindicated in presence of repeated episodes of hypoglycaemia. There are no absolute limitations for diabetic workers working shifts/night shifts (1).

Conclusion

Individuals with diabetes can serve as highly productive members of the workforce. Reasonable accommodations can readily be made that allow the vast majority of people with diabetes to effectively perform the job. In recent years, numerous

innovative drugs have become available and it is very important that the occupational physician knows the mechanism of action and the side effects since it could influence the worker's job.

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La gestione del soggetto lavoratore diabetico: difficoltà attuali e opportunità future alla luce dei nuovi progetti riservati ai pazienti cronici

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Key words: Diabetes

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Summary

«Managing people with diabetes in the workplace: current difficulties and future opportunities in the light of new projects for chronic patients». *Diabetes is growing rapidly in Italy as well as in much of the world. In addition to representing a health emergency, it involves a great deal of difficulty for patients who require close diagnostic and therapeutic control. Greater difficulties still are observed in workers with diabetes: the pathology itself sometimes becomes the object of discrimination when employed, and often work commitments are an important obstacle to the correct carrying out of regular diagnostic procedures and checks for monitoring the disease. Starting from 2020, as part of a project for the management of chronic patients by the Lombardy Region, a better organization of the diagnostic and therapeutic path of the diabetic subject is expected, managed in a more interactive way by the General Practitioner and the specialists, leading to a rationalization of costs, more accurate diagnostics and time savings for patients.*

Riassunto

La patologia diabetica è in grande crescita in Italia così come in buona parte del mondo. Oltre a rappresentare un'emergenza sanitaria, comporta una grande quantità di difficoltà ai pazienti che necessitano di stretto controllo diagnostico e terapeutico. Maggiori difficoltà ancora si osservano nei pazienti diabetici attivi dal punto di vista lavorativo: la patologia stessa a volte diventa oggetto di discriminazione all'atto dell'assunzione al lavoro e spesso gli impegni lavorativi sono un importante ostacolo alla corretta effettuazione di procedure diagnostiche e di visite atte a monitorare la patologia. A partire dal 2020, nell'ambito di un progetto di gestione dei pazienti cronici da parte della Regione Lombardia, si prevede una migliore organizzazione del percorso diagnostico e terapeutico del soggetto diabetico, gestito in maniera maggiormente interattiva dal Medico di Medicina Generale e dagli specialisti potendo portare a una razionalizzazione delle spese, una diagnostica più accurata e un notevole risparmio di tempo per i pazienti.

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Secondo i dati ARNO del 2019 le persone con diabete in Italia hanno superato i 4 milioni, il 6,2% dell'intera popolazione, mentre nel 1980 tali patologie coinvolgeva appena il 2,9% della popolazione. In prevalenza si tratta di soggetti con diabete mellito di tipo 2 (90%), che insorge soprattutto in età matura e tale percentuale è perciò destinata ad aumentare, anche solo per effetto dell'aumento della vita media della popolazione.

Per ogni diabetico lo Stato stanzia mediamente 4.000 euro all'anno, per un totale di circa 16 miliardi di euro, ovvero il 15% del Fondo Sanitario Nazionale.

Non a torto la lotta al diabete è considerata una delle tre emergenze sanitarie mondiali: in Europa circa 60 milioni di persone sono colpite da questa patologia con un tasso in continua crescita, superando già il 10-12% in alcune Nazioni. L'Italia si attesta lungo la media europea, sia nella popolazione in toto (dai 15 anni in su) che nella sola popolazione over 65, nonostante la nostra nazione sia quella con il maggior numero di anziani.

Il diabete è una patologia che interessa tutte le aree geografiche e le persone di tutte le età, ma ad essere più svantaggiati sono il centro-sud e la componente femminile, considerata la elevata percentuale di anziani: la maggiore diffusione si evidenzia in Calabria, Basilicata, Sicilia, Campania, Puglia, Abruzzo, Umbria e Lazio; mentre i tassi più bassi si hanno nel Trentino-Alto Adige, in Liguria e Valle d'Aosta.

Ad essere più colpite sono le classi economicamente e socialmente più svantaggiate.

Il diabete riduce l'aspettativa di vita di 5-10 anni e ne pregiudica anche la qualità; il danno vascolare provocato dal diabete rappresenta la principale causa di cecità.

Ogni medico di famiglia ha mediamente in cura più di un centinaio di diabetici (fra 80 e 150 persone), che vanno da lui a farsi visitare con una frequenza di 8-15 volte l'anno.

Il diabetico si trova ad affrontare nel mondo del lavoro diversi problemi:

1) Stress: attualmente le condizioni di lavoro sono nettamente migliorate sia in termini di entità della fatica sia in termini di grado di rischio fisico e/o chimico, ma sono aumentate le occasioni di stress legate ai lavori a turni e/o notturni; lo stress psichico è legato alla personalità del soggetto, al suo adattamento al lavoro o all'ambiente: c'è chi per evitare lo stress legato al lavoro può tardare l'ingresso in ufficio in modo da evitare il traffico mattutino soprattutto nelle grandi città. Ad aumentare lo stress contribuiscono altri fattori come l'apprensione continua per la rincorsa al successo e al lavoro dirigenziale, fattori che possono determinare un certo livello di ansia che può riflettersi sulla glicemia senza considerare come ad un aumento dell'attività lavorativa possa correlarsi una diminuzione dell'attività fisica. Infine, anche lavori che richiedono una concentrazione continua e prolungata possono essere fattori di stress lavorativo che influiscono sulla glicemia.

2) Attività e sforzi fisici: questo fattore può causare ipoglicemie nel caso di lavori ove è richiesto uno sforzo fisico notevole (lavaggi a mano delle auto, movimentazione carichi, etc.), oppure iperglicemie nel caso di lavori sedentari (impiegati, rappresentanti di commercio, ecc.).

3) Alimentazione: per questo fattore sussistono problemi legati alla mensa aziendale dove quasi mai sono previste pietanze dedicate al diabetico.

4) Rispetto degli orari del pasto: il problema è marcato nel caso di alcune categorie lavorative, ad esempio gli insegnanti, i cuochi, i baristi e i camerieri.

5) Trasferta: questo fattore riguarda i rappresentanti di commercio o i funzionari pubblici o privati che per ragioni di lavoro siano costretti a spostarsi sul territorio nazionale e straniero per le ragioni già sopra dette.

Inoltre, non bisogna dimenticare alcune condizioni di ridotta attitudine al lavoro che differenziano i soggetti diabetici dalla restante popolazione e riguardano:

1) Guida professionale.

2) *Lavori ad altezza dal suolo*: il problema riguarda principalmente le crisi ipoglicemiche che potrebbero far precipitare il lavoratore al suolo.

3) *Rotazione su turni*: risulta pregiudicato l'equilibrio glicemico non venendo mai rispettati gli orari dei pasti.

4) *Lavoro notturno*: uno studio (pubblicato dall'Harvard School of Public Health) ha dimostrato che chi fa il turno di notte ha una possibilità di

ammalarsi doppia rispetto agli occupati di giorno. Lavorare di notte, quindi, è un importante fattore di rischio per la salute e può provocare o peggiorare diabete e obesità. L'indagine prende in esame due gruppi di donne, rivelando che quelle di loro impiegate durante le ore notturne (almeno tre volte al mese) hanno una possibilità di ammalarsi di diabete due volte maggiore rispetto agli occupati di giorno.

Basterebbero già questi primi numeri a far comprendere quanto sia centrale il ruolo del Medico di Medicina Generale (MMG) nella cura e nella gestione del diabete. Un'interessante indagine condotta nel 2006 dalla Società Italiana di Medicina Generale e dall'istituto di ricerca Health Search, ha cercato allora di capire come e con quali risultati i MMG seguano i loro assistiti diabetici. Lo studio, basato su dati del 2005 e realizzato su un campione di oltre 602.000 pazienti sopra i 14 anni seguiti da 400 medici, ha individuato una percentuale di 5,59% diabetici (pari a oltre 33.600 persone), un quarto dei quali concentrati nelle regioni nord-occidentali (Piemonte, Valle d'Aosta, Liguria e Lombardia). L'analisi ha messo in evidenza le caratteristiche tipiche dei pazienti seguiti dal medico di famiglia, per lo più quelli le cui condizioni generali presentano minori difficoltà di gestione e pertanto comportano una minore necessità di fare ricorso allo specialista. Infatti, tra chi è in carico al medico di Medicina Generale, il 42% segue soltanto una terapia dietetica, una percentuale molto più alta di quella riferita all'insieme della popolazione diabetica; specularmente, molto più bassa del dato medio, sotto il 10%, è la quota degli insulino-trattati (il 6% circa con il solo ormone, il 4% con insulina in associazione con farmaci), il 48% è invece in cura con ipoglicemizzanti orali e altri medicinali specifici. Quasi tutti sono diabetici di tipo 2 e prevale decisamente la categoria dei sovrappeso: il 43,59% sono obesi e il 39,6% ha chili in eccesso. Soltanto il 17% rimane nella normalità. Un 18% fuma: è un valore inferiore alle percentuali relative alla popolazione generale (23% circa), ma bisogna ricordare che per un diabetico le sigarette costituiscono un fattore di rischio in più.

Nonostante i numerosi interventi legislativi e l'impegno civico profuso dallo Stato, non si è però ancora giunti ad una reale presa in carico della persona diabetica in tutte le regioni, con differenze nette tra di loro.

L'Associazione Cittadinanzattiva tra l'ottobre 2016 ed il marzo 2017, utilizzando una piattaforma online, ha svolto in Italia un'indagine sul diabete, riuscendo a coinvolgere 4-927 diabetici e 245 sanitari e le istituzioni sanitarie regionali di 15 regioni (Abruzzo, Basilicata, Friuli-Venezia Giulia, Lazio, Liguria, Lombardia, Marche, Molise, Piemonte, Puglia, Sardegna, Toscana, Trentino-Alto Adige, Valle d'Aosta, Veneto); la Regione maggiormente rappresentata è stata la Lombardia (19,3%), seguita dal Veneto (9,5%), dal Lazio (9,4%) e dalla Toscana (8,2%).

I circa cinquemila diabetici partecipanti all'indagine erano in maggioranza uomini (58,4%), mentre l'età variava:

00 - 19 anni 17,5%
20 - 39 anni 20,8%
40 - 64 anni 41,8%
65 - 74 anni 13,4%
75 - 85 anni 06,5%.

La situazione si capovolge, invece, per ciò che concerne i 245 professionisti sanitari, che sono in maggioranza donne (65%) con un'età compresa tra i 45 ed i 65 anni; per quanto attiene, invece, la professione esercitata si tratta soprattutto di diabetologi/endocrinologi (39,3%) ed infermieri (36,8%), mentre i MMG sono al terzo posto (7,6%).

La prima domanda a cui hanno risposto gli intervistati è quale sia la figura di riferimento nella gestione del diabete e la stragrande maggioranza degli intervistati l'ha individuata nel proprio diabetologo (81,7%) e nel diabetologo pediatrico (14,1%).

L'unico problema sollevato riguardava la carenza nei servizi, soprattutto per quanto riguarda l'impossibilità di avere sia un unico specialista di riferimento che un accesso senza appuntamento, ma soprattutto una tempistica spropositata per ottenere un appuntamento.

Altra figura di riferimento, ma con una ben differente percentuale di scelta (14,2%), è il MMG. Vi è infine una percentuale, seppur minima, di diabetici che si cura da solo (1%), rivolgendosi a stampa e siti web (0,2%).

Per quanto concerne la frequenza di visite del diabetologo, la maggioranza dei diabetici si fa visitare

da tre a cinque volte in un anno (27,8%) e il 13,8% anche oltre cinque.

Per quanto riguarda il MMG o il Pediatra di Libera Scelta (PLS), la maggioranza dei diabetici non fa riferimento a lui per la cura del diabete (29,8%), mentre chi lo fa si fa visitare sempre da tre a cinque volte l'anno (15,1%).

In realtà, a nostro parere, la percentuale di visite reale è quella indicata dalla Società Italiana di Medicina Generale (SIMG), per un semplice motivo: tutti i MMG segnano sul pc le visite effettuate ed hanno software costantemente (ed obbligatoriamente) aggiornati, mentre gli specialisti no; inoltre, i diabetici non considerano che quando si recano dal proprio MMG per un problema non diabetologico finiscono sempre per discutere con lui anche del diabete!

Sin dal Piano Nazionale Diabete, approvato nel 2012, si sottolineava l'importanza dell'integrazione fra le cure primarie e la medicina specialistica, ma si segnalava in un passaggio del piano stesso che "solo il 29% dei centri diabetologici dichiara di aver adottato dei modelli di integrazione/comunicazione con i MMG".

Secondo i diabetici l'integrazione fra la medicina di famiglia e quella specialistica non esiste. Infatti, il 62,8% degli intervistati ha affermato di "dover fare da tramite tra MMG e Specialista" e solo nel 5,7% dei casi esisteva una procedura codificata di comunicazione tra di loro. Leggermente più ottimista è invece la visione degli specialisti, secondo i quali esisterebbe un sistema di comunicazione codificato nel 19% dei casi, ma verrebbe attivato solo in base alle necessità (55%).

In base alla nostra esperienza di MMG al momento attuale non esiste ancora una procedura codificata di comunicazione ed integrazione tra MMG e Specialista, per il resto si comunica solo per particolari situazioni cliniche e quasi sempre a far da tramite è il diabetico od i suoi familiari.

Un punto dolente è quindi allo stato attuale la mancata necessaria integrazione tra ospedale e territorio (Lombardia esclusa, come si vedrà dopo), con l'adozione di un sistema assistenziale multidisciplinare con la definizione dei rispettivi compiti e delle modalità di integrazione; basta pensare che attualmente tali equipe sono solo "ospedaliere": in esse la figura maggiormente presente è ovviamente il diabetologo (81,7%), l'infermiere è presente nel 43,2% dei casi e quello specializzato nel 35,8 ma non vi è un solo MMG. Una figura importante come il dietista, invece, è presente solo in un nel 30% e l'oculista nel 15%!

In tutto questo l'organizzazione dei servizi sanitari regionali non aiuta, a cominciare da chi sta cercando di ottenere una diagnosi. C'è chi ha atteso oltre un anno per la prima visita diabetologica ed un anno e mezzo per quella endocrinologica, c'è chi rinuncia ad effettuare i controlli attraverso il servizio pubblico per le attese troppo lunghe e preferisce farsi seguire privatamente.

Un altro dato di cui si deve tenere conto è quello relativo ai PDTA (Percorso Diagnostico Terapeutico Assistenziale); se solamente il 12% dei pazienti dichiara di essere inserito in un percorso, tale percentuale sale notevolmente quando la stessa domanda viene posta ai professionisti sanitari che dichiarano che il 43,2% dei propri pazienti è inserito in un PDTA. C'è da dire che dove il Percorso esiste davvero (solo Regione Lombardia) e non è solo un atto formale, gli effetti sono estremamente positivi, come il maggiore controllo della malattia, a cominciare dai livelli di glicemia, continuando con un migliore controllo del peso corporeo (16,4%), fino ad una maggiore continuità delle cure e migliore organizzazione: controlli effettuati tutti in un solo giorno, possibilità di parlare sempre con lo stesso diabetologo, una migliore qualità di vita.

Il diabete interessa non solo come concezione biologica di malattia, ma soprattutto sotto l'aspetto economico-sociale, perché spesso crea problemi sulla prognosi lavorativa.

Diverse ricerche hanno dimostrato che agenti occupazionali sono direttamente coinvolti nella patogenesi del diabete mellito. Alcune caratteristiche lavorative rivestono un ruolo importante nell'insorgenza e/o nelle complicanze del diabete mellito: per tali motivi il diabete si può considerare una patologia lavoro-correlata. I diabetici sono nelle condizioni fisiche e psichiche di praticare qualsiasi lavoro. Il lavoro, in particolare nel diabete di tipo 2, può essere un fattore causale o aggravante della patologia in seguito a fattori di rischio psicosociali (stress), per sforzi fisici eccessivi, per lavori notturni, per sedentarietà

ma anche per essere a contatto con agenti fisici quali esposizione ad agenti chimici, sbalzi termici, rumore intenso, disbarismi (a tal proposito è interessante notare come in una città come Milano, in cui vi sono svariati cantieri per la costruzione di più linee metropolitane sotterranee, siano in funzione numerosi "cassoni iperbarici" ed impianti iperbarici di soccorso, il problema è che non è affatto certo che gli operai che lavorano in tali cassoni siano stati ritenuti o meno idonei all'ambiente iperbarico, ambiente che, alla pari di quello subacqueo con cui condivide le stesse identiche leggi sia fisiche che antinfortunistiche, vieta tale attività a chi sia diabetico...).

Secondo un'indagine statistica, il 35% dei giovani diabetici ha avuto difficoltà al momento dell'assunzione in un posto di lavoro, mentre il 34% dei datori di lavoro non ha neppure preso in considerazione l'assunzione di chi è affetto da diabete. Si tratta di difficoltà e discriminazioni ingiustificate. In teoria non esisterebbe ostruzionismo da parte dei datori di lavoro ad assumere un lavoratore diabetico, tuttavia di fondo sussistono dei timori che il soggetto diabetico si ammali più facilmente con la conseguenza che in molti casi viene preferito il non diabetico proprio nella convinzione che costui non possa accampare giustificazioni di salute per chiedere un giorno di riposo o l'interruzione del lavoro per praticarsi l'iniezione di insulina o fare lo spuntino e così via.

Comunque, il problema che più complica la vita ai diabetici lavoratori è il dover impegnare un buona dose di tempo (e quindi chiedere e soprattutto ottenere ore di permesso) per sottoporsi ad esami e visite specialistiche.

Da questo punto di vista la scelta della Regione Lombardia sulla presa in carico dei pazienti cronici da parte dei MMG (riuniti in cooperative all'uopo costituite) è senza dubbio un importante passo avanti.

Basti pensare che i diabetici lavoratori hanno adesso a disposizione (come tutti gli altri pazienti cronici) dei centri di prenotazione telefonici (che fanno capo alle succitate cooperative di MMG) dedicati che provvederanno a prenotare esami e visite per loro; sia le ASST che le strutture sanitarie private convenzionate si sono accordate con l'Assessorato alla Salute per concedere alcuni slot riservati per i pazienti cronici con precedenza su tutti gli altri assistiti! Inoltre, proprio in questi giorni, la Regione Lombardia sta redigendo il protocollo che consentirà a sanitari esperti, di eseguire nei confronti degli assistiti cronici (diabetici lavoratori inclusi) tutta una serie di esami sia in erogazione diretta, sia utilizzando la telemedicina, direttamente negli studi dei propri MMG ovviamente senza alcun aggravio di costi.

L'elenco di tali prestazioni è estremamente interessante: un panel di esami ematochimici tarato per i diabetici, fundus oculi, monitoraggio pressorio 24h, elettrocardiogramma, spirometria, ecografia addome completa, ecocolordoppler tronchi sovraaortici, ecocolordoppler arterioso e venoso arti inferiori. Questo significa che i lavoratori diabetici in una sola mattinata o pomeriggio potranno d'ora in poi fare tutti gli esami necessari al monitoraggio della propria patologia.

Per quanto concerne la condivisione tra specialisti e MMG della gestione dei diabetici lavoratori, quest'ultima è pesantemente spinta dalla Regione Lombardia: i MMG hanno infatti avuto il compito di redigere i PAI (Piani Assistenziali Individuali per assistiti cronici); gli specialisti non possono più modificarli senza prima interfacciarsi con i MMG. Ciò porterà all'eliminazione di doppioni di esami con conseguente risparmio sia economico che di tempo, cosa che invece attualmente accade specie se un diabetico (lavoratore e non) soffre di un'altra patologia cardiovascolare o respiratoria (entrambi gli specialisti prescrivono esami quasi sempre uguali ma in diversi periodi dell'anno).

Per chiudere il circolo bisogna citare i PRESST (Presidi Socio Sanitari Territoriali) che sempre in questi giorni sono in fase di partenza in Lombardia, si tratta di Poliambulatori di Specialisti e MMG operanti in strutture ospedaliere o poliambulatori polispecialistici; l'accesso a questi PRESST sarà riservato solo ai pazienti cronici (quindi anche diabetici lavoratori), in essi oltre agli esami sopradescritti si potranno effettuare anche le visite specialistiche, con ulteriore risparmio di tempo per gli utenti.

Gli autori non hanno dichiarato alcun potenziale conflitto di interesse in relazione alle materie trattate nell'articolo

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Environmental pollution and risk of type 2 diabetes mellitus: a short narrative review

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Key words: Air pollution; noise; type 2 diabetes mellitus

Parole chiave: Inquinamento atmosferico; rumore; diabete mellito di tipo 2

Summary

Background: *Exposure to air pollution (AP) and environmental noise influences the risk of cardiovascular diseases. These pollutants might also play a role in type 2 diabetes mellitus (T2DM).* **Objectives:** *To summarize the current evidence on the association between AP, noise and T2DM.* **Methods:** *We searched PubMed for pertinent literature up to March 17 2019, and summarized in a narrative review the 158 retrieved works.* **Results:** *In 2009, a first murine model suggested that air pollution might cause insulin-resistance. One of the most relevant ecological studies that followed showed concordant trends among diabetes prevalence and average concentrations of fine particulate (PM2.5) in US counties. In 2015, a robust meta-analysis estimated a RR of 1.10 (95%CI: 1.02-1.18) for 10 μg/m³ increase in PM2.5, and of 1.08 (1.00-1.17) for the same increase in nitrogen dioxide. Even exposures to increasing levels of ozone seem to be associated with higher incident cases of T2DM (+18% per 6.7 ppb). Studies on noise as well, although more limited, seem to indicate an association with an increased risk of T2DM.* **Discussion:** *Adequate control for confounders and potential effect modifiers is often highlighted as a critical aspect, together with uncertainty deriving from accurate definition of diagnosis. Open issues are related to critical exposure windows and the role of specific components of the pollution mixture in determining health effects. Current evidence seems to indicate an association between AP and T2DM, but some aspects still need to be elucidated. Greater uncertainty characterizes the association between noise and T2DM.*

Riassunto

«Inquinamento ambientale e rischio di diabete mellito di tipo 2: una breve revisione narrativa». **Introduzione:** *L'esposizione a inquinamento atmosferico (IA) e rumore ambientale influenza il rischio di patologie cardiovascolari. Tali inquinanti potrebbero avere un ruolo anche nell'insorgenza di diabete mellito di tipo 2 (DM2).* **Obiettivi:** *Sintetizzare le evidenze di letteratura ad oggi disponibili sull'associazione tra IA, rumore e DM2.* **Metodi:** *È stata condotta una ricerca in PubMed al 17 marzo 2019, sintetizzando in una revisione narrativa le evidenze dei 158 lavori individuati.* **Risultati:** *Nel 2009, un primo modello murino suggerisce come l'IA possa provocare insulino-resistenza. Seguono studi ecologici, di cui il più significativo mostra andamenti concordi tra prevalenza di diabete e concentrazioni medie di particolato fine (PM2.5) in contee statunitensi. Nel 2015, una robusta meta-analisi stima un RR di 1,10*

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(IC95%: 1,02-1,18) per incrementi di 10 μg/m³ di PM2.5, e di 1,08 (1,00-1,17) per analoghi incrementi di biossido di azoto. Anche esposizioni a livelli crescenti di ozono sembrerebbero comportare un incremento di casi incidenti di DM2 (+18% ogni 6,7 ppb). Le indagini condotte sul rumore, seppur più limitate, sembrano anch'esse indicare un'associazione con un aumentato rischio di DM2. **Discussione:** *L'incapacità di tenere adeguatamente conto di fattori confondenti e di potenziali modificatori d'effetto viene spesso segnalata come aspetto critico, insieme all'incertezza derivante dalla definizione della diagnosi. Problemi aperti riguardano l'individuazione di finestre di esposizione critiche e il ruolo delle specifiche componenti della miscela inquinante nel determinare effetti sulla salute. Le evidenze ad oggi disponibili sembrano indicare un'associazione tra IA e DM2, anche se rimangono aspetti da approfondire. Maggiore incertezza caratterizza l'associazione tra rumore e DM2.*

Introduction

The health effects of exposure to air pollution are well known, since many studies documented an association between both gaseous and particulate pollutants and health outcomes, especially respiratory and cardiovascular effects (3, 17). More recently, air pollution has been suggested to have a role also in metabolic dysfunction, and thus potentially increase the risk of type 2 diabetes mellitus (T2DM) (22).

Among other environmental pollutants, even exposure to noise (especially from aircrafts and road traffic) has been found to influence the risk of heart disease and stroke (12). However, evidences on the association between noise and diabetes are still inconsistent.

With the present narrative review, we aim to briefly summarize the current evidences on the association between environmental pollutants (especially air pollution and noise) and diabetes, and highlight criticisms and open issues on the topic.

Methods

We searched the electronic literature database PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) for pertinent literature up to March 17 2019. As this was meant to be a quick and narrative review on the topic of environmental pollution and T2DM, we decided to tailor our search using the following string: ("air pollution"[MeSH] OR "particulate matter"[MeSH] OR "nitrogen dioxide"[MeSH] OR ozone[MeSH] OR noise[MeSH]) AND "Diabetes Mellitus, Type 2"[MeSH]. We applied no filters for study design or language. We screened titles and abstracts for pertinence and retrieved potentially relevant articles as full texts.

Results

The PubMed search returned 158 publications. Some articles intercepting the topic dated back in the '90s, with no publication though directly addressing the link between exposure to environmental toxicants and T2DM. As a matter of fact, the works published between 1990 and 2008 mostly considered diabetic subjects as a hypersusceptible population where to study and better capture health effects (other than diabetes) associated with exposure to noise (14) or air pollution (8, 19).

In 2009, Sun and colleagues published the first article recovered by our search explicitly addressing, in a murine model, the question of whether air pollution is associated with T2DM (or related traits): they observed that a 6-month exposure at cumulative concentration levels of particulate matter with diameter less than or equal to 2.5 μm (PM2.5) induced insulin resistance in high-fat-fed nonatherosclerotic mice (24).

In the last decade, the interest for this topic has clearly increased, with a peak of articles between 2014 and 2016 (Figure 1).

In 2010, Pearson and colleagues published an ecological study assessing the relationship between PM2.5 annual mean levels and diabetes prevalence for the years 2004-2005, at the county level in the entire United States territory. In multivariate linear regression models (adjusted for socioeconomic covariates, behavioral risk factors, population density, and latitude), they observed a 0.78% increase

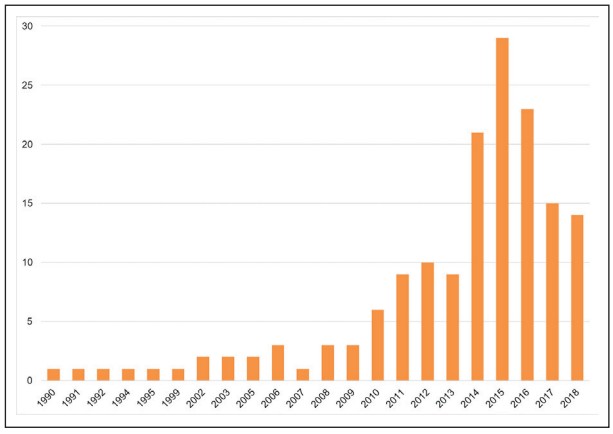

Figure 1 - PubMed results as of March 17 2019 for the search string: ("air pollution"[MeSH] OR "particulate matter"[MeSH] OR "nitrogen dioxide"[MeSH] OR ozone[MeSH] OR noise[MeSH]) AND "Diabetes Mellitus, Type 2"[MeSH]. X-axis: publication year; Y-axis: number of publications

(95% Confidence Interval [CI]: 0.39-1.25) in diabetes prevalence for each 10 μg/m^3 increase in PM2.5 concentration in 2004. Results in 2005 were comparable, with an estimated increase in diabetes prevalence equal to 0.81% (95%CI: 0.48-1.07). Interestingly, they found a similar association between increasing PM2.5 levels and diabetes prevalence after restricting the (univariate) analyses to counties with PM2.5 values below the 15 μg/m^3 limit set by the Environmental Protection Agency. Given the study design, the authors acknowledge the possibility of potential ecological biases.

In the following years, some more robust cohort studies have been published, also investigating the association between T2DM and air pollutants other than PM. For example, Andersen et al. followed over 57,000 participants of the Danish Diet, Cancer, and Health cohort between 1993-1997 and 2006, assessing the relationship between nitrogen dioxide (NO_2) exposure (estimated at the residential address since the early '70s) and incidence of diabetes (2). A 4% increase in diabetes was observed (95%CI: 1.00-1.08) per interquartile range (IQR) increase in NO_2 (4.9 μg/m^3), when restricting the analysis to confirmed diabetes cases in fully adjusted models.

Together with the work by Andersen and colleagues, an additional longitudinal study on NO_2 (16) and 3 others on PM2.5 (6, 7, 21) were considered in a sound meta-analysis by Eze and colleagues in 2015 (11). The pooled risk estimates for T2DM were equal to 1.10 (95%CI: 1.02-1.18) for 10 μg/m^3 increase in PM2.5 and 1.12 (95% CI: 1.05-1.19) for the same increase in NO_2. This latter estimate slightly decreased to 1.08 (95%CI: 1.00-1.17) when including in the analysis also results from two cross-sectional studies (5, 9). Interestingly, for both pollutants effects were more evident among females, with a risk ratio of 1.14 (95%CI: 1.03-1.26) for PM2.5 and of 1.15 (95%CI: 1.05-1.27) for NO_2.

Ozone was investigated too as potential environmental risk factor for T2DM. A large cohort study conducted on over 45,000 African American women living in metropolitan areas of the United States observed an 18% increased risk of incident diabetes (95%CI: 1.04-1.34) for an IQR increase of 6.7 ppb in ozone concentration. Interestingly, NO_2 seemed to act as effect modifier of the ozone-diabetes association, as higher hazard ratios for ozone levels were observed in areas with lower NO_2 (15).

Other than on diabetes itself, some other evidences have been produced, documenting an association between air pollution exposure and diabetes-related traits or preclinical factors, such as glycated hemoglobin, insulin resistance or glucose intolerance (26).

Finally, also environmental noise has been hypothesized to have a direct effect on the risk of diabetes. The only meta-analysis identified on the topic summarized evidences from five investigations on residential noise exposure and estimated a 19% increase in T2DM risk (95%CI: 1.05-1.35) for exposure levels (Lden) = 60-70 dB vs. Lden < 60 dB (10).

Discussion

The amount of studies investigating the association between exposure to air pollutants and risk of diabetes has been increasingly growing in the last 10 years. Although evidences produced so far suggest that air pollution may play a minor role on human health if compared to other factors (e.g. lifestyle or genetics), *"the pervasive, persistent, and lifelong exposure to air pollutants may arguably make this an important determinant of cardiometabolic health, especially in areas that have high levels of air pollution*" (23). This appears particularly clear if we consider, for example,

a recent large cohort study conducted on about 1.7 million US veterans with no previous history of diabetes. Using the Global Burden of Disease (GBD) study methodologies, the authors estimated that, in 2016, ambient PM2.5 contributed to about 3.2 million incident cases of diabetes worldwide (95% Uncertainty Interval [UI] 2.2-3.8) and that the age-standardized burden of incident diabetes attributable to PM2.5 per 100,000 population (Figure 2) was 40.4 (95%UI 29.7-51.1) globally (4).

Most of the reviews retrieved by our search try also to describe potential biological pathways underlying the association between air pollutants and diabetes: the main hypothesis relates to pollutants exacerbating an inflammatory status, with subsequent dysregulation of the glucose metabolism through several mechanisms (e.g. cytokine release, immune cells activation, altered glucose homeostasis through defective insulin signaling in tissues, etc.) (11, 23).

Some methodological aspects arise as critical in many of the works recovered by our search.

The first one is bias related to confounder adjustment: although most of the studies did adjust their models for basic T2DM risk factors (i.e. age, body mass index, socio-economic status, smoking, family history of diabetes, physical activity), some did not consider other elements, such as diet or environmental tobacco smoke (11). The relevance of properly adjusting for confounders is highlighted by the findings of a recent cross-sectional study by O'Donovan and colleagues. After collecting data from over 10,000 participants in three diabetes-screening studies in the UK, they found nitrogen dioxide and particulate matter concentrations to be associated with T2DM in unadjusted models. However, the observed associations were not consistent after further adjustment for demographic and lifestyle factors, and neighborhood green space (18).

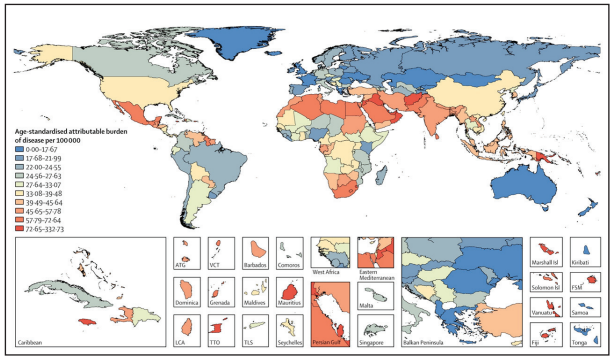

Figure 2: Age-standardized burden of incident diabetes attributable to PM2.5 per 100,000 population. List of abbreviations: ATG=Antigua and Barbuda; VCT=Saint Vincent and the Grenadines; LCA=Saint Lucia; TTO=Trinidad and Tobago; Isl=Island; FSM=Federated States of Micronesia; TLS=Timor-Leste. Adapted from Bowe et al., 2018 (4) under the CC BY 4.0 license.

Another critical point relates to bias due to outcome assessment: some studies relied on self-reported doctor-diagnosed diabetes (7, 9, 15), while others identified cases through linkage with established databases (2, 6). Both methods have limitations: relying on self-reported diagnoses entails the risk of disease misclassification, while record-linkage studies might bring to loss of cases, especially when the only informative source available is represented by hospital discharge registries.

As with most health effects associated with air pollution, even for T2DM an open question regards whether critical windows of exposure exist throughout the lifetime. To address this issue, Alderete and colleagues enrolled over 300 overweight and obese Latino children (8-15 years) and found that higher NO_2 and PM2.5 levels were associated with a faster decline in insulin sensitivity; they also observed NO_2 to negatively affect pancreatic β-cell function (1). Childhood exposure to ambient air pollution might thus be responsible for rapid metabolic dysfunction and contribute to the development of T2DM (20).

Another question regards what components of the pollutants mixture (especially particulate matter) play a role in influencing the risk of T2DM. To this extent, a study conducted in Hong Kong among residents aged 65 years or above observed an association between elemental carbon, organic carbon, nitrate, and nickel (out of 17 chemical components of PM) and daily emergency hospital admissions for T2DM (25). These findings thus suggest that PM constituents from combustion-related particles may be responsible for acute exacerbations of T2DM symptoms or complications.

Finally, other lifestyle and environmental factors (e.g. diet, noise) might act as effect modifiers of the air pollution-diabetes association. This has been

suggested, for example, by an experimental study conducted on male mice, which documented how exposure to PM2.5 potentiated T2DM development in high-fat diet (HFD)-fed mice if compared to mice only exposed to PM2.5, only treated with HFD, or to non-exposed non-treated referents (13).

Investigations on noise and T2DM still represent a small number of studies, and are characterized by a greater uncertainty and methodological challenges, especially for what concerns the heterogeneity of techniques applied to assess noise exposure (10).

Conclusions

The existing evidence indicates a positive association between air pollution and T2DM risk. Nonetheless, high-quality studies assessing dose-response effects are still needed to evaluate the role of the various pollutants, properly understand potential confounders and effect modifiers, and minimize the risk of bias.

Findings on the effects of noise on diabetes risk are still scarce and prevent firm conclusions.

No potential conflict of interest relevant to this article was reported by the authors

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Nutraceuticals in the management of type 2 diabetes

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Key words: Nutraceuticals; type 2 diabetes; hyperglycemia; dyslipidemia

Parole chiave: Nutraceutici; diabete di tipo 2; iperglicemia; dislipidemia

Summary

Background: *The prevalence of type 2 diabetes mellitus (T2DM) is dramatically increasing worldwide. Hyperglycemia and dyslipidemia, the two major components of this metabolic disorder, lead to accelerated ath-erosclerosis, coronary heart disease, chronic kidney disease and increase in the mortality rate. In recent years a growing number of hypoglycemic drugs have become available. However, in a remarkable number of patients the disease control is not fully satisfactory. Thus the search of new antidiabetic agents with minimal side effects is mandatory. In this context, nutraceuticals (bioactive compounds mostly of plant origin) can play a positive role in the management of T2DM, also in association with hypoglycemic drugs. An interesting feature of some nutraceuticals is their ability to improve not only the glycemic control but also the lipidic profile (berberine), the antioxidant status (silymarin) or endo-thelium dependent -vasodilator function (Pycnogenol) of the patients.*

Riassunto

«Nutraceutici per il trattamento del diabete di tipo 2»*. L'incidenza del diabete mellito di tipo 2 è in drammatico aumento a livello mondiale. L'iperglicemia e la dislipidemia, due importanti componenti di questa complessa malattia del metabolismo, determinano accelerazione dell'aterosclerosi e possibile comparsa di malattia coronarica e nefropatia con aumentata incidenza di mortalità. Negli ultimi anni un crescente numero di farmaci ipoglicemizzanti è stato reso disponibile per l'utilizzo clinico. Tuttavia, in un numero consistente di pazienti il controllo della malat-tia non risulta del tutto soddisfacente. In questo contesto, l'utilizzo di nutraceutici, composti bioattivi di origine prevalentemente vegetale con minimi effetti collaterali per il paziente (purché sia individuato il corretto dosaggio) , può svolgere un ruolo terapeutico positivo. Infatti, i nutraceutici possono essere cosomministrati con i farmaci ipoglicemizzanti coadiuvandone l'azione terapeutica. Inoltre, alcuni nutraceutici possiedono l'interessante proprietà di essere in grado di migliorare, oltre il controllo gli-cemico, il profilo lipidico (berberina), di ridurre lo stress ossidativo (silimarina) e di migliorare la funzione endoteliale vasorilassante (Picnogenolo).*

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Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disorder affecting a growing number of patients all over the world. T2DM is caused by abnormal insulin activity and/or release. The two major components of this metabolic disorder, hyperglycemia and dyslipidemia, lead to accelerated atherosclerosis, coronary heart disease, chronic kidney disease and increase in the rate of mortality. Despite the availability of several hypoglycemic drugs, in a remarkable number of patients the disease control is not fully satisfactory. Thus the search of new antidiabetic agents with minimal side effects is mandatory. Nutraceuticals are nutrients and/or bioactive compounds mostly of plant origin, with possible beneficial effects on human health. Plant-derived natural agents have been widely used since ancient times for a vast variety of diseases. A growing number of nutraceuticals are currently proposed to treat metabolic disorders, including diabetes mellitus. Nutraceuticals may improve glycemic control and often exert a beneficial effect on cardiovascular risk factors linked to T2DM such as dyslipidemia and hypertension with minimal side effects. In this review we take into consideration only nutraceuticals having enough evidence regarding their efficacy and safety in T2DM patients.

Nutraceuticals in T2DM

Berberine

Berberine, an isoquinoline alkaloid, is present in several plants such as *Berberis vulgaris*, *Berberis aristata* and *Coptis chinensis* (16). It is commonly used for gastrointestinal tract infections in China. Berberine has anti-microbial, glucose- and cholesterol-lowering and antioxidant effects (16). Berberine activates AMP-activated protein kinase (AMPK), a cellular energy sensor that increases fatty acid oxidation, glucose uptake and lipolysis, while inhibiting gluconeogenesis, fatty acid synthesis and cholesterol synthesis (19).

The hypoglycaemic, lipid-lowering and antioxidant properties of berberine have been widely investigated in animal models. In impaired glucose tolerance (streptozocin-treated) rats (21), treatment with berberine for 4 weeks significantly decreased fasting blood glucose, total cholesterol, free fatty acid and apoliprotein B levels; blood glucose levels after oral glucose tolerance test were also reduced (21). In high glucose and high fat diet-induced diabetic hamsters, berberine administration for 6 weeks significantly reduced glucose and insuline levels and ameliorated glucose tolerance tests (22). Furthermore total cholesterol, low density lipoprotein cholesterol (LDL-C), free fatty acid and triglyceride levels as well as markers of oxidative stress (thiobarbituric acid-reative substance and 8-isoprostane) were also decreased (22). Berberine was found also capable to reduce body weight and adipose tissue mass as well as insulin resistance in obese db/db mice (20). In this animal model, berberine also increased energy expenditure, limited weight gain, improved cold tolerance and increased brown adipose tissue activity, suggesting a potential therapeutic role of berberine in the treatment of obesity (41).

Clinical studies confirm the hypoglycaemic and lipid-lowering effects of berberine. A pilot study was conducted in 2008 to assess the efficacy of berberine in patients with T2DM (38). Adults with newly diagnosed T2DM were treated with berberine (500 mg 3 times daily) or metformin (500 mg 3 times daily) for three months (study A). The decrease in fasting and postprandial blood glucose and hemoglobin A_{1c} was similar in patients treated with berberine or metformine. Total cholesterol and triglycerides significantly decreased only in the berberine-treated group. In study B berberine (500 mg 3 times daily for 3 months) was administered to poorly controlled T2DM on-going treated with antidiabetic drugs. Berberine in combination therapy further decreased fasting and postprandial blood glucose, hemoglobin A_{1c} , fasting insulin and homeostasis model assessment of insulin resistance (HOMA-IR). Total cholesterol and LDL-C were decreased significantly as well (38). In patients treated with berberine alone no severe gastrointestinal adverse effects were recorded. In combination therapy the adverse effects (diarrhea, constipation, flatulence, abdominal pain) disappeared in 1 week after reduction of berberine dos-

age from 500 mg to 300 mg 3 times daily. Thus, the optimal dose of berberine with minimal side effects seems to be 300 mg 3 times daily, especially in combination therapy with antidiabetic drugs. In another study, T2DM patients with dyslipidemia were treated with berberine (500 mg 2 times daily) for 3 months (40). Fasting and postprandial blood glucose, hemoglobin A_{1c}, total cholesterol, LDL-C and triglycerides were all significantly reduced in the berberine-treated group. During the period of the study no serious adverse events occurred. Only a small number of patients receiving berberine (8.7 %) experienced mild to moderate constipation. No episode of hypoglycemia was reported. In 2010, a trial with daily administration of 1000 mg berberine confirmed the hypoglycaemic action of the phytochemical (39). The fasting blood glucose- and hemoglobin A_{1c}-lowering effects of berberine were found similar to those of metformine and rosiglitazone. Berberine was also found capable to increase the percentages of peripheral blood lymphocytes that express insulin receptor (39). Berberine and rosiglitazone, a thiazolidinedione (TZD), work through different mechanisms. TZDs decrease insuline resistance by activating peroxisome proliferator-activated receptor- g(PPARg) thus increasing body weight gain. Contrary to TZD, berberine reduces the expression of PPARg, thus preventing weight gain by suppressing preadipocytes differentiation (15,42). Therefore berberine may be a good choice in overweight or obese TDM2 patients. The effect of berberine on inflammatory parameters in TDM2 patients was investigated by Chen et al (2). In newly diagnosed T2DM patients administration of berberine (300 mg 3 times daily for 8 weeks) markedly reduced C-reactive protein (CRP), tumor necrosis factor (TNF)-a and lipopolysaccharide (LPS) levels. At the end of the trial fecal *Bifidobacterium* species were significantly modified. *Bifidobacterium longum*, *Bifidobacterium adolescentis* and *Bifidobacterium infantis* correlated significantly with TNF- aand LPS levels, suggesting the capability of berberine to modulate fecal microbiota thus reducing the expression of the inflammatory parameters TNF-a and LPS (2).

Silymarin

Silymarin is a standardized extract of *Silybum marianum* (milk thistle) seeds containing several flavolignans amongst which the most important is sylibin (silibinin). Milk thistle has been used since ancient times to treat a range of liver and gallbladder disorders (hepatitis, cirrhosis and jaundice). Silymarin has antioxidant and anti-inflammatory properties. It inhibits lipid peroxidation (37), prevents glutathione depletion (34) and activates antioxidant enzymes that protect DNA from degradation (18). Concerning the anti-inflammatory effects, a strong inhibitory effect of silibin on LTB4 (leukotriene B4) formation has been demonstrated (4). Silymarin also exerts an inhibitory effect on nitric oxide (NO) production and inducible nitric oxide synthase (iNOS) gene expression (17). Inhibition of intrahepatic expression of TNF- , aINFg , interleukin (IL)-2 and IL-4 have been also demonstrated (30). The antioxidant and anti-inflammatory properties of silymarin may induce a positive effect on diabetic metabolic abnormalities. Administration of silymarin to cirrothic diabetic patients (600 mg daily) for 12 months significantly reduced fasting plasma glucose and insulin, glicosuria and daily insulin requirement (35). Serum oxaloacetic transaminase (SGOT) and glutamic pyruvic transaminase (SGPT) were also significantly improved in silymarin-treated group (35). Supporting the antioxidant effect of the compound, plasma malondialdehyde (MDA) levels were significantly decreased by silymarin treatment (35). In a 4-month trial, silymarin (200 mg 3 times daily) (11) significantly decreased fasting blood glucose, HbA_{1c}, SGOT and SGPT levels. These findings indicate that silymarin, at the dosage of 600 mg/daily, may exert antidiabetic effects also after a short administration period. The effects of silymarin on antioxidant status were reported by Ebrahimpuor Koujan in 2015 (9). T2DM patients received 140 mg silymarin, 3 times daily for 45 days. Silymarin treatment significantly increased superoxide dismutase (SOD), glutathione peroxidase (GPX) activity and total antioxidant capacity (TAC) while decreasing plasma MDA and hs-CRP levels. Contrary to berberine, silymarin seems to have no effect on lipid profile (36). No mayor side

effects have been reported for silymarin (36), thus this phytochemical may be considered as a useful complementary medication in T2DM.

Berberol

Despite the known favourable effects of berberine on glycemic control and lipidic profile, the efficacy of this phytochemical is limited by its poor oral bioavailability (3). In fact, the amount of berberine capable of crossing enterocytes is greatly reduced by a P-glycoprotein-mediated gut extrusion process (26). Silymarin is a known P-glycoprotein inhibitor (43). Thus combination of berberine with silymarin may be suitable to enhance the oral bioavailability and increase the clinical effectiveness of berberine. Berberol is a commercial nutraceutical mixture composed by

588 mg of *Berberis aristata* extract (standardized based on 85% berberine) and 105 mg of *S. marianum* extract (standardized based on 60% flavolignans) (5).

T2DM patients with suboptimal glycemic control despite the use of antidiabetic drugs were treated with Berberol for 3 months (6). At the end of the treatment HbA_{1c} ,basal insulin and HOMA-IR, total cholesterol, LDL-C and triglycerides were all significantly reduced (6). The decrease in basal insulin and HOMA-IR confirms the capability of Berberol to increase insulin sensitivity and makes this nutraceutical combination a good candidate as an adjuvant therapy in poorly controlled T2DM patients. Berberol (1000 mg/day of berberine and 210 mg/day of silymarin) was compared with berberine alone (1000 mg/day) in a 4-months clinical trial (7). Berberol demonstrated to be more effective than berberine alone in reducing HbA_{1c} while both treatments similarly reduced fasting blood glucose, total cholesterol, triglycerides, SGOT and SGPT levels (7). As regard the safety of the nutraceutical combination, no patients reported any serious adverse event (myopathy or liver toxicity). Only about 15% of patients reported a mild transient abdominal discomfort. In 2015 a clinical trial investigated the role of Berberol in diabetic and hypercholesterolemic patients intolerant to statins (8). Patients were divided into three groups (low-dose statin-treated, ezitimibe-treated and patients not treated with antihyperlipidemic drugs) and treated for 1 year with Berberol. At the end of the study fasting blood glucose, HbA_{1c} , total cholesterol and LDL-C were significantly reduced in all groups of patients without any serious side effects (8). Therefore Berberol may be suggested as a safe and effective supplement to improve the lipidic and glycemic profile of hypercholesterolemic T2DM patients intolerant to statins (8).

Curcumin

Curcumin is a polyphenol with diarylheptanoid structure derived from the rhizome of *Curcuma Longa* which is used as a spice in Asian cuisine. This phytochemical has anti-inflammatory, antioxidant, immunomodulating and anticancer properties and its effects on cancer, heart failure, T2DM and depression have been clinically investigated (33). Curcumin inhibits Nuclear factor-kB (NF-kB) signalling pathway, one of the most important pathways in the cellular and molecular mechanisms of inflammation and down-regulates the expression of TNFa, Il-1, Il-6, Il-8 and CRP (27,28). In obese diabetic rats, curcumin decreased plasma glucose and decreased insulin resistance by reducing serum free fatty acids (FFAs) and increasing fatty acid oxidation in skeletal muscle (24). In humans, curcumin (300 mg/day for 3 months) significantly reduced fasting blood glucose and HOMA-IR in overweight/obese T2DM patients (25). Serum total FFAs and triglycerides were also reduced while lipoprotein lipase (LPL) activity increased (25). These findings suggest that the hypoglycemic effect of curcumin may be at least in part related to the ability of the phytochemical to decrease serum FFAs generation, which represents one of the major factors inducing insuline resistance. In keeping with this view, *in vitro* experiments demonstrated the ability of curcumin to improve FFAs b-oxidation through upregulation of phosphorylated AMP-activated protein kinase pathway (24). Due to its low bioavailability, curcumin must be used at high dose to achieve therapeutic levels. To improve the biovailability of curcumin a formulation of curcumin as a nanomicelle structure (Nano-curcumin) has been studied (29). Administration of Nano-curcumin (80

mg/die) for 3 months to T2DM patients, significantly decreased fasting blood glucose, HbA_{1c}, triglycerides and BMI (Body Mass Index) (29). These results suggest that administration of curcumin as nanomicelle may be a promising strategy to increase curcumin bioavailability and its therapeutic efficacy.

Pycnogenol

Pycnogenol is an extract of bark from the French maritime pine (*Pinus pinaster Ait.*) standardized to 70 ± 5% procyanidins. It represents a concentrate of water-soluble polyphenols (36). Pycnogenol has strong antioxidant and anti-inflammatory effects and endothelium-dependent vasodilator activity (10,30). The improvement of endothelial-dependent vasodilator function leads to a decrease in blood pressure levels in hypertensive subjects (14,44). Another effect of Pycnogenol is inhibition of a-glucosidase. Inhibition of a-glucosidase causes decreased glucose reabsorption and postprandial hyperglycemia (13). The inhibition of a-glucosidase provided by pycnogenol is more potent than that provided by green tea extract (IC_{50} about 5 mg/ml vs IC_{50} about 20 mg/ml) (12). In 2010, Stuard et al (32) investigated benefits of Pycnogenol as an adjunctive treatment to ACE-inhibitor ramipril in metabolic syndrome patients with hypertension and microalbuminurea. Pycnogenol (150 mg daily) taken in addition to ramipril (10 mg daily) further decreased blood pressure, fasting blood glucose, HbA1c , 24 hour urinary albumin and serum creatinine. C-reactive protein (CRP) levels decreased significantly only in the pycnogenol-treated group (32). In a more recent study (1) the effects of 6 months supplementation with Pycnogenol (150 mg daily) were studied in subjects with metabolic syndrome. Pycnogenol significantly decreased blood pressure, fasting blood glucose, and triglycerides levels while increasing HDL-C levels (1). Waist circumference was significantly reduced in patients with metabolic syndrome (both males and females) treated with Pycnogenol. No side-effects due to the treatment with the phytochemical were observed. This study (1) indicates a role for Pycnogenol for improving health risk factors in patients with metabolic syndrome. To investigate the anti-diabetic effects of pycnogenol, 77 patients with T2DM (taking standard anti-diabetic drugs) were treated with 100 mg pycnogenol for 12 weeks (23). Pycnogenol significantly lowered plasma glucose levels as compared with placebo. HbA1c was also lowered; however, the difference as compared with placebo was statistically significant only for the first month of treatment. In the Pycnogenol-treated patients plasma levels of endothelin-1, a potent vasoconstrictor peptide secreted by endothelial cells, were significantly decreased, while 6-ketoprostaglandin F1a levels, the metabolite of prostacyclin (a prostaglandin with vasodilator and antithrombotic activity) were elevated compared with placebo during the entire treatment period (23). These results indicate that supplementation of Pycnogenol to conventional diabetes treatment is able to reduce glucose levels and improve endothelium-dependent vasodilator function.

Conclusions

The clinical studies so far performed with nutraceuticals have some limitations such as the limited duration of the trials and the small sample size of the enrolled patients. However, the available data indicate a promising role of some nutraceuticals in the menagement of T2DM. Berberine, silymarin and Berberol have the strongest evidence of beneficial effects in T2DM patients. In this context, an interesting feature of some nutraceuticals is the ability to improve not only the glycemic control but also the lipidic profile (berberine and Berberol), the antioxidant status (silymarin) or endothelium-dependent vasodilator function (Pycnogenol) of the patients. The dosage of the nutraceutical is an important variable. The administered dose should be sufficient to provide therapeutic activity (taking into account that natural compunds have mostly low biovalability) without or with minimal side effects. Promising strategies to increase the biovailability and the therapeutic efficacy of nutraceuticals are the co-administartion of absorption enhancers or alternative delivery systems to traditional oral formulation. In conclusion, a place for nutraceuticals in the treatment of T2DM patients is emerging. However, future well-designed clinical trials are needed to confirm the efficacy and safety of nutraceuticals in the menagement of type 2 diabetes.

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Episodio lipotimico in pilota militare diabetico: percorso diagnostico e gestione dell'idoneità al volo

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Key words: Diabetes; lipothymic episode; military pilot; flight fitness management

Parole chiave: Diabete; episodio lipotimico; pilota militare; gestione idoneità al volo

Summary

«Lipothymic episode in a diabetic military pilot: diagnostic pathway and flight fitness management». *We report a case study of a military helicopter pilot, 56-year-old with a lipothymic episode during a mission in Afghanistan. He had increased cardio and cerebrovascular risk factors, suffering from type II diabetes mellitus under diet therapy. The management of the clinical case consisted basically of 2 phases: acute management in an advanced field hospital which excluded the presence of cerebral ischemic events and assessment of the fitness to fly. In Italy second-level investigations of neuroradiological relevance were carried out which excluded changes in the flow of the intra and extra-cranial circulation, highlighting more of an initial damage to the microcirculation with findings compatible with chronic microvasculopathy. A cardiologic evaluation was also carried out without signs of ischemic heart disease. Nevertheless, the patient presented also a metabolic syndrome so a complete medical evaluation had to be performed to assess the fitness to fly according to the current standards for flying safety.*

Riassunto

Riportiamo in questo lavoro il caso di un militare, pilota di elicottero dell'età di 56 anni, che ha presentato un episodio lipotimico durante una missione in Afghanistan. Il soggetto aveva un aumentato rischio cardio e cerebrovascolare ed era affetto da diabete mellito di tipo II in regime dietetico. La gestione del caso clinico è consistita essenzialmente di 2 fasi: la gestione in acuto, in ospedale da campo avanzato, che ha escluso la presenza di eventi ischemici cerebrali e la idoneità al trasporto aereo del soggetto in patria. In Italia sono state condotte indagini di secondo livello di tipo neuroradiologico che hanno escluso alterazioni di flusso a carico del circolo intra ed extra-cranico, evidenziando un quadro di micro-vasculopatia cronica iniziale. È stata eseguita anche una valutazione cardiologica che ha escluso la presenza di segni di cardiopatia ischemica. Nel complesso il paziente è stato inquadrato e gestito nell'ambito della sindrome metabolica, pertanto è stato necessario eseguire una valutazione medica completa ad hoc per valutarne l'idoneità al volo secondo gli standard attuali per la sicurezza del volo stesso.

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Pilota militare di elicottero, Uomo di 56 anni con segni antropometrici indicativi per moderato aumento del rischio cardiovascolare: altezza 174 cm, peso corporeo 82 kg, BMI 27,1 (sovrappeso secondo OMS 2004), circonferenza addominale 102 cm (aumentato rischio cardiovascolare OMS, 2008), rapporto addome/fianchi 1,02, rischio cardiovascolare a 10 anni 4,7%, basso rischio MCVI (progetto Cuore, ISS, 2004), non fumatore, pratica attività sportiva non agonistica di tipo aerobico. Non familiarità per cardiopatia ischemica, nessun precedente di interesse cardiologico. In anamnesi presentava diabete mellito di tipo II in regime di controllo alimentare.

Case report

Nel 2015 il soggetto ha presentato episodio lipotimico durante una missione estera in Afghanistan al di fuori dell'attività volativa. Viene trasportato presso ospedale da campo attrezzato in teatro, tipo ROLE 2 spagnolo, dove mostrava parametri nella norma e TC encefalo negativa in acuto per episodi ischemici o emorragici.

Viene successivamente rimpatriato e trasferito presso Ospedale Militare "Celio" a Roma per completamento diagnostico da cui emergono i seguenti principali reperti:

ECO TSA mostrava placca ateromasica con riduzione del calibro del 30% a livello della biforcazione della carotide interna e riduzione di flusso a livello dell'arteria vertebrale a dx. E' stato quindi sottoposto ad Angio-RMN encefalo che ha escluso malformazioni del circolo intra ed extra cranico, evidenziando un quadro di leucoencefalopatia su possibile base vasculopatica cronica. E' stato sottoposto ad Holter pressorio ed ECG risultati nella norma. All'eco cardiaca frazione di eiezione del 65% con segni di ipertrofia miocardica. Test ECG da sforzo dubbio per ridotta riserva coronarica pertanto si richiede cine-angio RMN da stress con dipiridamolo che escludeva segni di ischemia coronarica inducibile. Profilo lipidico colesterolo tot 158 mg/Dl, HDL 43 mg/Dl.

Provvedimenti terapeutici

Follow-up semestrale polispecialistico, assunzione di cardioaspirina e riso rosso fermentato in regime di controllo alimentare.

Provvedimenti medico-legali e idoneità al volo

Idoneo al pilotaggio con altro pilota a bordo senza limitazioni di impiego per mesi 6 (sei) ai sensi dell'art. 584 comma 2 D.P.R. 15/3/2010 n.90 e M_D ARM003 del 6/7/2015

Conclusioni

Nel presente lavoro viene presentato un caso di pilota militare in missione fuori area che presenta episodio lipotimico in soggetto con fattore di rischio cardio e cerebrovascolare aumentato, affetto da diabete mellito di tipo II in regime di controllo alimentare. Il management del caso clinico è consistito sostanzialmente in 2 fasi: gestione in acuto in ospedale da campo avanzato che ha escluso la presenza di eventi ischemici cerebrali e valutazione dell"aviotrasportabilità del soggetto stesso. Nella seconda fase al rientro in Italia sono state effettuate indagini di secondo livello di pertinenza neuroradiologica che hanno escluso alterazioni di flusso del circolo intra ed extra cranico evidenziando più un danno iniziale del microcircolo con reperti compatibili con microvasculopatia di tipo cronico in fase iniziale trattata mediante assunzione di terapia antiaggregante. Dal punto di vista cardiologico non segni di ridotta riserva coronarica o del ritmo cardiaco in soggetto diabetico nell'ambito di un contesto dismetabolico. I provvedimenti intrapresi mirano a un controllo dello stile di vita e alla prevenzione tenendo conto dei fattori di rischio descritti. I provvedimenti medico-legali ai sensi delle normative vigenti in Italia mirano al mantenimento degli skills professionali senza trascurare la sicurezza del volo mediante una idoneità con altro pilota esperto a bordo e follow up semestrale specialistico. Come mostrato in fig. 1 e 2 il paziente mostra parametri compatibili con sindrome metabolica confermati anche dal calcolo del rischio cardiovascolare associati a diabete. La sindrome metabolica è una condizione caratterizzata da una serie di fattori di rischio, che determinano una maggior probabilità di soffrire di patologie cardiovascolari o diabete, in questo caso già presente. Il problema maggiore di questa condizione è che i singoli fattori di rischio, se presi isolatamente, non appaiono preoccupanti e

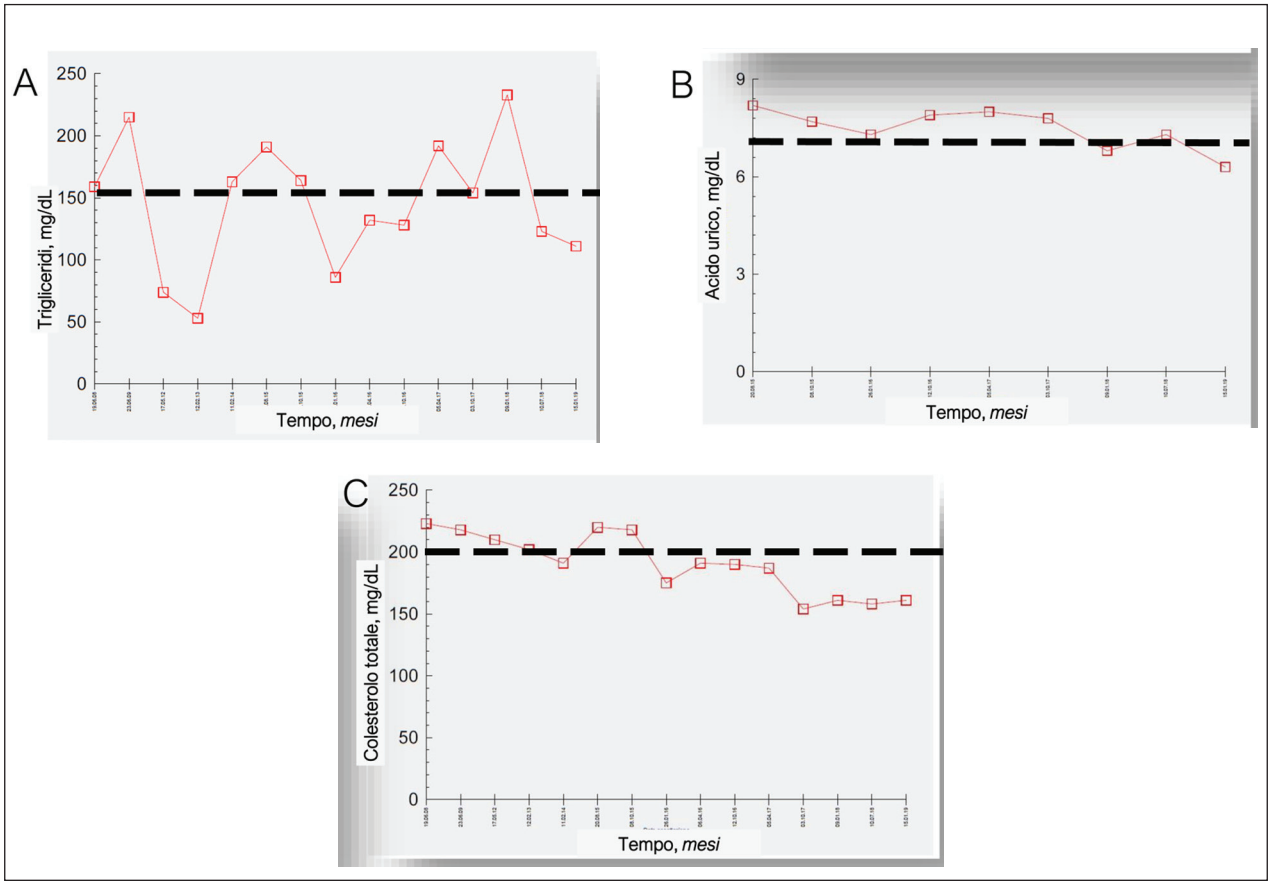

Figure 1 - Andamento nel tempo di A) trigliceridi, B) Acido urico e C) colesterolo tot.

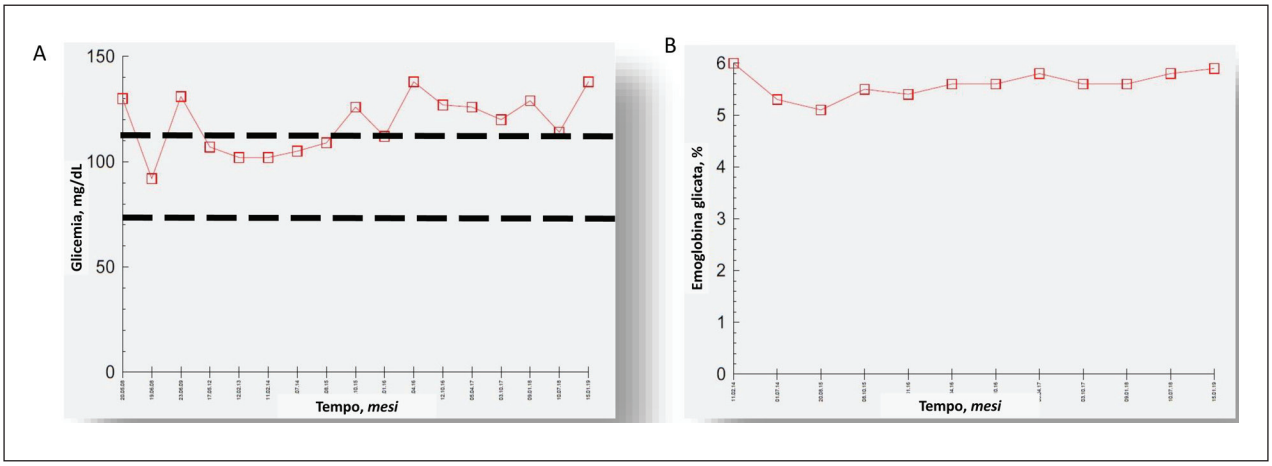

Figure 2 - Andamento nel tempo di A) glicemia a digiuno, B) emoglobina glicata.

anzi risultano entro i limiti clinici normali. Se però vengono considerati in un insieme univoco, allora diventano preoccupanti e si parla di sindrome metabolica. E' per questo motivo che spesso e volentieri diagnosticare questa condizione è complesso: perchè ogni valore clinico, preso singolarmente, risulta del tutto nella norma. Sicuramente il miglioramento dello stile di vita può agire molto sui fattori di rischio che determinano la sindrome metabolica, in particolare la dieta e l'attività fisica anche nel caso descritto hanno contribuito a migliorare i parametri ematochimici nel tempo oltre che garantire un miglioramento clinico del soggetto che grazie all'interazione tra i vari specialisti e, in particolare nell'ottica di una visione integrata dal punto di vista cardiovascolare, diabetologica e occupazionale può permettere di contenere i fattori di rischio e mantenere per quanto possibile gli skills professionali (Iavicoli I., 2019)

Gli autori non hanno dichiarato alcun potenziale conflitto di interesse in relazione alle materie trattate nell'articolo

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Prevention and screening of diabetes through a workplace campaign: an experience in advanced tertiary sector

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Key words: Diabetes; prevention; screening; health promotion; office worker; occupational health

Parole chiave: Diabete; prevenzione; screening; promozione della salute; lavoratore d'ufficio; salute sul lavoro

Summary

Introduction: *Worldwide, diabetes and its complications are a health priority. In Italy, its social global impact on private life and occupation relationships is not always considered. In adults the physiopathology is not completely understood yet, but it surely involves many relevant risk factors. Corporate social responsibility actions can play a significant role in life style through information and education, but the level of uncertainty about the screening cost-effectiveness ratio is high.* **Objectives:** *To evaluate a diabetes screening and educational program, in the workplace.* **Results:** *An information campaign about diabetes was addressed to 4,232 office workers. In this group, 425 volunteers without a prior diagnosis of diabetes (average age of 44 years, average Body Mass Index 24.4 kg/m^2) participated in individual moments with the company physicians (assisted calculation of "Diabetes risk score", screening by fasting blood glucose, and specific counseling). The prevalence of elevated capillary blood glucose was 16% (n = 68) and new diagnosis of diabetes was made in 1.6% of workers participating in the screening (n = 6).* **Discussion:** *A diabetes prevention campaign was carried out on Italian office workers in order to develop targeted preventive strategies. The campaign was aimed at primary and secondary prevention.* **Conclusions:** *The collaboration of the "company system" provided useful and effective support for a successful implementation of preventive diabetes campaign. The company's occupational physician's involvement was strategic.*

Riassunto

«Campagna di prevenzione e screening del diabete in ambito aziendale: una esperienza nel settore terziario avanzato». **Introduzione:** *Il diabete e le sue complicanze costituiscono una priorità sanitaria. In Italia non è sempre considerato l'impatto sociale che può avere (privato e lavorativo). Si ignorano i dettagli fisiopatologici ma molti fattori di rischio sono chiari. Interventi sullo stile di vita sono sicuramente utili, mentre permane un alto grado d'incertezza sull'effettivo vantaggio costi-benefici dello screening. Azioni di responsabilità sociale delle imprese possono svolgere un ruolo rilevante.* **Obiettivi:** *Sperimentare e valutare un programma di screening e formazione sul diabete sul luogo di lavoro.* **Risultati:** *Un gruppo di 4.232 impiegati d'ufficio ha partecipato a una campagna d'informazione sul diabete. Di questi, 425 volontari senza una precedente diagnosi di diabete (età media 44 anni, BMI medio 24,4 kg/m^2) hanno partecipato al momento individuale con il medico aziendale (calcolo assistito del "punteggio di rischio di diabete", screening mediante glicemia capillare a digiuno e consulenza mirata). Nel 16% dei partecipanti allo screening (n = 68) si è riscontrata iperglicemia e nell'1,6% (n = 6) è stata in seguito posta una nuova diagnosi di diabete.*

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Discussione: *Su un campione d'impiegati è stata impostata e condotta una possibile campagna di prevenzione del diabete, al fine di sviluppare strategie preventive mirate in ambito lavorativo in Italia. La campagna condotta era mirata alla prevenzione primaria e secondaria.* **Conclusioni:** *Una collaborazione costruttiva del "sistema aziendale" consente di fornire un supporto utile ed efficace a una corretta attuazione di una campagna preventiva sul diabete sul luogo di lavoro. Il coinvolgimento del medico del lavoro dell'azienda è strategico.*

Introduction

Diabetes is a global health emergency. Recent large-scale epidemiological studies showed that over the past 30 years diabetic cases in the adult population have increased, reaching 347 million cases worldwide, and also cases of prediabetes were growing fast (10). The disease is very heterogeneous, clinically complex with the involvement of target organs complications (i.e. heart, eyes, blood vessels, nerves, kidneys). Type 1 diabetes usually develops in children or young adults until 30 years of age. Risk factors research is still ongoing and primary prevention can't be performed. People who have prediabetes (called impaired glucose tolerance or impaired fasting glucose) do not properly process sugar (i.e., glucose). Sugar levels will be higher than normal, but not high enough to be classified as diabetes. Without a change of diet and more physical activity, about half of the people with prediabetes will develop diabetes type 2. Diabetes type 2 has traditionally been seen as a disease that occurs slowly over time and could be managed rather than cured. The exact reasons why this disease develops are still unknown, but many relevant risk factors have been identified. Today, diabetes really is a highly preventable condition. There is no widespread perception of what diabetes is and what social impact it may have on a population. In Italy, the total direct and indirect costs of diabetes for the National Health Service is estimated at up to 30 billion Euros per year. Many patients with diabetes and many non-specialist doctors underestimate the disease and so prevention strategies are not more implemented (6). Diabetes is often first diagnosed in people who show clear signs and symptoms of complications even before reporting those specific to the disease itself.

Diabetes also has a relevant impact on the quality of life, private as well as working (e.g.: main cause of blindness in adulthood). For this reason, lifestyle preventive interventions are certainly useful (many risk factors are also common in the primary prevention of other important chronic diseases, such as cardiovascular ones). For these reasons an adequate specialized care and therapy that stop the evolution of the disease and its complications are also required and highly recommended (3).

However, there is a high degree of uncertainty about the actual cost-effectiveness advantage of secondary prevention interventions through screening, particularly if it is performed in the general population rather than in greater risk groups (11). Epidemiological studies are limited and the levels of evidence are based on the experts' opinion: "there are doubts about whether it should always be recommended, but it is believed that its execution should be carefully considered - level of recommendation B " (1).

General health balance and workplace screening are realistic opportunities contemplated by the European legislation for the protection of workers' health and safety. In Italy, occupational physicians operating within companies have a leading role in promoting and protecting health in the workplace and collaborate in the implementation and enhancement of voluntary "health promotion" programs, according to the principles of social responsibility (Legislative Decree 81/2008, article 25, c.1, let. a) within the frame of the International Code of Ethics for Occupational health professionals (by ICOH).

The advanced tertiary sector provides services with high innovative content directed to other organizations using the most recent technologies. Intellectual performance is made available as a "network" rather than a "structure"; human resources, with their professional and relational contribution, are considered a central value. The organizational setting leads workers to consolidate their confidence,

and decision-making autonomy is supported and delimited by reliable regulations. Workers have to feel themselves in a framework defined as "freelancers in a corral" (4). Alterations of personal health related to the expansion of the working space-time are counterbalanced by an increasing attention to wellness. In this perspective, corporate social responsibility actions play a significant role both in awareness-raising and prevention activities and management of physical, mental and social well-being of a worker affected by a chronic disease. This working context appears to be useful to support a prevention campaign on a chronic and complex pathology such as diabetes.

Methods

The preventive diabetes campaign was part of a health promotion program carried out between November 2013 and February 2014 and directed/targeted at a number of companies related to an Italian multinational information technology consulting group. Companies in Lombardy, Piedmont, Puglia, Lazio, Campania, and Veneto Regions were involved in the study.

Informed consent from workers included in the study was obtained before review of the medical records. During data collection and analysis, anonymity and privacy was respected.

All 4,232 employees involved (average age 45 years, range 24-55; females 33%; average Body Mass Index 24.1 kg/m^2, range 18.2-32.3 kg/m^2; smokers 10%) can be classified as office workers with task of "Video Display Unit (VDU) operator" (health risks: VDU, organization and stress, use of company car).

During the periodical health check for renewing pass-issue, data on family history, personal physiologic (including lifestyle characteristics), pathological and occupational history, general clinical examination, musculoskeletal and visual symptoms and sign, anthropometric measurements (weight, height) were collected by trained health occupational physicians using standardized methods (i.e., same methods/equipment in all locations). Results of the complementary investigations such as clinical laboratory analysis (i.e. blood glucose, glycated hemoglobin, thyroid function, etc.) performed by specialists were also included.

An information campaign to increase awareness about diabetes was addressed to all workers, by sending an e-mail message, posting streamers or flyers in high traffic areas (i.e. break areas), and setting up a dedicated website where more informations were made available.

A total of 425 employees without a prior diagnosis of diabetes (mean age 44 years, range 25-55; females 32%; average Body Mass Index 24.4 kg/m^2, range 19.1-32.3 kg/m^2; smokers 11%), equal to 10% of all workers, spontaneously agreed to participate in a private examination with the company doctor. Assisted calculation of the probability of a non-diabetic person to develop Type 2 Diabetes in the following 10 years by means of "Diabetes risk score" (9), a extemporaneous screening by measuring of fasting blood glucose, and targeted counseling with possible referral to General Practitioner for further investigations have been carried out. Individuals screened positive for diabetes based on standard criteria for Fasting Plasma Glucose test (FPG): normal value up to 99 mg/dL (5.5 mmoles/L) was considered.

The analytical system used for the determination of fasting glucose with glucometer was Bayer's CONTOUR XT (Biosensor: Glucose Dehydrogenase converts Glucose from sample into Gluconolactone, Enzyme: Flavin Adenine Dinucleotide) conforming to ISO 15197: 2013 and more stringent quality parameters tested by Scandinavian evaluation of laboratory equipment for primary health care. Diabetes diagnosis was confirmed by a second level specialist center. Each participant received a report both hand-written and by e-mail containing all the suggestions of preventive improvement required (weight check-up, diet control and physical exercise).

Individual follow-up was performed during each mandatory clinical examination (periodic health surveillance).

Results

All workers were involved in the awareness-raising information phase regarding diabetes. Out of 4,232 participants, those already known to have diabetes were 67 (1.6%).

The slogan chosen for the campaign, "Play in advance with diabetes", led to immediate emotional

involvement as it recalls the rapid action of soccer players. The campaign was launched in concomitance with World Diabetes Day, reinforcing the link with a large-scale issue. The explicit invitation and the information provided helped reduce one's risk factors (extra weight, inactivity, high blood pressure, irregular sleep), and adopt a healthier lifestyle (eating a healthy low-fat and low-sugar diet, high-fiber foods and lots of fresh fruit and vegetables, keeping weight under control, and staying physically active). In-depth information was made available in simplified language, regarding each of the main clinical situations (gestational diabetes, prediabetes, type 1 diabetes, and type 2 diabetes), and attention was paid also to the unchangeable risk factors (age, family history).

During the voluntary screening (425 employees), the prevalence of elevated capillary blood glucose was 16% (n = 68), 18% and 14% in men and women respectively. After a 1-year follow-up a new diagnosis of diabetes was made in 1.6% of workers participating in the screening (n = 6).

Discussion

The present report shows a possible integrated strategy of diabetes prevention campaign, in a sample of Italian office employees. To our knowledge this is the first study carried out to investigate a diabetes preventive campaign including screening of elevated capillary blood glucose among not preselected individuals to develop targeted preventive strategies in Italian workplaces.

Preliminary results agreed with those of studies conducted in France where the prevalence of elevated capillary blood glucose was 20% (vs. 16%) (5). According with previous studies men generally tend to have higher levels of blood glucose compared with women (7) and type 2 diabetes is more prevalent in men (11). In our experience, diagnosis of diabetes was made in 1.6% of participants vs. 4% of a recent screening study conducted in the USA (2). Different results could probably be explained by the lower BMI values found in the workers we studied. The lower finding of diabetics compared to a screening study conducted in Canada (8) could be related to failure to pre-select the subjects at greater risk (1.6% vs. 8%).

The consistency of the new diagnoses of diabetes could hardly justify a screening investigation on a not pre-selected high risk population. In the workplace, the possibility that this diagnosis involves a colleague acts as a powerful message to stimulate a radical change in the own and family members lifestyle.

The campaign conducted was not only aimed at secondary prevention but settled with a vision of medium-long term primary prevention targets. The implementation of illness prevention (lower onset of the disease) in the working context appears to be an excellent opportunity to educate consciences and behaviors. Wellness intervention programs with workers health and wellness strategy may also lead to greater uptake by employees. The follow-up study will make it possible to have clearer understanding of the impact of our campaign on the working population.

The involvement of companies of the advanced tertiary sector played a role in defining and managing the prevention campaign combined with screening. In particular, a strong social support received from work organization and colleagues have certainly helped to maximize efficiency of the campaign.

The workplace environmental experience, based on a "moderate" open space (i.e.: without cubicles, with large aggregation areas, etc.), also facilitated the realization and contributed to the positive impacts.

In conclusion, the preliminary results of our experience demonstrated that a workers' prevention diabetes campaign can be implemented successfully. A collaboration of the "company system" is helpful to provide support to increase awareness of diabetes with positive implications on physical, mental and social well-being. The involvement of the company occupational physician not only provided a practical, accurate and reliable operator in carrying out the screening, but also allowed effective actions useful to therapy compliance and lifestyle improvement. Coordination between general practitioner and the specialist seemed to be necessary.

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Recurrent hypoglycemia in Diabetes Type 1: a case report

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Key words: Diabetes type 1; hypoglycemic episodes; office worker; occupational health

Parole chiave: Diabete tipo 1; episodi di ipoglicemia; lavoratore d'ufficio; salute sul lavoro

Summary

Introduction: *Insulin as diabetes therapy, if not well accepted by the patient, can worsen life quality and lead to compromised glucose control. Diabetic emergencies, such as hypoglycemia, can occur. According to social responsibility, corporate actions plays a relevant role in supporting the well-being of diabetic workers.* **Objectives:** *To report a case of management of severe recurrent hypoglycemic crises.* **Results:** *An advanced tertiary sector office worker (health risks: VDU, organization and stress, no company car use), suffering from Diabetes Type 1 with recurrent severe hypoglycemic crisis during the working time was brought to the attention of the occupational physician. The patient was followed by a high-level specialized diabetic center, but an unusual personality and bizarre ideas on self-regulation of diabetes resulted in rejection of continuous infusion with insulin pump in favor of multiple daily insulin injections therapy.* **Discussion:** *Advanced tertiary sector, characterized by a space-time expansion of the working time, didn't facilitate acceptance of the regularity in insulin therapy and meals. Company prevention system intervention is useful to achieve a satisfactory balance: social support, availability of a refrigerator for medicines and an infusion pump.* **Conclusions:** *A constructive action of the "company system" can be useful to provide effective support in the management of diabetic therapy, with real positive implications on health status.*

Riassunto

«Ipoglicemie ricorrenti in Diabete Tipo 1: caso clinico». **Introduzione:** *La terapia insulinica del diabete, se non ben accettata, può determinare un rilevante impatto sulla qualità di vita e comportare problemi nel controllo glicemico. Possono così verificarsi emergenze diabetiche, come crisi ipoglicemiche severe. Nell'ottica della responsabilità sociale, l'azienda può attuare azioni di rilievo mirate a supportare l'equilibrio di benessere del lavoratore affetto da questa patologia cronica.* **Obiettivi:** *Presentare un caso di gestione di gravi crisi ipoglicemiche ricorrenti.* **Risultati:** *Giunge all'attenzione del medico aziendale il caso di un lavoratore del settore terziario avanzato (rischi per la salute: VDT, organizzativi e stress, no auto aziendale), affetto da Diabete di tipo 1 con gravi crisi ipoglicemiche ricorrenti in orario lavorativo. Il lavoratore era seguito da un centro specialistico diabetologico di secondo livello; la sua originale personalità e la convinzione di potersi agevolmente auto-gestire nella quotidianità lo avevano portato al rifiuto dell'applicazione di una pompa con infusore continuo di insulina, preferendo continuare con una terapia multiniettiva.* **Discussione:** *Il lavoro nel settore terziario avanzato, caratterizzato da una dilatazione spazio-temporale del momento lavorativo, non facilita la necessaria regolarità nell'assumere la terapia ed i pasti. Un intervento del sistema della prevenzione aziendale coordinato con gli specialisti diabetologi ha permesso di raggiungere un equilibrio soddisfacente in più passaggi: supporto sociale dei colleghi, disponibilità di frigorifero per medicinali prima e di pompa ad infusione poi.* **Conclusioni:** *Azioni costruttive del "sistema aziendale" possono costituire un concreto ed efficace supporto per riconciliare la gestione della terapia diabetica e il lavoro, con concrete implicazioni positive sullo stato di salute.*

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Introduction

Treatment of diabetes type 1 involves, in addition to a specific nutritional intervention, insulin therapy according to the recommended basal-bolus scheme. The therapy can be carried out by multiple daily insulin injections or, in the case of poor glycemic control and /or recurrent hypoglycemia, by continuous infusion with insulin pump (2). Poor compliance of patient could influence the quality of their private and working life. Hypoglycemic crises are particularly important also because they generate considerable apprehension in people who assist diabetic patients, especially if they occur at the workplace.

Education and improvement of insulin therapy play an important role to reduce poor compliance.

According to social responsibility, corporate actions could play a relevant role in the integrated management of support for the physical, mental and social well-being of the diabetic worker.

Methods

We reported a clinical case of an employee in the advanced tertiary sector suffering from diabetes type 1 with severe recurrent hypoglycemic episodes during working hours.

Informed consent of the patient included in the study was obtained before the consultation of the medical records. During data collection and analysis, anonymity and privacy were respected.

Family history, personal physiologic, pathological and occupational history and general clinical examination were collected by the company occupational physician, during periodical check for renewing pass-issue. The occupational physician also collected the reports drawn up by company first aid workers, who helped the colleague during the hypoglycemic crisis. Additional investigations such as high-level specialized laboratory analysis were also ruled out.

Case report

Female 45 years old, normal weight (58 Kg, Body Mass Index=23.1), non-smoker, office worker in the same multinational company of advanced services for nineteen years, with the task of "Video Display Unit (VDU) operator" and role of Executive Assistant (health risks: VDU, organization and stress, without use of company car). The diagnosis of "diabetes mellitus type 1" was made at the age of 26 and was confirmed by a high level specialist center. Insulin therapy was started and good glycemic compensation (HbA1c 6.3% - 46 mmoles/moles, confirmed by diary with a good preprandial control) was obtained within one year. However the space-time expansion of the working time did not facilitate acceptance of the necessary regularity in therapy and meals, compromising glucose control. The unusual personality of the patient and her bizarre ideas on the self-regulation of her diabetes resulted in wide variations of insulin dosage and in refusal of continuous insulin infusion with insulin pump (recommended by the specialized center for diabetics) in favor of multiple daily insulin injections (5 doses / day). The pathologic history shows a Transient Ischemic Attack (TIA) due to therapeutic mistake when she was 37 years old and a silent heart attack at 43 years of age. No ergophthalmologic and musculoskeletal abnormality was revealed by medical examination.

At workplace, in a short period of time, three episodes of severe hypoglycemia occured (glucose < 70 mg/dL - 3.88 mmoles/L, with unconsciousness), always late in the morning or early in the afternoon. During all the crisis, intervention of both the company first aid workers and the external public first aid were needed. The impact on physical, mental and social well-being involves not only the worker (who minimized and underestimated her situation), but also the work colleagues who were scared and worried. The company first aid team (concerned about the severity and frequency of the interventions), and the company management (worried about collaborator's health and business continuity) were also involved.

Early cooperation between company occupational physician and high-level specialized center for diabetics started and a reinforcement activity in an opportunistic context was planned in order to increase empowerment and to accept treatment indications. The company also facilitated the therapeutic

management of the disease and made available a medical refrigerator (continuous temperature monitoring, connection to the electricity line with a UPS, access limitation by personal code) to keep personal medications in optimal conditions.

A collaboration between the occupational social context, performed by the company health service and prevention and protection service, was also set up. Strong support to the worker was implemented (i.e.: supporting the maintenance of regular times dedicated to the consumption of food avoiding inappropriate overlapping of meetings and / or requests, etc.).

The worker found her own glycemic balance and her well-being; no other hypoglycemic crisis occurred during the working day. After one year, the worker agreed to equip herself with an infusion pump to simplify the management of insulin therapy and to improve glycemic control.

Discussion

Severe hypoglycemic crises during insulin therapy represent the most important complication of diabetes mellitus type 1 and can lead to death. These events commonly appear at the beginning of therapy or when a change occurs in one daily life; they are closely related to understanding of real needs of the substitution therapy, as happened also in this case report. Educational reinforcements adapted to the age and sociocultural context of the patient (5) represented the best preventive results in the medium term.

The collaboration with a high-level diabetes center is an excellent opportunity to have an easily available coordinated team offering the best prospective for treating diabetes and its complications (1). However, this was not sufficient in the management of this case. To overcome the criticalities connected to an inadequate management of insulin therapy, the involvement of the company occupational physician allowed an effective and efficient coordination between the general practitioner and the specialist. Appropriate enhancement actions were useful to assure to the best lifestyle and insulin therapy management supporting the worker to accept a continuous infusion pump instead of multiple daily insulin injections.

In this case report the discouragement and depressive implications were effectively counterbalanced by the strong social support received from work organization and colleagues, in synergy with the reinforcement interventions suggested by the corporate prevention system and implemented within the workplace social context.

Psycho-behavioral characteristics have led the worker to not completely accept her situation as a "chronic patient dependent on a therapy" and the diagnosis of type 1 diabetes made in adulthood has contributed to this non-acceptance. The fact of being employed in a company of the advanced tertiary sector created some difficulties for the regularity of meals and therapeutic doses. Companies operating in this sector of activity provide services with high innovative content, directed exclusively for other companies; for the success of this system the human resource is considered crucial, with the need for flexibility, dynamism and adaptability (3). In this work context there is a time-space expansion combined with an increase in social conditioning. An eventual substratum of personal insecurity, aggravated by the fear of losing one's professionalism, could become critical when regular rhythms of working time are need, as in the case of insulin therapy. The technological evolution in insulin treatment now provides new, more performing opportunities that are well suited also to this working context (4).

In conclusion, an action of the "company system" provided an useful and effective support to reconcile the management of diabetic therapy and work, with positive implications on physical, mental and social well-being.

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Caso clinico - Novelis Italia

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Parole chiave: Metalmeccanica; obesità; diabete

Keywords: Engineering; obesity; diabetes

Riassunto

Introduzione: *Operaio di 55 anni dipendente di un'azienda metalmeccanica multinazionale che produce nastri e lastre in leghe di alluminio. Ispettore dell'impianto laminatoio su tre turni.* **Obiettivi***: Nel 2009***,** *a seguito di visita periodica, con BMI di 32.9, viene inviato al Day Hospital Obesità e Lavoro presso la Clinica del Lavoro di Milano, senza adesione motivazionale.* **Metodi:** *Nell'agosto 2012 il dipendente reca certificato del CPS con diagnosi di "Disturbo dell'umore" e il consiglio di astensione dai turni di lavoro notturni. Impostata terapia specialistica e follow-up trimestrale delle visite periodiche. Nel settembre 2013, come da indicazione psichiatrica del CPS, riprende gradualmente la turnazione notturna, due-tre al mese. Nuovo accesso autonomo a MAC nel luglio 2017, con BMI di 42.78. Diagnosi: "Obesità di III classe con sindrome metabolica, diabete tipo 2 di prima diagnosi, dislipidemia, sospetta sindrome da apnee notturne". MAC di controllo nel gennaio 2018: "Obesità di II classe con calo ponderale in precedente obesità di III classe e sindrome metabolica". Adeguata adesione motivazionale ai provvedimenti terapeutici e miglioramento dei comportamenti alimentari disfunzionali.* **Risultati:** *MAC del gennaio 2019 "Ulteriore calo ponderale (25 Kg), diabete 2 in buon controllo glicometabolico".* **Discussione:** *Negli anni, grazie alla continua attività di sensibilizzazione sia durante le visite periodiche, sia attraverso numerose campagne preventive in azienda e grazie in particolare alla collaborazione con centri specialistici di eccellenza, si è giunti ad un successo terapeutico e di performance lavorativa.*

Summary

***«Case report - Novelis Italy»*. Introduction:** *A 55 years old employee of a multinational engineering company producing aluminum ribbons and alloys. Mill inspector on three shifts.* **Objectives:** *In 2009 during a periodic evaluation he presented a BMI of 32.9. The plant occupational health physician sent him to the Obesity Center at "Clinica del Lavoro" in Milan, but the employee wasn't motivationally engaged.* **Methods:** *In August 2012 a Public Psychiatric Center diagnosed him with mood disorder and suggested to avoid night shifts. He began psychiatric therapy and a three-month medical follow-up in the plant. In September 2013, as recommended by the Psychiatric Center, he restarted to gradually work night shifts, for not more than two or three nights a months. In July 2017 he spontaneously went to the Obesity Center presenting a BMI of 42.78. This was the diagnosis: "Third class obesity with metabolic syndrome, diabetes type 2 at first comparison, dyslipidemia, suspected sleep apnea syndrome". New examination in the center in January 2018: "Second class obesity with weight decrease in previous third class obesity and metabolic syndrome". Adequate adherence to therapy and improving of dysfunctional eating behaviors.* **Results:** *New control January 2019:"Further weight decrease (25 kg), diabetes type 2 in a good metabolic control".* **Discussion:** *Over the years, thanks to the continuous sensibilization during medical examinations and through some preventive health campaigns, thanks especially to the collaboration of specialized high level hospital centers, we have achieved a therapeutic success associated with an increase of working performance.*

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Introduzione

Il contesto aziendale è costituito da un'industria metalmeccanica multinazionale che opera nel settore dell'alluminio: si tratta del principale produttore di laminati in alluminio e il più grande riciclatore di alluminio al mondo. Fornisce soluzioni innovative ai mercati delle lattine per bevande, automobilistico e delle specialità di fascia alta.

In Italia produce in due stabilimenti situati nell'hinterland milanese, Bresso e Pieve Emanuele. L'impianto di Bresso possiede la linea di verniciatura liquida in continuo più produttiva d'Europa e una linea di verniciatura a polveri. Lo stabilimento di Pieve è dotato di più linee di colata continua e di laminazione a freddo per la realizzazione di rotoli di alluminio finiti o destinati alla verniciatura.

Il caso in oggetto è un operatore di 55 anni con la mansione di addetto alla linea di ispezione dell'impianto laminatoio presso lo stabilimento di Pieve. E' in azienda dal 2000, in precedenza come disegnatore tecnico.

Metodi

A seguito della visita medica periodica del settembre 2009, a fronte di un riscontro di obesità di prima classe (BMI 32.9), il medico del lavoro lo invia al Day-Hospital Obesità e Lavoro della Clinica del Lavoro di Milano. Nell'agosto 2012 il lavoratore presenta al medico del lavoro un certificato del CPS recante la diagnosi di "Disturbo dell'umore" con il consiglio di astensione dai turni di lavoro notturni. Viene altresì impostata terapia psichiatrica dal CPS. Il medico del lavoro rilascia l'idoneità alla mansione con la limitazione prescritta dal CPS e imposta un programma di follow-up trimestrale di visite mediche periodiche. Nel frattempo il dipendente esegue, inviato dal Medico Curante, una serie di prestazioni presso il servizio di Psicologia dell'Ospedale di Pavia che rilascia la diagnosi di "Disturbo depressivo con tratti di personalità che rendono difficile l'adattamento". Nel settembre 2013 viene rilasciata l'idoneità alla mansione con la ripresa graduale dei turni notturni, non più di 2-3 al mese, come da indicazione del CPS. Nel novembre 2016 viene ricoverato in PS per crisi ipertensiva. Nel luglio 2017 effettua volontariamente un nuovo accesso al MAC della Clinica del Lavoro di Milano, con un peso di 139,4 kg e un BMI di 42.78 e la diagnosi alla dimissione di "Obesità di III classe con sindrome metabolica, diabete tipo 2 di prima diagnosi, dislipidemia, sospetta sindrome da apnee notturne". Questa volta vi è un'adeguata capacità di adesione alle cure. Viene prescritta Metformina Cloridrato 1000 mg alla sera. Riferisce buon controllo glicemico domiciliare con media di 128 mg/dl. Riferisce, inoltre, un miglioramento dello stato di salute e del tono dell'umore. Nel novembre 2017 viene ricoverato sempre presso la Clinica del Lavoro di Milano per accertamenti in merito alla sindrome da apnee notturne. L'esito è di un livello di grado lieve, non meritevole di trattamento. Nel gennaio 2018 effettua un MAC di controllo. La diagnosi è di "Obesità di II classe con calo ponderale in precedente obesità di III classe e sindrome metabolica". La specialista Psicologa del Centro riscontra un'adeguata capacità di adesione motivazionale ai provvedimenti terapeutici proposti e un miglioramento dei comportamenti alimentari disfunzionali.

Risultati

Al MAC del gennaio 2019 la diagnosi è risultata di "Ulteriore calo ponderale (25 kg) in precedente Obesità di II classe con sindrome metabolica. Diabete tipo 2 in buon controllo glicometabolico".

Discussione

Il raggiungimento del successo terapeutico e di performance lavorativa del caso analizzato può essere considerato un esempio di efficacia di una serie di azioni condotte negli anni in azienda. Si tratta di attività che spaziano dalla sensibilizzazione individuale da parte del medico del lavoro durante le visite mediche periodiche, nel caso specifico portate ad una periodicità trimestrale, alla sensibilizzazione collettiva, rivolta alla popolazione lavorativa come gruppo omogeneo, attraverso numerose attività di promozione della salute. A partire dal 2007 in azienda, infatti, in collaborazione con centri specialistici ospedalieri, sono state condotte numerose campagne di promozione della salute: nello specifico, la

campagna di disassuefazione dal fumo di sigaretta (1), quella di prevenzione del sovrappeso/obesità (2)(3), di valutazione ematica della vitamina D nei turnisti unitamente alla MOC calcaneare (4), dipromozione dell'attività fisica attraverso l'apertura di un'area wellness con la presenza di trainer dedicati, quella attuale di prevenzione del diabete. Elemento fondamentale per il medico del lavoro sul territorio, oltre alla disponibilità del management aziendale, è la collaborazione con centri specialistici ospedalieri, in grado di offrire l'attività di cura del singolo attraverso canali di comunicazione facilitati, ma soprattutto attraverso azioni preventive e studi di ricerca, azioni fondamentali per il wellbeing aziendale.

Gli autori non hanno dichiarato alcun potenziale conflitto di interesse in relazione alle materie trattate nell'articolo

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Unknown diabetes: a case report

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Parole chiave: Diabete tipo 2; retinopatia; lavoratore d'ufficio; salute sul lavoro

Summary

Introduction: *Diabetes is often diagnosed in people who already show clear signs and symptoms of complications. This leads to a significant impact both on general health costs and quality of life (private and working). Corporate social responsibility actions could play a significant role managing and supporting physical, mental and social well-being of the worker affected by diabetes.* **Objectives:** *To report a case of management of unknown diabetes.* **Results:** *Type 2 Diabetes in an office worker (health risks: VDU, organization and stress, use of company car), with sudden visual impairment, detected during a health surveillance periodical consult. The diagnosis was "diabetes mellitus with proliferative retinopathy, macular edema and predominantly sensitive polyneuropathy".* **Discussion:** *The most important impairment concerned the distance visual acuity, with the consequent impossibility to drive a car. The worker continued to work in the same advanced tertiary sector company adapting to the new condition of susceptibility (transition from customer directed operations to manager of working groups, limited VDU use, and no company car use). The depressive implications, caused by the impacts in lifestyle, have been effectively counterbalanced by the strong social support received from the work organization and colleagues.* **Conclusions:** *A constructive reaction of the "company system" is able to provide an useful and effective support to manage diabetes and work, with tangible positive implications on overall health status.*

Riassunto

«Diabete misconosciuto: caso clinico». **Introduzione:** *La diagnosi di diabete è spesso posta in persone che mostrano già chiari segni e sintomi di complicanze. Ciò comporta un rilevante impatto sui costi sanitari generali nonché sulla qualità della vita personale (privata e lavorativa). Interventi nell'ambito della responsabilità sociale delle imprese possono svolgere un ruolo significativo anche nella gestione integrata del sostegno al benessere fisico, mentale e sociale del lavoratore affetto da questa malattia cronica.* **Obiettivi:** *Presentare un caso di identificazione e gestione di diabete misconosciuto.* **Risultati:** *Diabete di tipo 2 in un impiegato (rischi per la salute: VDT, organizzazione e stress, uso dell'auto aziendale), con improvvisi sintomi visivi rilevati durante un controllo periodico di sorveglianza sanitaria. La diagnosi finale è "diabete mellito con retinopatia proliferativa, edema maculare e polineuropatia prevalentemente sensitiva".* **Discussione:** *Il danno più importante ha coinvolto il visus per lontano, con la conseguente impossibilità di guidare un'auto. Il lavoro è continuato nella stessa azienda del settore terziario avanzato, adattando il ruolo alla nuova condizione di suscettibilità (passaggio da attività dirette presso i clienti a gestore di un gruppo di lavoro, uso limitato di VDT, nessun uso di auto aziendale). I risvolti depressivi per i relativi impatti sulla vita sono stati efficacemente controbilanciati dal forte sostegno sociale ricevuto anche dall'organizzazione del lavoro e dai colleghi.* **Conclusioni:** *Una reazione costruttiva del "sistema aziendale" consente di fornire un supporto utile ed efficace per conciliare la gestione della patologia diabetica e del lavoro, con implicazioni positive concrete sullo stato di salute generale.*

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Introduction

In 2016 there were over 3 million Italian people suffering from diabetes corresponding to 5.3% of the entire population (3). In the last thirty years the prevalence has almost doubled and in the majority of cases (over 90%) the diagnosis of Diabetes Type 2 is made, involving people in adulthood.

Often people who do not seem to belong to major risk groups (i.e. low education, overweight, advanced age), as well as people who already show clinical complications are diagnosed with diabetes. Diabetes could lead to difficult management of the chronic medical therapy and changes in lifestyle. Diabetes complications have then a significant impact not only on the general health costs, but also on the people's quality of life, private as well as at work.

Corporate social responsibility actions could play a significant role in awareness-raising, prevention activities and management in physical, mental and social well-being of the diabetic worker.

Methods

Free agreement of patient included in the study was obtained before the consultation of the medical records. During data collection and analysis, anonymity and privacy were respected.

We report a case of unknown Diabetes Type 2 in an office worker with sudden visual impairment.

Family history, personal physiologic, pathological and occupational history, general clinical examination, history of ocular disease, visual symptoms and sign were collected by the company occupational physicians during periodical medical consult for renewing pass-issue. The results of complementary investigations such as clinical laboratory analysis (i.e. blood glucose, glycated hemoglobin, thyroid function, etc.), optical coherent tomography (OCT), brain computed tomography (CT) and magnetic resonance imaging (MRI) were also collected. The diagnosis was confirmed by a second level specialist center.

Case report

A 50 year-old male, normal weight (73 Kg, Body Mass Index=24.2), non-smoker, office worker in the same multinational company of advanced services for 32 years (hired in 1984), with the task of "Video Display Unit (VDU) operator" (health risks: VDU, organization and stress, use of company car). Personal history shows a familiarity for diabetes (maternal grandfather in old age) and cardiovascular diseases (father with middle-aged heart attack). The personal physiologic and pathological history revealed no abnormalities except the common childhood rashes and a good correction of medium severity myopia with lenses in use (-6.00 diopter at right eye and left eye). No other ergophthalmologic and musculoskeletal abnormality was revealed by medical examination.

During a health surveillance periodical medical consultation, blurred vision (especially for distance), eye heaviness, general fatigue, and limbs discomfort (especially for the lower ones) were reported. These symptoms did not resulted related to workplace conditions (i.e.: use of most recent and ergonomic VDU devices, lightness and chair optimal, etc.) but they impact on the working performance. Musculoskeletal physical examination was normal. The ergophthalmological medical examination detects a binocular distance visual acuity with use of his lenses of 3/10 (Monoyer illuminated optotype at 3m), and a binocular near visual acuity with use of his lenses of 5J (Jaeger standard optotype EN 473 ISO 8596/1996 - UNI EN ISO 8597/1996).

In agreement with the general practitioner and an ophthalmologist, further clinical investigations were required. After excluding other relevant diseases in the differential diagnosis, the focus was on possible diabetes. The diagnosis of "diabetes mellitus with proliferative retinopathy, macular edema and predominantly sensitive polyneuropathy" was confirmed by a second level specialist center. A laser therapy was then performed to stabilizing but not improving the ocular disease. The patient received insulin and metformin therapy and glycemic compensation (HbA1c 6.5% - 48 mmoles/moles, confirmed by diary with a good pre-prandial control) was obtained within a year.

The serious non-reversible blindness leeds to the loss of the minimum requirements for diving license set established by the Italian Highway Code. The employee continued to work in the same company

adapting his role to the new condition (transition from customer directed operations to manager of working groups, limited VDU use, and no company car use). The National Social Security Institute (INPS) recognized a civil disability of 80% which allowed the inclusion of the worker among the protected categories.

Discussion

Working in a company of the advanced tertiary sector played a particular role in managing the personal impacts on the psychophysical and social well-being. These work organizations provide services with high innovative content, targeted exclusively to other organizations. Intellectual performance is the considered as a "network" rather than a "structure" so far human resource is considered central (2). Discouragement and depressive implications caused by the diagnosis were effectively counterbalanced by the strong social support received from work organization and colleagues.

Diabetic retinopathy is one of the most important ocular complication of diabetes mellitus and affects more than a third of patients. It generally remains silent until the macula is affected; symptoms that may occur include floaters (spots or dark threads that "float"), blurred vision, dark areas, loss of visual acuity and difficulty in perceiving colors (4). It is common for these symptoms to be slowly progressive. When retinal lesions become clinically evident therapy improvement could be limited. This happened also in the case we report.

The most important impairment concerned the distance visual acuity, with the impossibility to drive for both private and business trips. The worker had to get adapted to reaching the company headquarters by public transport (subway station available at less than 100m). He also had to accept to no longer being able to go frequently to customer sites (he was used to travel by company car for about 40,000 Km/year) having to move from the role of "on-site consultant" to that of "remote consultant" (suspension of the use of the company car).

Near visual acuity was found to be less compromised, allowing him to continue using VDU, with interventions aimed at alleviating asthenopia. A larger screen was provided and the occupational physician defined both the limitation in the timing of VDU use (no more than 4 hours/day) and the prescription of compensatory rests (20 minutes every hour of use of the VDU) more frequents compared to the minimum due by Italian law (15 minutes every two hours).

The involvement of the company occupational physician allowed an efficient coordination with the general practitioner and the specialist. Appropriate enhancement actions were useful for therapy and lifestyle. The glycemic control remains today the most important of the modifiable risk factors to stop or reduce the progression of diabetic retinopathy (1).

In the new work organization, the risk of social self-isolation was avoided by exploiting the worker's professional skills and moving him to a second-level coordination role in which he could give the benefit of his experience to a group of colleagues, without the need to travel.

Also the workplace environmental experience of the company headquarters, based on a "moderate" open space (i.e.: without cubicles, luminous, with large spaces of movement, aggregation areas, etc.) contributed to the positive impacts.

In conclusion, a positive reaction of the "company system" can really be helpful supporting and managing diabetes and work, with concrete positive implications on his physical, mental and social well-being.

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Critical issues and perspectives of the diabetic worker

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The condition of chronic hyperglycaemia due to shortcomings in insulin secretion and/or action is characteristic of different metabolic disorders that are commonly referred to as diabetes (1). According to the diagnosis and classification criteria of the American Diabetes Association (ADA) there are different types of diabetes (1). Type 1 diabetes is caused by a cellular-mediated autoimmune destruction of the pancreatic β-cells and usually determines an absolute insulin deficiency, whereas type 2 diabetes is characterized by an insulin resistance, commonly associated with a relative insulin deficiency (1). In the long run, if not adequately controlled, the condition of sustained and prolonged hyperglycaemia can result in extremely important and severe complications such as nephropathy, retinopathy, peripheral and/or autonomic neuropathy and sexual dysfunction (1, 2, 10). Recently, it was estimated that 422 million adults aged over 18 are living with diabetes, South-East Asia and Western Pacific Regions being the areas with the largest numbers of affected people (9). In this regard, it should be noted that the majority of diabetic subjects are diagnosed with the disease when they are in full working age. For example the International Diabetes Federation estimated that there are 326.5 million people of working age (20-64 years) with diabetes (4) and the forecasts for the near future do not seem to be promising, considering that a net increase of about 2% of global prevalence of the disease in adults is expected by 2040 (5).

These figures clearly show the need of special attention to the complex relationship between this pathology and the working conditions experienced by diabetic workers in order to guarantee, even in workplaces, an optimal management of diabetes, thus ensuring the well-being of workers, together with implementing their work ability. In Italy, a working group of the Italian Society of Occupational Medicine (SIML), the Italian Diabetes Society (SID) and the Italian Association of Medical Diabetologists (AMD) has been actively involved in this topic for several years and has recently published a consensus paper reviewing some specific occupational risk factors, suggesting strategies and tools to properly treat diabetes in the workplace, as well as supplying practical guidance to face the issue of fitness for work (3). Nevertheless, much work remains to be done on this topic and further research is needed in order to address other occupational risk factors, implement job retention strategies and improve the working conditions of diabetic workers.

In this context, an event was recently held in Milan entitled "Approccio multi-disciplinare al lavoratore con diabete: dialogo tra medici del lavoro, diabetologi e specialisti" [Multi-disciplinary approach to the worker with diabetes: dialogue between occupational physicians, diabetologists and specialists] which pointed out that a key role to achieve the aforementioned goals lies in the close collaboration between occupational physicians (OPs), diabetologists and other specialists (including where necessary, cardiologists, nephrologists, ophthalmologists, neurologists). In their Editorial, Perseghin and Riboldi highlighted how the multidisciplinary analysis of the interplay between the characteristics of the specific job requirements on the one hand and the

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individual's health status of the diabetic worker on the other is a formidable working tool. It effectively manages any criticality related to the therapeutic treatment (e.g. hypoglycaemia), the complications of diabetes (which, in turn, represent the main potential obstacle to the issue of fitness for work) and to the possibility of safely and effectively undertaking the working activities.

In detail, the risk of hypoglycaemia and the presence of chronic complications might represent an element of criticality mainly when the diabetic worker is faced with some particular occupational risk factors such as those described and discussed in the priority list of the consensus document of Iavicoli et al. (3). In this regard the case reports, included in this special issue, allow a further step in the analysis of this problem by evaluating new occupational risk factors and introducing fresh elements for discussion. For example, the studies by Cirla and Martinotti, describing two cases of diabetes in office workers exposed to video display units (VDUs), work-related stress and use of company car, showed that the aforementioned multidisciplinary approach to the diabetic worker is strongly encouraged, especially when the complications of the disease become an obstacle to the job performance (e.g. use of VDUs) or pose a safety risk (use of company car).

Cirla observed that type 2 diabetes is characterized by an asymptomatic phase between the actual onset of diabetes hyperglycaemia and clinical diagnosis. This phase has been estimated to last at least 4-7 years; consequently 30-50% of type 2 diabetic patients remain undiagnosed. Thus, untreated hyperglycaemia is an explanation for the relatively high prevalence of retinopathy in newly diagnosed diabetic people. The workplace health screening program could be an opportunity to check diabetes and its complications. According to Martinotti hyperglycaemia may be responsible for serious chronic damage .among patients with type 1 diabetes. Insulin pump therapy, compared with injection therapy shows lower risks of severe hypoglycaemia, diabetic ketoacidosis and better glycemic control.

On the other hand, also the case report proposed by Belluigi, regarding a diabetic worker exposed to shift-work and night-time work, showed that a concerted and synergistic interaction of OPs and diabetologists allows to obtain a greater probability of therapeutic success; it improves also the work skills of affected workers. With regard to this last issue it is noteworthy to underline that the effective cooperation, experienced in the aforementioned studies, between the various specialists has guaranteed the identification and the adoption of the best and most appropriate reasonable accommodations for diabetic workers. Belluigi also pointed out that more than 90% of the patients with type 2 diabetes are overweight or obese and weight loss slows the progression of diabetes complications. Both drugs and nutritional advice have a major role in the treatment approach. In the case reported, an appropriate balance of energy requirements together with metformin reached the metabolic target.

The effective cooperation experienced in the above mentioned studies has also worked positively in the case of the Airforce pilot affected by Type 2 diabetes (with medico-legal implications) reported by Palumbo and Marfia. Here again the multidisciplinary approach and the close cooperation between military doctors, diabetologist, cardiologist and OPs has allowed him to retain his professional skills and fly in utter safety. Marfia has shown that in a patient with well controlled type 2 diabetes, cardiovascular autonomic neuropathy may be present with an annual incidence of 1.8 %. It is possible to perform non-invasive specific tests in order to evaluate autonomic cardiovascular function.

The need for greater integration and more effective collaboration between OPs and other medical specialists, aimed at a better and more effective management of the diabetic worker (and related issues in the workplace), has been underlined and promoted by this working group since the beginning of its activities. Unfortunately, it is widely acknowledged that communication between OPs and other physicians, especially general practitioners (GPs), is often lacking or very poor, at best inadequate and sometimes also conflictual (7, 8). Actually, this sort of incommunicability would seem to involve several medical specialists. Indeed, in their article Banchini and Santelia pointed out that in Italy only 29% of diabetes centres have adopted integration/communication models or tools to cooperate and share information with GPs, while in general there is still no codified collaborative procedure between these professional figures. These considerations highlight

what is undoubtedly a weakness of the diabetic patients' (worker or not) management system which also severely limits their quality of life, as when they are prescribed identical diagnostic tests by different specialists at different times. However, at the same time the awareness of this issue offers a great opportunity since, considering the central role of GPs (in Italy each GP treats an average of over a hundred diabetics who visit him/her 8-15 times a year), the definition of integrated diagnostic and therapeutic pathways shared between GPs, OPs and diabetologists would greatly contribute to improving the well-being of the diabetic worker. In fact, data from the Lombardy Region demonstrate that where this shared and multidisciplinary approach is implemented, the results are encouraging, showing a better control of blood sugar levels and body weight.

In this regard, the main therapeutic target is to maintain optimal blood glycaemic levels in order to avoid (especially in the long run) the occurrence of the chronic diabetes-related complications which could importantly compromise the working capacity of the diabetic subject. In most cases the pharmacological treatment with insulin or oral agents, such as sulfonylureas and glinides, represents the cornerstone on which the therapeutic strategy is based. However, it should be noted that the administration of these drugs significantly increases also the risk of hypoglycaemia which, in turn, especially in the presence of particular occupational factors, can pose a serious risk to the health and safety of the diabetic worker exposing him to sudden loss of consciousness. Therefore, as well argued in two articles included in this special issue, the search and definition of effective therapeutic schemes using drugs capable of guaranteeing a good control of the glycaemic levels with minimal side effects is an urgent need. In detail, De Gennaro Colonna described the main characteristics of nutraceuticals (bioactive compounds mostly of plant origin), their beneficial effects and the potential use of these compounds in the treatment of type 2 diabetes mellitus in association with the traditional hypoglycaemic drugs. It is noteworthy to underline that the data available so far demonstrate that these drugs, in addition to improving a good hypoglycaemic control, have also important positive effects on the lipidic profile, the antioxidant status or endothelium dependent-vasodilator function.

On the other hand, it is also important to point out that maintaining an optimal glyceamic control cannot be exclusively based on pharmacological therapy but also requires other types of interventions such as diet and therapeutic education. In this context, Orsi and Resi, describing the main physio-pathological characteristics, the diagnostic criteria and the therapeutic strategies of the disease, highlighted the key role of the OPs in the prevention and management of diabetes. In fact, a modern OP is a leading expert not only in the assessment of fitness for work but also in the evaluation of work ability, the management of employee's wellness programs and the implementation of workplace health promotion (6). Considering that a healthy lifestyle is essential to allow to adequately manage the diabetic disease, the importance that the role and functions of OPs have in this area is quite evident. They individually both raise the awareness of the diabetic worker and contribute to the realization of adequate and specific health promotion campaigns in the workplace regarding the adoption of a healthy diet, increased physical activity, smoking cessation plan and maintenance of a healthy body weight. For example, the diabetes prevention and screening strategy provided through a workplace campaign by Cirla and Martinotti in a company of the advanced tertiary sector demonstrated the strategic role played by the OPs.

Last but not least, it should be noted that several research groups, starting from the evidence that some risk factors are implicated in the etiopathogenesis of cardiac and lung diseases, have recently investigated the possible association between the occurrence of diabetes and the exposure to different environmental pollutants. In this regard, Carugno carried out an interesting literature review on this topic, focusing on the exposure to air pollution (AP) and environmental noise and their possible role in increasing the risk of diabetes. This is an important topic since these factors might also be present in the workplace. Current evidence points to a possible correlation between AP and diabetes, whereas the results concerning exposure to noise and this disease are limited. Nevertheless, it is essential to consider the findings of these studies with great caution since there are still many critical aspects that need to be clarified such as for example the influence of the various pollutants included in the definition of air pollution or the role played by possible confounders factors.

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