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Antibiotic resistance: is knowledge the only driver for awareness and appropriate use of antibiotics?

D. Zaniboni[1], E. Ceretti[2], U. Gelatti[2], M. Pezzotti[3], L. Covolo[2]

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Abstract

Background. *The fight against antibiotic resistance (AR) is nowadays a world priority. Antibiotic resistance is largely associated with the overuse of antibiotics and a lack of awareness of the problem.*
Considering the large use of antibiotics in the paediatric age, the aim of this study was to investigate the knowledge and perception of antibiotic resistance in a sample of parents.
Methods. *A cross-sectional study was conducted on a sample of parents of children aged 0-14. Data on antibiotic use and awareness of antibiotic resistance were collected by a self-administrated questionnaire. The potential predictors of the antibiotic resistance awareness were evaluated using a multivariate logistic regression model.*
Results. *The questionnaire was completed by 610 parents of which 91% (n=553) used antibiotics for their children. Summarizing the answers related to antibiotic resistance knowledge and perception, 36% of parents gave a correct answers to at least 9 of 12 questions. Fever seemed to represent a reason of anxiety in parents. Using a 10-point scale, the perceived anxiety by parents was measured based on a situation when the child wakes up in the morning with a fever at 38°C and the doctor suggests to wait at least 48 hours before administering the antibiotic. Almost half of parents (49%) indicated a low degree of anxiety (1-4), 31% medium (5-6), and 20% high (7-10).*
Multivariate analysis showed that a good level of education, healthcare occupation and low grade of anxiety are associated with antibiotic resistance awareness.
Conclusions. *The awareness of antibiotic resistance is not strong. The study highlights the need to put effort on tailored education programs aimed to improve knowledge of antibiotic resistance and guide mainly anxious parents to appropriate management of disease of their children.*

Introduction

Infectious diseases have been the first determinant of mortality in humans. Especially in the 19th century tuberculosis, pneumonia, diarrhoea and diphtheria were the main causes of death in children and adults. Antibiotics have allowed a breakthrough in the treatment of infectious disease modifying morbidity and mortality of the population (1). These achievements are now at risk mainly because of the excessive and/or inappropriate use of antibiotics, which has led to antibiotic resistance (AR). According

[1] *Post-graduate School of Public Health, University of Brescia, Italy*
[2] *Department of Medical and Surgical Specialties, Radiological Sciences and Public Health. Section of Public Health and Human Sciences. University of Brescia, Italy*
[3] *Degree Course in Health Care, University of Brescia, Italy*

to the World Health Organization (WHO), there is an increasing emergency and we are observing a spread of multi-resistant bacteria. AR has already reached alarming levels in many parts of the world: it is estimated to be responsible for 25,000 deaths per year in the EU and 700,000 globally and it might cause more deaths than cancer by 2050 (2). Recent data indicate that in Italy AR remains among the highest in Europe (3). Another reason for concern is that development, manufacture and marketing of new antibiotics have significantly slowed down in the past 20 years (4). Resistant microorganisms exist in humans, animals, food and the environment. This makes AR a complex epidemiological issue (2).

Despite the burden of AR is increasingly prominent, the level of awareness of the relationship between the use of antibiotics and the development and spread of AR is still low (5, 6). Among the initiatives aimed at fighting the AR problem, the European Parliament has launched the *2017 European One Health Action Plan against Antibiotic Resistance*. This consists of a series of actions to ensure that antibiotics remain an effective tool against infectious diseases: to strengthen infection prevention and control measures, to promote the prudent use of antibiotics, to better address the role of environment, to improve the availability of antibiotics, to improve awareness and understanding of AR (2).

Paediatric population is the category of patients who receive the largest amount of prescriptions of antibiotics (7). Results of a cross-sectional survey involving Italian primary care paediatricians and parents during 2002-2003 shows that antibiotics were prescribed in 40.4% of respiratory tract infections (RTIs) and 84.2% of parents expected to receive a drug prescription (8). It was shown that parents tend to overestimated antibiotic benefits despite being aware of potential harms (9). Previous studies (10, 11) comparing parents with other adults suggested that parents are more cautious with antibiotics for their children also because aware about side effects of antibiotics. Nevertheless, it was shown that fever was the most important drive for giving antibiotics to their children. Fever is often a self-limiting symptom (12), however it continues to be a major concern for parents and often causes inappropriate management of antibiotics in their children (13, 14). In this context, the aim of the study was to investigate the knowledge, attitudes and practice of a sample of parents about the use of antibiotics in paediatric age.

Materials and methods

A cross-sectional study was carried out in Brescia, a Northern Italy town, from July to October 2017. Data were collected through a self-administered questionnaire. Participants were recruited on a voluntary basis applying two procedures: (a) online using social media (Facebook and WhatsApp) and (b) on paper in waiting rooms of vaccination clinic at the "Clinica Pediatrica - Spedali Civili di Brescia". The paper questionnaires were distributed by a healthcare assistant and completed independently by the parents while waiting for the visit. When both parents were present, only one was asked to participate. Only participants aged >18 years were recruited. Participation was voluntary and anonymous. The questionnaire was composed of 20 items addressed to parents of children in the paediatric age-group (0-14 years). Data collected were: socio-demographic characteristics of parents (six items); consumption of antibiotics by their children (one item); attitudes and behaviours related to the administration of antibiotics (six items); source of information about antibiotics and AR (three items); knowledge about use of antibiotics and adverse reactions (two items); knowledge and perception about AR (one item requesting AR definition and

one item composed by eleven statements). In particular, the knowledge and perception of AR was mostly based on the 2015 WHO questionnaire (5) and a questionnaire translated into Italian language published by Prigitano et al (6).

The answers regarding the statements on AR knowledge and perception were based on a "totally agree/agree/ poorly agree/ disagree/don't know" scale. For each statement a score=1 was given to the correct answer (totally agree/agree if statement was true and poorly agree/disagree if statement was false) and a score=0 was assigned to incorrect answers, including "don't know" option. A variable summarizing the scores of the eleven statements (Table 1) in addition to the answer on AR definition was created. Considering the quartiles, we defined as "good" AR awareness the total points of at least 9 corresponding to the 75% of 12 correct answers.

In regard to attitudes and behaviours related to the administration of antibiotics, we developed some questions taking the survey of Bert et al (7) as starting point. One item included four sub-items, particularly, four situations that could favour a pressure on parents and influence the decision to give antibiotic to children were investigated. Parents were asked to indicate a response according to a five-point Likert-scale.

Parents were asked to express a degree of anxiety on a scale of 1(=Null) to 10 (=High) at the question that represented a simulation of a usual situation: "Your child wakes up in the morning with a fever at 38°C. Your doctor/paediatrician tells you that at least 48 hours must pass before administering the antibiotic. On a scale of 1 to 10, what is your degree of anxiety for a situation like this?" The perceived anxiety was categorized as follow: low (score 1-4), medium (score 5-6), and high (score 7-10) degree of anxiety.

Before starting the survey, the questionnaire was administered to a small sample of population (20 participants not working in the health context and without a degree) to understand if the questions made sense and were comprehensible. No problems were detected.

Comparisons between groups were made by using the χ^2 test or Fisher's exact probability test. A multivariable logistic regression model was performed to assess the potential predictors of the AR awareness. The covariates to be included into the final model were selected using a stepwise forward selection process, with a univariate $p<0.05$ as the main criterion. Results were expressed as OR with 95% CI, and a two-tailed $p<0.05$ was considered significant for all analyses. Statistical analyses were performed using STATA (Stata Statistical Software: Release 14.0 College Station, TX: Stata Corporation).

Results

Of 260 questionnaires distributed at vaccination clinic, 239 (92%) were completed by parents. Of 419 respondents online, 371 (86%) completed the survey. The sample was therefore represented by 610 parents. The participants, aged 38.9±6.8 years (median 39 years), were mainly female (89.2%) and with a good level of education (high school or more, 82%). The majority of participants (78.4%) had an occupation and in particular the 9.5% worked in health field. Most of parents (57.4%) had more than one child. Ninety-six percent (n=553) of parents used antibiotics for their children.

Almost all parents (97.4%) refer to the family doctor or paediatrician as a source of information, and declared that they stop giving antibiotics to their children when all the doses of the prescription were taken, regardless of symptoms (96.4%) and reported that it is not correct to use antibiotic prescribed to other children having the same disease of their children (92.6%). Thirty-one percent of parents reported to have used sometimes the

Table 1 - Knowledge and perception of antibiotic resistance

	N (%)
Many bacteria are becoming increasingly resistant to treatment with antibiotic [a] (TRUE)	
Totally agree/Agree	457 (74.9)
Poorly agree/Disagree	62 (10.2)
I do not know	91 (14.9)
Antibiotic resistance is only a problem for people who take antibiotics regularly [a] (FALSE)	
Totally agree/Agree	202 (33.1)
Poorly agree/Disagree	265 (43.5)
I do not know	144 (23.4)
Bacteria which are resistant to antibiotics can be spread from person to person [a] (TRUE)	
Totally agree/Agree	284 (46.6)
Poorly agree/Disagree	128 (21.0)
I do not know	197 (32.4)
Infections supported by antibiotic-resistant bacteria are more dangerous than those sustained by other bacteria (TRUE)	
Totally agree/Agree	347 (56.9)
Poorly agree/Disagree	71 (11.6)
I do not know	192 (31.5)
In Italy antibiotics are used extensively in agriculture and in animal farms for human consumption [b] (TRUE)	
Totally agree/Agree	382 (62.6)
Poorly agree/Disagree	72 (11.8)
I do not know	156 (25.6)
If bacteria are resistant to antibiotics, it can be very difficult or impossible to treat infections they caused [a] (TRUE)	
Totally agree/Agree	436 (68.5)
Poorly agree/Disagree	67 (10.6)
I do not know	128 (20.9)
Antibiotics could be sold without a prescription (FALSE)	
Totally agree/Agree	29 (4.8)
Poorly agree/Disagree	522 (85.6)
I do not know	59 (9.6)
New antibiotics are produced every year (FALSE)	
Totally agree/Agree	199 (32.6)
Poorly agree/Disagree	138 (22.6)
I do not know	273 (44.8)
Antibiotic resistance is a problem that can affect me or my family [a] (TRUE)	
Totally agree/Agree	295 (48.4)
Poorly agree/Disagree	200 (32.7)
I do not know	115 (18.9)
Antibiotic resistance is a problem present in other countries but not in Italy [a] (FALSE)	
Totally agree/Agree	54 (8.9)
Poorly agree/Disagree	371 (58.6)
I do not know	198 (32.5)
There is not much people like me can do to fight antibiotic resistance [a] (FALSE)	
Totally agree/Agree	128 (19.4)
Poorly agree/Disagree	328 (51.4)
I do not know	178 (29.2)

[a] from 2015 WHO questionnaire (5); [b] from Prigitano et al.(6)

antibiotic prescribed in previous situations but for the same type of disease, without consulting the doctor.

Most of parents (72%) knew the definition of AR. As shown in Table 1, 75% of the sample was aware of the increase in the AR phenomenon. However, less than 50% of parents agreed that AR could affect them in the first person or their family, that resistant bacteria can transmit from one individual to another (47%) and were aware that AR is a problem that affects not only people who regularly take antibiotics (44%). About one third of the sample did not know that resistant bacteria can transmit from one individual to another (32%), that infections supported by antibiotic-resistant bacteria are more dangerous than those sustained by other bacteria (32%) and that AR could be present in other countries except Italy (32.5%). Nineteen percent of the sample stated that "people like me can do little to fight antibiotic resistance" and 29% did not know it. Summarizing the scores to the answers AR-related, 35.9% (n=219) of parents gave a correct answers to at least 9 questions. The AR score was used as dependent variable in the Multivariable logistic regression analysis. The results showed that a good level of education (OR=4.6), healthcare occupation (OR=2.8) and not being anxious (OR=1.8) were factors associated with knowledge and awareness of AR. Being female was inversely associated to (OR 0.5) (Table 2).

At the question "In case of fever and having antibiotic at home, when do you give the drug to your children?" the 62.6% answered "when fever begins with 40°C", 19.9% "only after doctor's visit" and the rest (17.5%) when the fever reaches 38°C.

In case the child wakes up in the morning with a fever at 38°C and the doctor suggests parents to wait at least 48 hours before administering the antibiotic, 48.8% (n=270) of parents declared that to use antibiotics indicated a low degree of anxiety, 31.3% medium, and 19.9% (n=110) high.

Compared to parents with low degree of anxiety (score 1-4), parents more anxious (score 7-10) were less educated (77.3% vs 85.9%, p=0.04). Furthermore they reported in higher percentage to have used sometimes the antibiotic prescribed in previous situations but for the same type of disease (42.7% vs 23.0%, p<0.001) and answered that they don't know whether it is correct to use antibiotic prescribed to other children having the same disease of their children (12.7% vs 4.4%, p=0.006).

Four situations that could favour a pressure in parents and influence the decision to give antibiotic to children were investigated.

Table 2 - Multivariable analysis on knowledge and perception of antibiotic resistance

		OR (CI95%)	*P value*
Age (risk increase per year)		1.0 (0.97-1.03)	NS
Gender	Male	1	
	Female	0.54 (0.29-0.98)	0.04
Educational level[a]	Low	1	
	High	4.56 (2.44-8.54)	<0.001
Healthcare job	No	1	
	Yes	2.77 (1.47-5.22)	0.002
Anxiety grade	High	1	
	Low/medium	1.81 (1.25-2.62)	0.002

[a]High level: secondary school and university degree; Low level: primary and middle school
NS: not significant

Table 3 - Percentages of parents' responses to question: "How much do the following situations influence the decision to give the antibiotic to your child?"

	Not at all N (%)	Little N (%)	Somewhat N (%)	Much N (%)	Very much N (%)
Loss of school days	355 (64.2)	109 (19.7)	67 (12.1)	16 (2.9)	6 (1.1)
Loss of workdays	322 (58.3)	121 (21.9)	74 (13.4)	30 (5.4)	6 (0.9)
Extracurricular commitments of children (e.g. sports activities)	410 (74.3)	96 (17.4)	31 (5.6)	16 (2.7)	-
Personal extracurricular commitments	412 (74.5)	94 (17.0)	26 (4.7)	20 (3.6)	1 (0.2)

Parents were asked to indicate a response according a five-point Likert-scale. The distribution of responses are shown in Table 3. All the proposed situations have little or no influence on the decision-making about antibiotic administration in the majority of cases, particularly for parents that reported low grade of anxiety compared to those who can be considered anxious (score 7-10). Respectively: "loss of school days" 91.5% vs 72.3%, $p<0.001$; "loss of working days" 86.7% vs 78.2%, $p=0.04$; "extracurricular commitments of children" 96.7% vs 90.0%, $p=0.02$ and finally "personal extracurricular commitments" 95.6% vs 90%, $p=0.055$.

Overall, 21.8% of the sample declared that antibiotics can be used to treat flu and 8.1% didn't know it. Twelve percent of participants reported that antibiotics can be used to treat chicken pox and 16.1% didn't know it. Similarly, 11.3% reported that antibiotics can be used to treat measles but 33.3% declared that they didn't know it. Only 5.7% of sample reported that antibiotic can be used for cold and 3.6% declared that they didn't know it. Considering the anxiety variable, those with a score 7-10 thought the antibiotics can be used to treat flu more than parents no/little anxious (score 1-4). Respectively flu, 29.1% vs 11.9%, $p<0.001$ and cold 10.9% vs 0.7%, $p<0.001$. No statistical difference between the two groups was found in case of chicken pox and measles.

Discussion

Overall, only 36% of the sample had a good awareness of AR. Several participants did not perceive AR as an important problem in their lives. Only half of all respondents believed that AR can put themselves or their family at risk and thought they can contribute to prevent AR. These results are in agreement with other surveys. Hawkings et al (15) showed that less than a quarter of the sample indicated that they could positively influence the situation by expecting antibiotic prescription less often. Similarly, the 2015 Wellcome Trust study (2015) (16) showed that citizens resist joining the AR cause because they feel powerless to do anything about it.

The results of this study showed the majority of parents use antibiotics correctly. However, a lack of knowledge of diseases that can be treated with antibiotics should be underlined. Twenty-two percent of parents admitted the possibility of treating flu with antibiotics. These data are partly consistent with other studies. Ivanovska et al (17) showed that 40% of parents believe that antibiotics could kill viruses. Similarly, 33% of Italian parents agree or strongly agree that antibiotics are useful for viral infections (7) and this results in bad habits and inappropriate attitudes on antibiotics administration to their children.

In addition to AR awareness, a possible predictive factor of inappropriate use of antibiotics could be anxiety. It is reasonable to believe that anxiety could influence negatively a decision-making (18, 19). Interestingly, it was shown that anxious parents about the severity of a child's illness are 30% more likely to expect an antibiotic prescription (20).

In this study we found that being less anxious was associated with AR awareness, adjusting for age, gender, education, and being a healthcare worker.

In case of fever onset at 40°C, most of parents (63%) reported to give the antibiotic to their children and only 20% declared to give the drug after medical evaluation. Faced with an usual situation, when the fever of child is not high (38°C) and the doctor suggests to wait for antibiotic administration, 20% of parents reported a high level of anxiety and 31% a medium level. The fever is often seen as a disease rather than a symptom and this result confirms the concern of parents in relation to fever management of their children (21). It is interesting to note that, in the recent report of the European Commission on AR (22), it was shown that respondents in Italy are the most likely to say they take antibiotics to treat a fever (25%) after Bulgaria (28%), and comparing 2016 to 2009, the proportions using antibiotics for a fever have increased the most in Italy (+14%).

In fact, fever represents a physiologic response and it is rarely associated with serious infection (<1%) in primary-care settings in industrialized countries (23) and, as clearly specified by Italian Pediatric Society guidelines, "in itself, the degree of fever should not be taken as an indicator of the risk for severe bacterial infection" (24). Nevertheless, it was shown that high fever is the most important drive for parents to give antibiotic to their children (11). It should be considered that fever is one of the aspects, in addition to duration of symptoms and missed school, on which parents rely to assess the severity of illness (25). In fact, parents often expect antibiotics because they believe that antibiotics treat more severe illnesses (26).

In this study we explored the possibility that the decision to give antibiotic to children could be influenced by situations that could favour a pressure on parents, leading them to take inappropriately drugs only to be sure that the children feel good. It is well known that the concern of parents can influence also the antibiotic prescribing of health professionals (27).

Possible source of stress could be the loss of school or working days and not being able to participate in a sports competition or any other important event due to the child's disease. All situations investigated seemed not to have a role in decision making but mainly in parents who reported a low level of anxiety.

The major limitation of the study is that the sample is not representative of general population. However, the results are similar to surveys carried out on other Italian samples (6, 7, 28).

Another limitation is that we did not use an objective method (i.e. standardized scale) to measure the anxiety level. We only considered the perceived anxiety based on a simulated situation and yet a situation that is not problematic from a clinical point of view, considering that we asked parents to image a child with a fever at a temperature not high (38°C). On the other hand, the percentage of parents who indicated a high level of anxiety is not negligible and this is an aspect that would probably be worth looking into.

Finally, health literacy skills were not evaluated. Anyway, even if literacy skills take into account different factors such as ethnic status, age, income etc., education is one of the main predictor of health literacy (29). In fact, we found that most of participants had a high level of education and it was the main factor strongly associated with AR awareness.

Despite we found that the behaviour of parents in finding information and

administering antibiotics to their children was quite correct, the perception of AR threat seemed not strong. In fact, child's health is the most important concern for parents, and the perception of negative consequences related to AR, projected into the future, could be overshadowed by this priority. In this regard, it may not be a case that the level of perceived anxiety of parents was inversely associated with AR awareness, taking into account education level.

Conclusion

Considering that children are the category of patients who receive the largest amount of antibiotic therapies, to strengthen the awareness regarding AR in parents is a challenge for public health. Tailored education programs are needed to improve not only knowledge and awareness about AR, but to create a means by which to instill greater reassurance in parents on disease management of their children. This goal can be achieved through an effective communication from medical professionals, given that most of the participants refer to the family doctor or paediatrician as a source of information (30). As clearly underlined in a recent review (27), in an effective communication between parents and clinicians, parental concerns need to be addressed.

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Riassunto

Resistenza agli antibiotici: la conoscenza è l'unico determinante per la consapevolezza e l'uso appropriato degli antibiotici?

Background. La lotta contro l'antibiotico-resistenza oggi è una priorità mondiale. L'antibiotico-resistenza è in gran parte associata all'abuso di antibiotici e alla mancanza di consapevolezza del problema. Considerato il grande utilizzo di antibiotici in età pediatrica, lo scopo di questo studio era indagare la conoscenza e la percezione dell'antibiotico-resistenza in un campione di genitori.

Materiali e metodi. È stato condotto uno studio trasversale su un campione di genitori di bambini di età compresa tra 0 e 14 anni. I dati sull'uso di antibiotici e la consapevolezza dell'antibiotico-resistenza sono stati raccolti attraverso un questionario auto-somministrato. I potenziali fattori associati alla consapevolezza dell'antibiotico-resistenza sono stati valutati utilizzando un modello di regressione logistica multivariata.

Risultati. Il questionario è stato completato da 610 genitori di cui il 91% (n = 553) ha usato antibiotici per i propri figli. Riassumendo le risposte relative alla conoscenza e alla percezione dell'antibiotico-resistenza, il 36% dei genitori ha dato una risposta corretta ad almeno 9 domande su 12. La febbre sembrava rappresentare un motivo di ansia nei genitori. Usando una scala da 1 a 10, è stato misurato il livello di ansia generato da una ipotetica situazione in cui il bambino si sveglia al mattino con la febbre a 38 °C e il medico suggerisce di attendere almeno 48 ore prima di somministrare l'antibiotico. Quasi la metà dei genitori (49%) ha indicato un basso livello di ansia (1-4), il 31% medio (5-6) e il 20% alto (7-10).

L'analisi multivariata ha mostrato che un buon livello di istruzione, l'occupazione in ambito sanitario e un basso grado di ansia sono associati alla consapevolezza dell'antibiotico-resistenza.

Conclusioni. Non è stata riscontrata una forte consapevolezza dell' antibiotico-resistenza. Lo studio evidenzia la necessità di porre maggior impegno in programmi educativi mirati volti a migliorare la conoscenza dell'AR e guidare i genitori maggiormente ansiosi a gestire in modo adeguato la malattia dei propri figli.

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Corresponding author: Dr. Loredana Covolo, Unit of Hygiene, Epidemiology and Public Health, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Italy
e-mail: loredana.covolo@unibs.it