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Original article

Prevention of acute GI disturbances with a functional food formulation designed to support and maintain intestinal barrier function during sports performance

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Summary. Gastrointestinal disturbances are very frequent among athletes undergoing strenuous and continuous training and an endurance race. We tested a mix of nutrients and antioxidants for preventing GI disturbances and dropouts at the "Tor des Geantes" ultratrail competition (330 km run). Athlets used the mix during training and competition and showed benefits, including more power and resistance and better gastrointestinal health. Even if not all of athletes took the mix on a regular basis during the race, the number of athletes pulling out of the race due to gastrointestinal problems was 4.2% (1/24) in the treatment group compared to 11.3% (6/52) in the control group.

Key words: gastrointestinal disturbances, intestinal ischaemia, strenuous physical exercise, sport diet, nutrition

Background

The prevalence of gastrointestinal disturbances (GIDs) during sports practice for athletes, such as long-distance runners, triathletes, and athletes involved in other types of wearing or long-lasting exercise is high (1-4). Sports requiring a short but very strenuous exertion can lead to diverse intestinal disturbances such as gastroesophageal reflux GER (2,3,5,6).

Marathon runners, for example, have long been studied by sport clinicians due to the frequency with which these athletes report disturbances related to their sports practice, with a prevalence of up to 50% (7,8). While some studies are focused on occult bleeding or bleeding which is sometimes overt, other studies investigated different symptoms and disturbances, like those in Table 1. Although in some athletes symptoms are also present during training, those symptoms tend to increase in frequency and severity during competition due to the longer length and higher intensity of the physical stress that the athletes are exposed to.

Among athletes playing long-range strenuous sports, dehydration and gastric emptying (GE) delay are the most frequent causes for gastrointestinal (GI) complaints, and gut ischaemia is the main cause for their nausea, vomiting, abdominal pain, and diarrhea (with blood traces) (9).

The cause for these changes in the normal physiology of the gastrointestinal tract is mainly due to reduced blood circulation (and consequently oxygen and nutrients) to the internal organs because of higher energy requirements by muscles, induced by athletic effort. In humans, during maximal exercise, blood flow to the gut is reduced by about 80% (7,10).

This condition of relative ischaemia is the most probable cause for a well-documented alteration of in-

Table 1. Various gastrointestinal symptoms during/after strenuous and continuous exercise

Upper GI Tract	Lower GI Tract
Gastric emptying (GE) delay	Abdominal pain
Gastroesophageal reflux (GER)	Bloating/borborygmus/ gas problems
Heartburn	Diarrhea
Dizziness/nausea/vomiting	Blood in the stools
Eructation	Stitch in right/left side

testinal permeability, inducing severe metabolic stress in athletes (11,12).

It is reasonable to think that acute GI symptoms can be more frequent and severe in athletes whose intestinal function is less stable, even in the absence of intestinal diseases.

A serious gut underperfusion often leads to shock-induced mucosal damage associated with invasion by Gram-negative intestinal bacteria and/or their constituents (endotoxins) into the blood circulation.

In a specific clinical trial, elevated plasma endotoxin concentrations were found in 81% of ultramarathoners (90 km-race), with 2% of them exhibiting extremely high values (13).

Additionally, any factors limiting sweating, such as a hot and humid environment and/or dehydration, has profound effects on muscle glycogen depletion and increases the risk for heatstroke.

Apart from mucosal damage and enhanced permeability, a serious gut underperfusion causes blood loss, microbiota invasion (endotoxemia) and food-born allergen absorption (with anaphylaxis) (9).

Anaphylaxis is observed during or soon after exercise, more often when the latter is preceded by the intake of food-born allergen (14).

In 2000, A.E. Jeukendrup hypothesized that the gastrointestinal disturbances (GIDs) observed during and after ultra-endurance exercise could be related to transition(passage or absorption) of endotoxins [lipopolysaccharide (LPS)] into circulation in association with cytokine production (15).

In that study, performed after a race involving triathletes, an elevation of the reactive C protein (CRP) was found.

The author concluded that LPS does enter into circulation after an ultra-endurance exercise, and may, together with muscle damage, be responsible for an increased cytokine response, and hence GI complaints in these athletes (15).

GI tract disturbances last days or even weeks in athletes undergoing strenuous and continuous physical stress, albeit running (even long distances) may actually have a therapeutical effect on mild gastrointestinal problems and IBS (16).

Nutritional practices can correlate with GI complaints. Athletes are generally warned against the risks of overhydration, and an excessive use of beverages with a very high osmolarity is not recommended (17).

Gastric emptying (GE) is thought to be negatively affected when the intensity of exercise exceeds 70% of VO2max, and this has been significantly associated with increased exercise-induced nausea (18).

The study

This study has been designed to ascertain if a mix of nutrients formulated to maintain and restore balance of the gastrointestinal barrier can:

a) (Primary objective) bring general and gastrointestinal benefits to athletes who train for endurance races;
b) (Secondary objective) reduce the gastrointestinal effects induced by physical stress, and the consequent pulling out of the race, compared to athletes not following the treatment.

Achievement of objectives has been measured through 3 questionnaires specifically formulated and administered based on this time-frame:

- 4 weeks before the endurance race (Form 1);
- At the end of training period, just before the race (Form 2);
- At the end of the race (Form 3, and Form 3bis as a control).

Fifty out of 705 athletes were enrolled at "Tor Des Géants 2013." Joining was voluntary, and there was no selection criteria. As a control (for Objective 2), a questionnaire (Form 3bis) administered by organizers of the race ("VDA Trailers"), and sent to all athletes has been used. In this questionnaire, the reason for pulling out of the race was asked.

The 50 enrolled athletes followed a supplementary plan with Nutrimonium at a dose of one portion/day starting 30 days before the race. The same dose was also used during the race. No changes to the athletes' diet was proposed. During the race, athletes ate/drank the following: water; food; hydrating substances (with the exception of those substances that have an effect on the gut, like probiotics and prebiotics). Some athletes took supplements and nonsteroidal anti-inflammatory drugs (NSAIDs).

The following *general nutritional indications* were provided to both groups throughout the race:

- During strenuous exercise, it is recommended to

drink 0.5 L/hour of water or low-osmolarity sports drink.
- It is recommended to drink beverages containing sodium and carbohydrate (CHO) (<10%).
- Glucose and fructose sources should be consumed to increase exogenous oxidation of CHO (19).

Tested formulation: Nutrimonium®

The tested product is a base functional food containing nutrients with the composition reported in Table 2.

The product is in the form of a powder to be reconstituted with water. The daily dose used in the study is equal to one portion, i.e. 11 grams of powder (1 sachet). Nutrimonium provides no calorie intake. It is sweetened with sugars from *Stevia rebaudiana*.

Materials and Methods

The race: the "Tor Des Géants" (TdG)

The "Tor Des Géants" is an ultra trail race of 330 kilometers, and a positive difference in altitude of 24,000 meters. This race requires continuous physical exertion for most of the 5-6 days (and nights) that are necessary to complete the course. Athletes have to spend their time doing physical activity for most of the time, thus reducing to a minimum sleep and time for personal care and feeding. 705 athletes started the race. The first athlete completed the course in 75 hours. Maximum expected time was 150 hours. Seven "life bases" and many supply points were available along the course, where food and beverages could be found.

Samples and data observed with 1st questionnaire

50 healthy adult athletes were enrolled, 44 men and 6 women. During the first 2 weeks of training, 3 athletes had to interrupt it and withdraw from the study and pull out of the race due to injuries (n. 2), and articular problems (n. 1).

Thus, in the first part of the study, the first questionnaire has been filled in by 47 athletes, with an average weight of 72.1 Kg, and a BMI of 23.15, which is higher, on average, compared to shorter races like marathons.

Table 2. Nutrimonium® composition (per 1 sachet/11 g - RI*)

Oligofructose-enriched inulin	1500 mg
Lactobacillus acidophilus NCFM (9 billion alive and viable bacteria)	
Bifidobacterium lactis Bi-07 (1 billion alive and viable bacteria)	
L-Glutamine	1500 mg
Vitamin A	600 µg - 75%
Vitamin B1	0,825 mg - 75%
Vitamin B2	1.05 mg - 75%
Vitamin B3	12 mg - 75%
Vitamin B5	4.5 mg - 75%
Vitamin B6	1.05 mg - 75%
Vitamin B12	1.88 µg - 75%
Vitamin C	60 mg - 75%
Vitamin D	7.50 µg - 150%
Vitamin E	9 mg - 75%
Biotin	37.5 µg - 75%
Folic acid	100 µg - 50%
Calcium bisglycinate	200 mg - 25%
Chromium picolinate	30 µg - 75%
Iodine	112.5 µg - 75%
Magnesium bisglycinate	93.75 mg - 25%
Manganese citrate	1.50 mg - 75%
Molybdenum	37.5 µg - 75%
Selenium (selenomethionine)	41.25 µg - 75%
Zinc citrate	7.50 mg - 75%
Curcume extract (95% of which is curcumin)	30 mg
Alpha lipoic acid	75 mg
Green tea extract (30% of which are polyphenols)	30 mg

**%RI = % Reference Intake (EU)*
In admixture with: maltodextrins, flavors, citric acid, silicon dioxide, potassium chloride, xanthane, cellulose gum, carrageenin, steviol glycosides

87% of the athletes reported regular bowel movements, and only 6.4% reported frequent diarrhea, or constipation (4.3%). Symptoms like abdominal swelling were reported by 28.3% of cases.

91% of athletes reported experiencing gastrointestinal disturbances during races in the last 2 years, and 65.9% of athletes said they had to pull out of a race on at least one occasion due to these problems.

Athletes taking part in the study followed no particular diet in 81.1% of cases.

4 athletes followed an hyperproteic diet; 2 athletes followed a gluten-free diet; and 1 athlete followed a vegetarian diet. 78.7% of athletes stated they used supplements while training. Among them, mineral salts (83%). Supplement use was higher during the race (83.0%), mainly for mineral salts and protein bars.

4.2% of athletes said they took drugs before the race to prevent gastrointestinal disturbances.

Global judgment on quality of life was very good (these are healthy individuals), with values between 6 and 10 (mean: 8.1).

After training: results of 2nd questionnaire

After 30 days, and soon before the race, the data collected through the 2nd questionnaire, administered at the end of the 30-day treatment period with Nutrimonium, can be observed.

The mean weight of the athletes changed to 70.9 Kg, with a mean reduction of 1.2 Kg.

Athletes stating to have regular bowel movements changed to 95.7% compared to 87.0% in the previous month (Fig. 1).

Frequency of abdominal swelling lowered from 28.3% to 17.0% (Fig. 2). Still 4 athletes reported frequent diarrhea (8.5%).

74.5% of athletes stated they did not have gastrointestinal disturbances during training.

Compliance to the treatment with Nutrimonium was very good. 91.3% of athletes took the product as suggested by the protocol.

51.1% of athletes noticed benefits compared to previous month (Fig. 4).

The most reported benefits were increased resistance (8/47) and better intestinal health (5/47). Other 5 athletes said they had more than one benefit.

Nutrimonium was excellently tolerated in 85.1% of cases without unwanted effects. 2 athletes reported "abdominal swelling" as an unwanted effect; 1 athlete reported "nausea".

At the end of training period, 14,9% of athletes suspended treatment due to the absence of benefits (n=3), or because of unwanted effects (n=2).

At the end of training period, judgment on quality of life increased to 8.4, i.e. 3.7% more than at the start of the treatment.

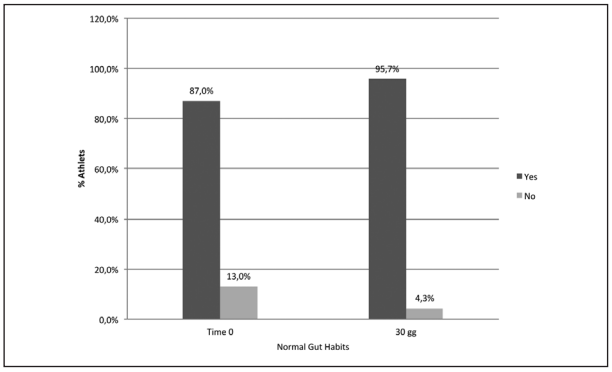

Figure 1. Gut habits regularity

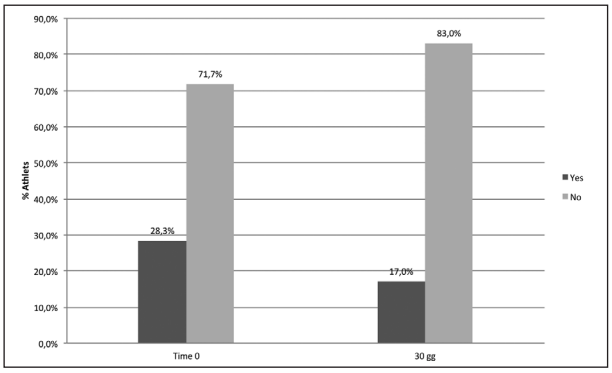

Figure 2. Bloating

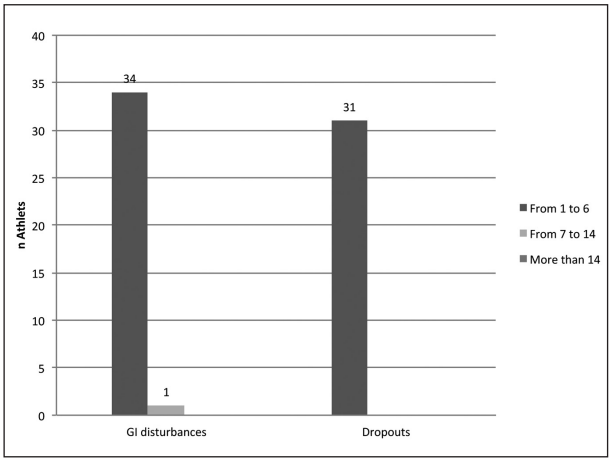

Figure 3. GI disturbances and dropouts due to GI problems in competitions of previous 2 years

The race: results of 3rd questionnaire

Taking Nutrimonium during the race was practically difficult. Runners could access their bags only during pauses at the "life bases" located along the course at a distance of 40-50 Km apart.

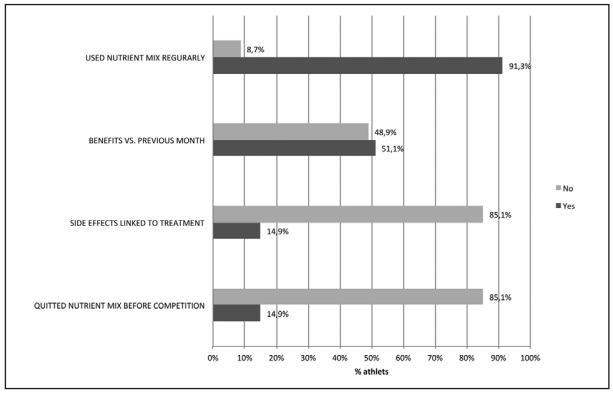

Figure 4. Benefits and compliance

Despite these difficulties, 36 out of 47 enrolled athletes took the product even during the race.

At the race's end, the mean weight of the athletes was 68.7 Kg, with a mean reduction of 2.2 Kg (3.1%). Three athletes reported they had severe gastrointestinal disturbances during the race, which led to pulling out of the race in one case.

21.4% of athletes had some gastrointestinal problem during the competition (Fig. 5) such as diarrhea, abdominal pain, abdominal swelling, or slowdown of digestion during the race.

Use of NSAID's or pain killers during the competition is very frequent (54.8%) to fight joint pain arising from overstimulation of the muscoloscheletal apparatus.

Joint pain/articular problems was the first cause of pull out from previous edition of competition: Tor des Geants 2013.

58.5% of athletes taking Nutrimonium during the race noticed benefits compared to previous races. In particular, more power and resistance (n = 9); better gastrointestinal health, or less gastrointestinal symptoms (n=9). Six athletes said they had more than one benefit.

Nutrimonium was also well tolerated during the race by 90.2% of athletes. Two cases of unwanted effects (one case of gastric pyrosis and one case of abdominal swelling) were reported.

In the treatment group, 23 athletes (48.9%) completed the race, and 24 (51.1%) pulled out.

The most common cause for quitting were articular problems (n =13). Only one athlete's quitting was due to gastrointestinal disturbances.

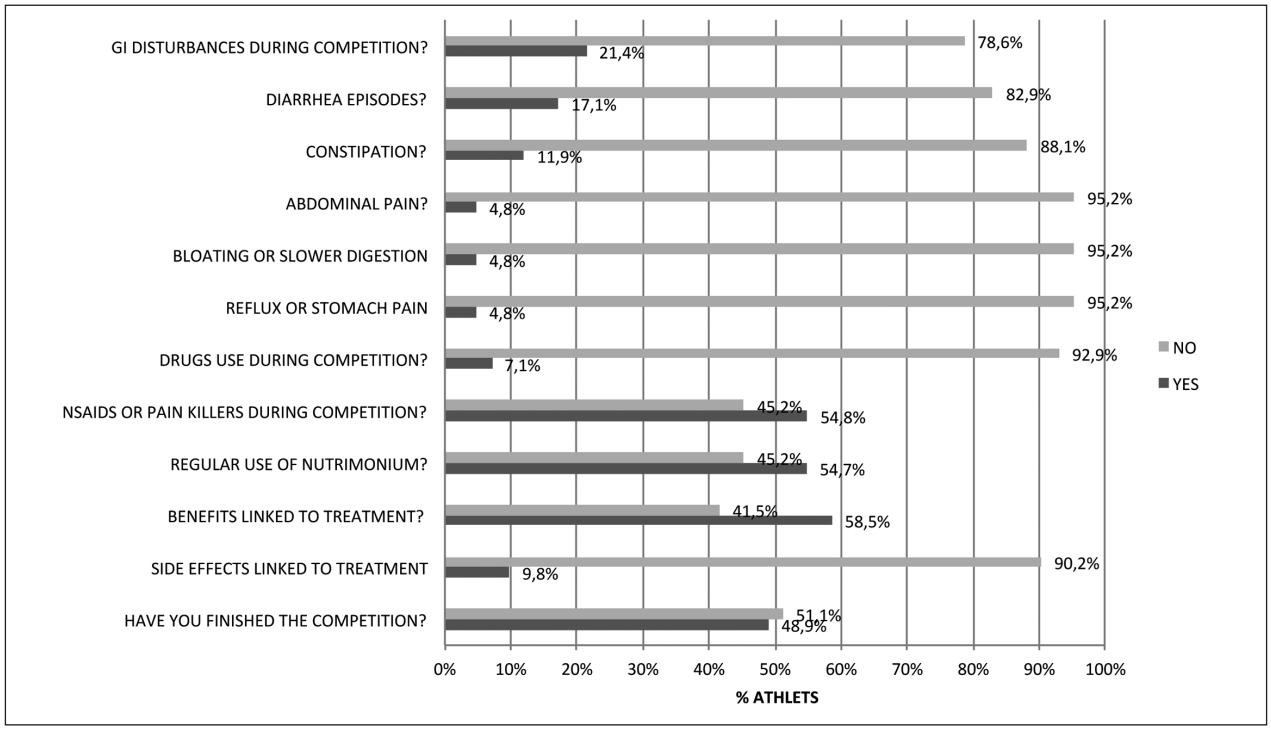

Figure 5. Competitions

The organizers' control questionnaire (Form 3bis)

The organizers of the race sent a multiple-choice technical questionnaire to all participants. Questions included the cause for pulling out of the race.

140 Italian athletes sent their answers.

52 of these athletes were forced to quit, 6 of them because of gastrointestinal problems (11.5%).

Discussion

Gastrointestinal disturbances (GIDs) are very common during endurance races, especially in running races. Although they are not the first cause for quitting the race, GIDs entail discomfort and effects leading to a reduction in performance and deprive one of the pleasure of completing the race. The hypothesis supporting this work is related to a likely change in intestinal wall function, which is induced by intermittent blood perfusion of digestive tract. Our aim was not to interfere with this specific aspect, but rather to reduce its effects through a mix of components with a synergistic function.

As it is a complex product with more significant chronic effects than acute ones, it was necessary to check for the occurrence of any changes in intestinal function during the previous weeks, as well. Bowel movement regularity is certainly one of the most significant markers. Checking for improvements (as a percentage) in subjects complaining of disturbances proves the positive effect of the product.

The mean compliance to protocol was high. We believe that if athletes hadn't had good sensations, dropout would have been higher. The absence of adverse effects should be noted, both chronically and during the race. We consider the reported good sensations to be significant.

Of particular interest are the reasons for which treated subjects pulled out of the race: Only 1 subject reported GIDs as the cause, while GIDs were definitely more frequent in control subjects.

Weight loss after ultra-endurance exertion was considered acceptable if less or equal to 2% (20). Weight loss is due to a reduced water content in almost all cases. However, we must also consider that the majority of data in the literature does not relate to races with a length equivalent to the TdG. An observational work on a 100-mile race reports data very similar to ours (21). It is also likely that a loss of cellular mass occurs (both in adipose and muscle tissues) over several days of race. Moreover, data exists concerning the likelihood that water content increases due to edemas formed (22). Given this preamble, the evaluation of weight loss is very complex. No data on body weight can be discussed as we did not monitor the volunteers' caloric intake.

Rules regarding the physiology of exercise cannot be changed, nor did we want to do that. Muscles need blood, and enteric circulation provides it. However, we must find a way so that those whose sport objectives are very high can find ways to train and adapt every organ to the type of exercise they practice. Feeling good after the practice of movement, even if very intense, still remains one of the main goals of promoting physical exercise, and also a duty for every instructor.

Evaluation of energy, water and mineral consumption during the race

The race called "Tor Des Géants" can be considered one of the hardest races in the world as it requires intense exertion for more than 21 hours per day for 3-5 days.

We estimated that athletes spent about 10,000-12,000 Kilocalories per day. In these conditions, the water-salt balance can also be a determining factor, and important problems may arise both in the case of dehydration and hyperhydration.

The dramatic reduction in sleeping hours leads to alterations in attention in many athletes, which often can result in hallucinations.

Possible insights

This study did not allow for data collection regarding the role of diet versus general state of health, particularly as a possible determining factor for the gastrointestinal disturbances mentioned above. In the future, it would be useful to compare a group with controlled feeding and supplements versus a control free-feeding group with or without supplements.

Conclusions

The problem of preventing gastrointestinal disturbances is addressed for the first time through supplements with a mix of nutrients in athletes undergoing strenuous and continuous training and an endurance race.

51.1% of the athletes who followed the treatment reported one or more benefits, including more power and resistance and better gastrointestinal health. At the end of the training period, judgment on the quality of life increased to 8.4, i.e. 3.7% more compared to previous month.

Bowel movement regularity increased from 87.0% to 95.7%.

Even if not all of athletes took Nutrimonium on a regular basis during the race, the number of athletes pulling out of the race due to gastrointestinal problems was 4.2% (1/24) in the treatment group compared to 11.3% (6/52) in the control group. Nutrimonium was well tolerated both during training (85.1% of athletes) and the race (90.2%).

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