Use of acetaminophen in young subelite athletes

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**Aim.** The purpose of the present investigation was to look for other drugs besides doping substances in the urine of subelite athletes submitted to heavy training.

**Methods.** One hundred and forty-one young subelite athletes (in sprint, cycling, middle distance running and handball) were included in the study, with a control group of 89 high school pupils. Drugs were researched by high performance liquid chromatography using a diode array detector.

**Results.** Among the 212 subjects who agreed to give a urine sample, acetaminophen was detected: 9.5% for the subelite athletes versus 1.3% for the control group with a greater difference for sprint and cycling training (26.7% and 20%, respectively). Acetaminophen is used to treat both acute and chronic pains. It relieves pain by elevating the pain threshold.

**Conclusion.** The use of acetaminophen has to be taken into account by medical staff, trainers and educators.

**Keywords:** Analgesic - Urine - Detection - Performance - Sport.

Training for sport in general and for endurance particularly requires long term efforts and can produce psychological and physical pains in adolescent athletes. Physical pain is the sign that the body needs temporarily to stop or reduce activity. Another way is to consume drugs (medicine or illicit drug) to stop the pain and then continue practicing at the same level.

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This behavior can be the beginning of a complex mechanism which can lead to addiction.

Most athletes will use over-the-counter pain relievers at some time. These drugs, in fact, are some of the most widely used and least understood of all drugs. They are reliable and effective when used appropriately for moderate pain relief. For example, acetaminophen has been used in soft-tissue injury, in the ilio-tibial band friction syndrome. Wagner et al. have shown that acetaminophen was among the most commonly prescribed drugs at the Tenth Pan American Games. Nevertheless, little data dealing with this practice in the young is available and in previously published papers, evaluation of such consumption is based on questioning or analysis of prescriptions.

Acetaminophen is used to treat both acute and chronic pains. It relieves pain by elevating the pain threshold, that is, by requiring a greater amount of pain to develop before it is felt by a person, and this drug reduces fever through its action on the heat-regulating center of the brain. It is probably the single most effective non-
prescription medication for lower back pain and has the fewest side effects. Acetaminophen was approved by the FDA in 1951, and is used for the relief of fever as well as aches and pains associated with many conditions. Acetaminophen relieves pain in mild arthritis but has no effect on the underlying inflammation process, redness and swelling of the joints. If the pain is not due to inflammation, acetaminophen is as effective as aspirin, and is as effective as the non-steroidal anti-inflammatory drug ibuprofen in relieving the pain of osteoarthritis of the knee. Perhaps the most notable property is that, unlike aspirin, acetaminophen does not have peripheral anti-inflammatory effects or blood-thinning properties. It is used to relieve mild to moderate pain or to reduce fevers. Acetaminophen is also known as paracetamol and N-acetyl-p-aminophenol (APAP). It is found in France as 1 000-mg and 500 mg immediate-release tablets. It can be found as liquid suspension, coated caplets, gels, gels, geltabs, and suppositories. Furthermore, acetaminophen is to be found as a component of combination drugs such as propoxyphene-acetaminophen (e.g. Di-analvic®), or codeine-acetaminophen (e.g. Paracétamol®, codeine). The maximum daily dose of APAP is 4 g in adults and 60 mg·kg⁻¹ in children. The toxic dose of APAP after a single acute ingestion is 150 mg·kg⁻¹ of approximately 7 g in adults, although at-risk dose hepatotoxicity may be lower in persons with alcoholism and other susceptible individuals. When dosing recommendations are followed, the risk of hepatotoxicity is extremely small.

In this study carried out on subelite adolescent athletes in the North-Pas-de-Calais region of France, we sought numerous licit and illicit substances and during urinary screening, acetaminophen was found and no other drugs were detected in these analytical conditions. Taking into account the popularity of this drug, we have chosen to only focus on this manuscript on acetaminophen consumption. The frequency is reported in this paper, the purpose being to examine the influence of the type of training sport practiced on this acetaminophen consumption.

Materials and methods

Participants

One hundred and forty-one young subelite athletes were included in this study (19.3±2.8 years, 63.5±9.9 kg, 174.2±8.9 cm). This population was made up of 86 men and 55 women. They were divided into groups of 35 endurance-trained runners, 15 sprinters, 56 handball and 15 cyclists. These athletes were chosen to represent endurance activity (runners, cyclists), speed (sprinters), and combined (handball players). All these athletes trained between 3 and 5 times per week and had practiced their respective activity for at least 8 years. The number of athletes is different according to sport and level practice in the North-Pas-de-Calais regions of France. The last group was composed of only males because no female section existed in this field. The control group consisted of 89 young adolescents (42 males and 47 females). Subjects in the control group were selected from their school or university and identified as individuals who did not engage in any regular exercise during their daily routine. They only practiced physical education at school (less than 4 hours per week). This study received the ethical committee approval statement on 4th April, 2000 (CP 00/10) and written informed consent was obtained from each participant.

Exercise protocol

The study was carried out during the middle of the athletic season (January - March). During this period, athletes trained 3-5 times a week, to be able to compete each week for the handball players or to compete at the end of this period for the runners, cyclists, and sprinters. Control subjects were controlled in the same period.

Urinary sampling

Urine was collected and transferred to the toxicological Laboratory and analyzed to find numerous substances.

To 1 mL of urine was added 0.5 mL acetate 1M buffer pH 3.5. The mixture was vortexed for 3 min. Then 3 mL of an extracting solvent (dichloromethane, dioxyle ether, hexane and isooamylic alcohol 3:5:2:0.05 V/V) was added and the mixture vortexed for 3 min; 0.5 mL saturated borate buffer pH 9 was added to another 1 mL of urine, after vortexing for 3 min, the mixture was extracted in the same conditions, as described above. The two organic phases were pooled and the solvent was evaporated to dryness under nitrogen. To the dry residue was added 100 μL of a mixture of acetonitrile-phosphate buffer 5 mM pH 3.6 (50:50 V/V) and 20 μL of the solution was
injected onto a column Symmetry C8 (250 mm×4.6 mm) (Waters®, France) equipped with millennium software (HPLC Alliance, Waters®, France). The column was eluted by a mobile phase: acetonitrile-phosphate buffer 50:50 V/V using a eluting gradient. The analytical method is sensitive and specific and the detection of acetaminophen is easy by absorption at 280 nm. Acetaminophen was identified by retention time and absorbance characteristics. The detection limit was 1 mg/L and the coefficient of variation was below 10% at a concentration of 5 mg/L⁻¹.

Statistical analysis

Ages, weights and sizes are presented as mean ± standard deviation values. Statistical analyses were performed using the RxC x² test ¹⁰ to analyze frequencies of positive subjects in different groups.

Results

Out of the 230 subjects who participated in this study, 212 agreed to give a urine sample. Anthropometric data on these subjects is presented in Table I. This study shows an intake of acetaminophen (Table II) which is more frequent in young subelite athletes (13/137), than in controls (1/75); 9.5% versus 1.3%, respectively, significant at the P<0.02 level.

Detected concentrations range from 1.6 to 132 mg/L. These values cannot be related to the ingested doses because of the variability in absorption, metabolism by different cytochromes P-450 and elimination. Acetaminophen is generally rapidly absorbed and metabolized, its half-life being about 2 hours.

As for training in different sports, the results show that two groups can be distinguished, the former including athletes from sprint (4/15) and cycling (3/15) training with 10% and 20%, respectively and is significantly different (P=0.05) from the second group: handball (3/53) and middle distance running (3/54) with 5.7% and 5.5%, respectively.

As regards possible differences between males and females, according to three sports practices, no significant difference was determined. For the male group, no significant difference could be established between different sports practice, but for the female group, a significant difference (P=0.05) was found between the sprint group (37.3%) and the other two groups (6.9% for handball and 6.2% for middle distance running).

Moreover, for the female group, these differences were maintained when compared to the control group (2.6%).

Discussion and conclusions

In this group of young athletes or control subjects, acetaminophen was detected. Intake appears to be greater and more frequent in young subelite athletes than in controls, with more marked differences for sprint and cycling. The need for continuous results during training sessions could explain the higher frequency of acetaminophen intake in the sprint group. For cycling, the same reason could be suggested, and possibly linked to the fact that these athletes were the youngest.

Athletes may consume acetaminophen for two purposes. First, to decrease the pain associated with a previous training period, and secondly to prevent further pain which could be the result of current and future intense training sessions. This appears as a false idea since a recent paper by Barlas et al.¹¹ showed the absence of any beneficial effect from medication with acetaminophen (1 000 mg) in the management of delayed-onset muscle soreness.

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<th>Table I. — Age, weight and size values (mean±standard deviation) of subelite athletes according to sport.</th>
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M: male; F: female.

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<th>Table II. — Detection of acetaminophen according to different sports and control groups.</th>
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M: male; F: female.
This drug is often automedication taken by sportive and non-sportive people. Use of acetaminophen can have important consequences.9 In acute overdose or when maximum daily dose is exceeded over a prolonged period, the normal metabolic pathways become saturated. Excess APAP is then metabolized in the liver via cytochrome P-450 enzymes to a toxic metabolite. This must be taken into account by medical staff, trainers and educators to give information on the use and severe adverse effects of this drug, particularly hepatotoxicity.12

Compared to a survey, our work presents some advantages: the intake of acetaminophen was directly established as it was not through simple questioning, and numerous other compounds were sought. Nevertheless, the athletes were aware of the analytical protocol. Consequently, some athletes may have chosen not to participate in this study because they consumed or had consumed medicine or illicit drugs. The percentage of acetaminophen consumers would be in this case underestimated in the hypothesis that illicit drug consumers also used acetaminophen.

Further investigations could be launched to specify whether acetaminophen consumption by athletes is a sporadic habit or a chronic one (i.e., young athletes could be in the habit of taking drugs to continue their practice).

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References