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Brief Communication

Effects of a single low-dose acetaminophen on body temperature and running performance in the heat: a pilot project

Martin Burtscher[1,2], Hannes Gatterer[1], Marc Philippe[1], Philipp Krüsmann[1], Stefanie Kernbeiss[1], Veronica Frontull[1], Philipp Kofler[1,3]

[1]Department of Sport Science, Medical Section, University of Innsbruck, Innsbruck, Austria; [2]Austrian Society for Mountain and High-Altitude Medicine, Innsbruck, Austria; [3]Centre of Technology of Ski and Alpine Sports, Innsbruck, Austria

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Abstract: Purpose: To examine the effects of a single low-dose (500 mg) acetaminophen on body temperature and running performance in the heat (30 °C). Methods: This is a randomized, cross-over pilot study performed in a climatic chamber at the Department of Sport Science of the University of Innsbruck. Seven male sport students (age, 25.9 ± 2.3 years; VO_2max, 67.3 ± 7.1 mL/min/kg) participated in the study. Each participant performed two prolonged exercise tests at a constant intensity on a treadmill at a temperature of 30 °C at an individual intensity corresponding to 70 % VO_2max. Two hours before exercising participants were randomly assigned to receive acetaminophen (500 mg) or placebo and performed the same test 2 weeks later with reverse pre-treatment. Results: After 20 min of running in the heat core temperature increase was less under acetaminophen (P = 0.004) and heart rates were higher (P = 0.02) compared to placebo. At the end of exercise neither running time nor body temperature nor ratings of perceived exertion differed between groups. Conclusion: Although the increase in core temperature was slightly reduced by acetaminophen after 20 minutes of running in the heat running performance remained unaffected after pre-treatment with a single low-dose of acetaminophen.

Keywords: Acetaminophen, heat, running, performance, thermoregulation

Introduction

Over-the-counter analgesics like acetaminophen (paracetamol) are commonly used by athletes primarily with the intention to reduce musculoskeletal pain [1]. Acetaminophen may be considered as selective cyclooxygenase-2 (COX-2) inhibitor without the antiplatelet and detrimental effects on gastrointestinal mucosa of COX-1 inhibition [2]. Acetaminophen is thought to elevate the pain threshold and exercise tolerance [3] but has also potent antipyretic actions and might therefore modify exercise thermoregulation and exercise tolerance in the heat as demonstrated with COX-2 inhibition [4]. Despite the common use of low-dose acetaminophen in sports, its effects on performance in the heat has not been studied. Based on its antipyretic and analgesic effects we hypothesized that pre-treatment with a single low-dose acetaminophen would improve exercise performance in the heat by lowering heat strain and possibly also by increasing the pain threshold as well.

Methods

Subjects and design

Seven healthy and well trained male sport students were subjected twice, in a double-blind cross-over fashion, to prolonged treadmill running in the heat either under acetaminophen or placebo. Characteristics of the participants are shown in **Table 1**. All participants provided written informed consent and the study was approved by the institutional ethical review board.

Table 1. Characteristics of study participants (N = 7)

Variable	Mean	SD
Age (years)	25.9	(2.3)
Body mass (kg)	70.3	(7.8)
Height (cm)	177.4	(8.6)
HRmax (bpm)	190.1	(11.7)
VO_2max (mL/min/kg)	67.3	(7.1)
VEmax (L/min)	162.1	(25.8)

HRmax: maximal heart rate, VO_2max: maximal oxygen uptake, VEmax: maximal minute ventilation.

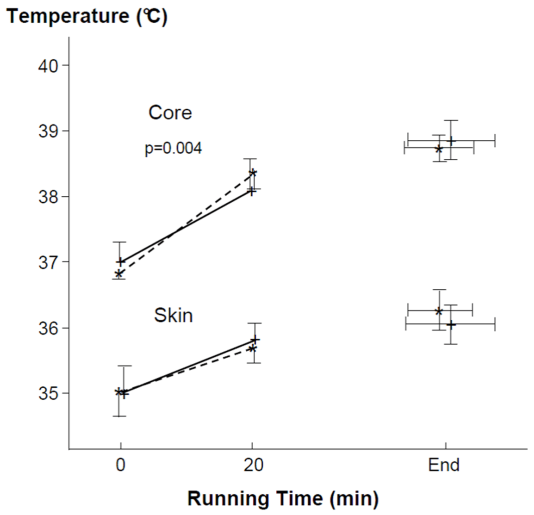

Figure 1. Core and skin temperatures at the beginning, after 20 minutes and at the end of exercising at 70 % VO_2max in the heat (30 °C) with acetaminophen (crosses and solid lines) or placebo (stars and dashed lines). Data are presented as means (SEM).

Routine examination and maximal spiro-ergometry

After routine examination subjects performed an incremental exercise test to exhaustion on a treadmill as described previously [5]. Gas exchange was measured by an open-circuit spirometric system (Oxycon mobile, Visasys Healthcare, Germany). Maximal oxygen uptake (VO_2max) was defined as the highest 30-s VO_2 average measured during incremental exercise.

Prolonged exercise testing and pre-treatment

Each participant performed two prolonged exercise tests at a constant intensity on a treadmill at a temperature of 30 °C and 50% relative humidity at an individual intensity corresponding to 70 % VO_2max. Participants wore usual running clothing (T-shirt and shorts) and were randomly assigned in a double-blind fashion to receive acetaminophen (500 mg) or identical-looking placebo 2 hours before the first exercise test. The delay of 2 hours was chosen based on the observation that maximal plasma concentration appears about 1.5 hours after acetaminophen administration in a non-fasted state [6]. About 2 weeks later subjects performed the same exercise test with reverse pre-treatment. Exercise was stopped whenever subjects wanted to do or because of complaints, when the supervising doctor decided to stop or when the core temperature increased above 39 °C.

Measurements

Body mass was exactly determined before and after exercise testing without clothing. Heart rate (HR) was measured continuously, VO_2 and the respiratory exchange ratio (RER), blood pressure, blood lactate, skin temperatures (Tskin) by infrared thermometry and core temperatures (Tcore) by infrared tympanometry and scoring of perceived exertion (RPE) [7] also used as an indirect measure of pain perception [3], were determined before starting, after 20 minutes of running and at the end of the tests. Mean weighted Tskin was calculated as: Tskin = 0.28Tsubscapular + 0.14Tforearm + 0.08Ttriceps + 0.22Tcalf + 0.28Tthigh. Metabolic heat production (MHp, W/m^2) was estimated from the VO_2 and RER by the equation: MHp = (0.23RER + 0.77) x (5.873VO_2) x (60/BSA); BSA is body surface area (m^2) [5].

Statistics

We used a sample size of 7 due to the within-subjects design, because previous research reported significant effects of COX-2 inhibition on Tcore responses during exercise in the heat [4], and due to the pilot character of the study. Data are presented as means (SD). Paired t-tests were used to compare differences between experimental conditions. Differences are considered statistically significant at $P < 0.05$.

Results

No adverse events occurred. After 20 min of running in the heat core temperature increase was less under acetaminophen compared to

Table 2. Comparisons of cardiorespiratory and metabolic responses after 20 min of running in the heat between acetaminophen and placebo pre-treatment

Variable	Paracetamol (N=7)		Placebo (N=7)		*P*-value
	Mean	SD	Mean	SD	
HR (bpm)	175.7	(14.9)	171.7	(14.2)	0.02
VO_2 (mL/min/kg)	52.2	(8.3)	52.6	(12.9)	0.93
RER	0.84	(0.08)	0.85	(0.07)	0.91
Blood Lactate (mmol/L)	5.9	(2.4)	6.1	(3.3)	0.73
RPE	14.7	(2.4)	14.3	(2.6)	0.68
MHp (W/m^2)	694.9	(100.3)	707.5	(96.7)	0.55

HR: heart rate, VO_2: oxygen uptake, RER: respiratory exchange ratio, RPE: ratings of perceived exertion, MHp: metabolic heat production.

Table 3. Comparisons of cardiorespiratory and metabolic responses at the end of running in the heat between acetaminophen and placebo pre-treatment

Variable	Paracetamol (N=7)		Placebo (N=7)		*P*-value
	Mean	SD	Mean	SD	
Running Time (min)	47.5	(15.5)	45.2	(13.1)	0.42
Delta Body Mass (kg)	1.17	(0.62)	1.13	(0.58)	0.50
Hematocrit (%)	44.2	(2.4)	44.5	(4.1)	0.90
HR (bpm)	185.0	(11.6)	185.3	(9.9)	0.88
VO_2 (mL/min/kg)	56.0	(10.2)	57.4	(6.8)	0.55
RER	0.82	(0.16)	0.84	(0.03)	0.76
BPsyst (mmHg)	121.3	(18.9)	133.0	(22.6)	0.15
BPdiast (mmHg)	70.0	(11.5)	76.6	(13.6)	0.22
Blood Lactate (mmol/L)	6.2	(1.9)	6.2	(2.4)	0.96
RPE	18.4	(0.79)	18.1	(0.69)	0.36

HR: heart rate, VO_2: oxygen uptake, RER: respiratory exchange ratio, BPsyst: systolic blood pressure, Bpdiast: diastolic blood pressure, RPE: ratings of perceived exertion.

placebo (P = 0.004) but did not differ between treatments at the end of exercising (**Figure 1**). No differences between treatments were found for skin temperatures after 20 min or at the end of running in the heat. With regard to cardiorespiratory and metabolic responses after 20 min of running in the heat only heart rates differed significantly between treatments being higher under acetaminophen compared to placebo (P = 0.02) (**Table 2**). No between-treatment changes of body mass (fluid loss), or cardiorespiratory and metabolic responses were detected at the end of running in the heat (**Table 3**).

Discussion

The main finding of this study was that a single low dose acetaminophen (500 mg) caused a lesser increase in core temperature associated with a larger increase in heart rate compared to placebo. Running performance in the heat (30 °C) did not differ between acetaminophen and placebo. It is well known that acetaminophen preferentially inhibits prostaglandin biosynthesis in the central nervous system thus lowering the hypothalamic set-point in the thermoregulatory centre resulting in elevated heat dissipation due to cutaneous vasodilation and sweating [8]. Heart rates increase as a counter-regulatory measure. Although participants under acetaminophen run on average 2.3 minutes longer compared to placebo this difference was not significant. This may be due to the small sample size and/or the use of a much lower dose of acetaminophen (500 mg) when compared to Mauger and colleagues (3 x 500 mg) [3] which is also supported by the observation that individual RPE changes under acetaminophen were not related to changes in individual running times.

There are at least two limitations. First, readings of infrared ear thermometry are known to be of limited accuracy but our research team is well trained to perform highly valid and reliable measurements [5]. Second, we cannot entirely exclude a Type II error with regard to RPE (and pain perception) but this was not a primary outcome measure. Generally, the use of pharmacological methods raises ethical concerns but the present study attempted to demonstrate potential pharmacological mechanisms of a single low dose acetaminophen affecting performance but does not recommend the use of such medication.

In conclusion, this is the first study evaluating effects of a single low dose (500 mg) administration of acetaminophen on thermoregulation and running performance in the heat (30 °C).

Although the increase in core temperature was slightly reduced by acetaminophen after 20 minutes of running in the heat running performance remained unaffected.

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Address correspondence to: Dr. Martin Burtscher, Department of Sport Science, Medical Section, University Innsbruck, Fürstenweg 185, 6020 Innsbruck, Austria. E-mail: martin.burtscher@uibk.ac.at

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