Effect of Thiamine Pyrophosphate on Levels of Serum Lactate, Maximum Oxygen Consumption and Heart Rate in Athletes Performing Aerobic Activity

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The aim of this study was to determine the effect of thiamine pyrophosphate (TPP) on serum lactate levels, maximum oxygen consumption (VO2max) and heart rate in male athletes performing aerobic activity. A double-blind, randomized, crossover study was performed in which lactate levels, VO2max and heart rates in 27 male athletes were compared at rest and after exercise, following administration of placebo (sodium chloride 0.9%) or TPP (1 mg/kg). At rest, serum lactate levels after placebo or TPP were similar; however, after exercise, the levels were lower in the athletes after taking TPP than after placebo. During exercise, VO2max in athletes on TPP was higher than on placebo. At rest, heart rate after taking placebo or TPP was similar but, after exercise, heart rate was lower after taking TPP than after placebo. It is concluded that TPP caused serum lactate levels and heart rate to be lower than placebo and VO2max to be higher in athletes performing aerobic physical activity.

KEY WORDS: THIAMINE PYROPHOSPHATE; SERUM LACTATE; MAXIMUM OXYGEN CONSUMPTION; HEART RATE; AEROBIC ACTIVITY

Introduction

Thiamine pyrophosphate (TPP) is the physiologically active form of thiamine (vitamin B1) and is essential in the metabolism of carbohydrates,1,2 participating as a co-factor for three enzymes: pyruvate dehydrogenase, α-ketoglutaric dehydrogenase and transacetylase. Pyruvate dehydrogenase is a multi-enzymatic complex which, under certain anaerobic conditions, decarboxylates pyruvate to acetyl-coenzyme A. Also, TPP takes part in the Krebs cycle during decarboxylation of α-ketoglutarate to succinyl-coenzyme A, favouring the oxidation of glucose to obtain adenosine triphosphate (ATP).3

Aerobic physical training results in increased maximum oxygen consumption (VO2max), which can reach 40 – 80 ml/kg per min, as a result of increased cardiac output and oxygen uptake by the muscles, and a decreased heart rate.4,5 As well as resulting in an increase in the availability of oxygen towards skeletal muscle, exercise increases
its vascularization and the formation of myoglobin. At the same time, the mitochondria increase in size and number, and also the levels and activities of various enzymes increase. These changes help to improve the individual's physical capacity towards exercise, which generates a decrease in muscle and blood lactate concentrations.6 – 8

There is evidence that the administration of thiamine (100 mg/day for 3 days) reduces serum lactate and improves resistance to fatigue.9 – 12 The administration of thiamine has also been shown to improve ergogenic capacity,13 although other studies concluded that thiamine is incapable of improving physical activity or the levels of serum lactate.14,15 Likewise, lactic acidosis is present in situations where a deficiency of thiamine and pyruvate dehydrogenase exists.16,17 From this evidence, it is possible to infer that TPP might affect the concentration of serum lactate by improving the oxidation of carbohydrates during aerobic metabolism. The objective of the present study was to investigate the effect of TPP administration in athletes who undertake aerobic activity. This work is relevant within this population as a physiological observation, since serum lactate levels are affected by pathological circumstances, chronic renal failure or chronic diabetes. To the best of the authors’ knowledge, no other report has been published on this subject.

**Subjects and methods**

**STUDY GROUP**

This randomized, double-blind, crossover study was conducted at the Faculty of Medicine, University of Colima, Mexico. Athletes aged 18 – 25 years old, who did exercise four times each week for 2 h and practised soccer as aerobic activity, were recruited. Persons presenting with physical, mental, emotional or psychiatric alterations, cardiac arrhythmia or electrolytic changes were excluded. The height, weight and body mass index of the volunteers were measured. All the participants signed letters of informed consent under the approval of the University of Colima Committee for Ethics, in compliance with the international standards set by the Declaration of Helsinki in 1964 (revised in 2000).

**ADMINISTRATION PROCEDURE**

Once the subjects were selected, they were given an intravenous placebo solution or a dose of TPP in two phases, with a latency period of 30 days between phases.

**Phase 1**

The placebo consisted of 80 ml isotonic saline (sodium chloride 0.9%) (Laboratorios Pisa, Guadalajara, Mexico) and the treatment consisted of 80 ml of isotonic saline plus 1 mg/kg TPP (Investigaciones Filosóficas y Científicas, Río Verde, Mexico). These solutions were administered intravenously with an administration time of 60 min. The TPP was previously dissolved in sterile bi-distilled water to obtain a stock solution with a concentration of 40 mg/ml. The placebo and treatment solutions were dissolved in bi-distilled water to the same final volume. At 24 h after administration, the subjects were submitted to physical exercise using a modified Pugh method.18 The exercise was performed in stages, using a treadmill with an elevation of 1º (to simulate wind resistance in cross-country running), at an initial speed of 4 km/h for a duration of 3 min/stage, with increments of 2 km/h between each stage until the end of the test (16 km/h). Lactate, heart rate and $\text{VO}_{2\text{max}}$ were measured before and after the application of the modified Pugh protocol.18

VM Bautista-Hernández, R López-Ascencio, M Del Toro-Equihua et al.

Effect of thiamine pyrophosphate
Phase 2
This phase was performed 30 days after phase 1 (TPP washout period). Subjects who were given the placebo in phase 1 received TPP and vice versa. The exercise protocol and the measurements of lactate, heart rate and \( VO_{2\max} \) were exactly the same as in phase 1.

MEASUREMENT OF LACTATE
An aseptic ear lobe was punctured to obtain a drop of capillary blood. The first drop of blood was discarded; the second one was applied to the reactive strip to be immediately read by an Accusport® analyser (Total Perfomance Inc, Mansfield, USA) at a wavelength of 660 nm.\(^ \text{19} \) It took 60 s for this instrument to determine the enzymatic and photometric measurements of the capillary blood sample. The analyser's effectiveness has been reported and validated previously.\(^ \text{20} \)

DETERMINATION OF HEART RATE
Heart rate was determined using a Polar™ pulsometer (Polar Co., Madrid, Spain) comprising a transmitter which picks up the heart rate signal and transmits it in radio frequency, to a receiver. The accuracy of these pulsometers is comparable with that of electrocardiographic equipment.\(^ \text{21–27} \)

MEASUREMENT OF \( VO_{2\max} \)
The PWC 170 test was employed for measurement of \( VO_{2\max} \); this is applicable to young adults who practice some aerobic activity and where \( VO_{2\max} \) is reached at a heart rate of 170 beats/\( \text{min} \). Whilst keeping heart rate constant during the physical activity, \( VO_{2\max} \) was determined using the formula: \(^ \text{28–31} \) \( VO_{2\max} = (3.656 \times v) - 3.99 \), where \( v \) is the velocity in km/h at which 170 beats/\( \text{min} \) are reached.

STATISTICAL ANALYSIS
The mean, SD and variance were calculated for the data. For inferential statistics, a paired Student’s \( t \)-test and 95% confidence intervals were calculated. Differences were considered significant when \( P < 0.05 \).

Results
A total of 27 male athletes (aged 18 – 25 years) who practiced aerobic activity on a regular basis were recruited and their general characteristics are shown in Table 1. Mean ± SD baseline serum lactate levels before exercise were similar between the athletes prior to administration of placebo or TPP (2.18 ± 0.16 versus 1.92 ± 0.11 mmol/l; Fig. 1A). There was, however, a significant difference in post-exercise serum lactate levels between the placebo and TPP treatments (4.56 ± 0.31 versus 3.34 ± 0.15 mmol/l; \( P = 0.00001 \)), indicating that lactate levels do not increase as much in the presence of TPP (Fig. 1B).

The difference in the post-exercise \( VO_{2\max} \) values between the placebo and TPP treatments indicated that oxygen consumption was significantly increased by TPP (placebo 41.9 ± 1.15 ml/kg per min versus TPP 48.2 ± 1.44 ml/kg per min; \( P = 0.000006 \); Fig. 2).

Mean ± SD baseline heart rate before exercise for the placebo and TPP treatments were similar (70.8 ± 2.3 versus 69.0 ± 2.5 beats/min; Fig. 3A), whereas the post-exercise heart rates between the placebo and TPP treatments were significantly different (placebo 187 ± 1.13 versus TPP 181 ± 1.29.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>20.0 ± 1.8</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.7 ± 0.1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.5 ± 6.3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>19.0 ± 0.4</td>
</tr>
</tbody>
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beats/min; \( P = 0.000006 \), indicating that heart rate did not increase as much in the presence of TPP (Fig. 3B).

A sensation of well-being was reported after TPP administration in 26 of the 27 subjects; two subjects presented with localized complaints (burning) at the moment of TPP application. No further adverse effects were observed.

**Discussion**

The objective of the present study was to determine the effect of TPP on the serum concentration of lactate, \( \text{VO}_{2\text{max}} \) and heart rate, in athletes who regularly practiced aerobic activity, by subjecting them to physical exercise with a modified version of the Pugh method.\(^{18}\) Participating subjects were randomly selected into this double-
Effect of thiamine pyrophosphate

blind study, where each subject was his/her own control in order to prevent extraneous factors influencing the results. When the subjects received TPP, serum lactate levels and heart rate were significantly less than placebo, and VO$_{2\text{max}}$ was significantly higher than placebo after performing physical activity. On the other hand, there was no significant difference in serum lactate levels and heart rate when measured at rest.

There do not appear to be any published data on the effect of TPP on athletes who practice an aerobic activity and are subjected to physical exercise. However, a decrease in serum lactate levels after exercise in sedentary individuals, in the presence of TPP, has been reported.\textsuperscript{32} In addition, several papers have shown the importance of TPP in the metabolism of carbohydrates (mainly in the decarboxylation of pyruvate), the improvement of diabetic acidosis and in acute myocardial infarction, as it favours the transport of oxygen towards ischaemic cells.\textsuperscript{11,12,33}

Different compensating mechanisms exist that can increase the capacity for aerobic metabolism of carbohydrates by reducing the amount of lactate produced during physical activity and mean that the lower serum lactate reported in the present study following TPP, may be explained as follows: (i) in terms of the multi-enzymatic complex of pyruvate dehydrogenase, which comprises three enzymes and five coenzymes, where TPP is one of the main coenzymes it could increase the movement of pyruvate towards the mitochondria and increase glycolytic activity; (ii) in terms of the Krebs cycle, in which oxidative decarboxylation of $\alpha$-ketoglutarate to succinyl-coenzyme A, with its respective liberation of carbon dioxide, is catalysed by a multi-enzymatic complex similar to that of pyruvate dehydrogenase where TPP produces a stable carbanion that reacts with the $\alpha$-carbon of $\alpha$-ketoglutarate – the latter is essential for the decarboxylation
of pyruvate to acetyl-coenzyme A, as well as the decarboxylation of α-ketoglutarate to succinyl-coenzyme A.

A muscle’s ability to extract oxygen from arterial blood is an essential factor in the global capacity of an organism to consume oxygen. This process involves capillarization, predominance of type I or type II muscle fibres, mitochondrial mass and multi-enzymatic complexes. The availability of more TPP, as in the present study, would increase the activity of the multi-enzymatic complex, which could favour disposition of pyruvate, increasing the activity of the aerobic cellular metabolic pathways of the Krebs cycle, thus resulting in an increase in oxygen consumption.

However, dynamic physical exercise training slows down the resting heart rate and decreases the heart’s response to effort. Heart rate at rest slows due to an increase in vagal tone, but the sympathetic nerve stimulus remains unchanged. During exercise, however, the sympathetic nerve stimulus and the release of catecholamine are proportionally smaller than those of an untrained individual. Yet, in the present study, a decrease in heart rate after exercise was achieved without any additional physical training by the athletes, which indicates that this is not a physical adaptation to exercise. It is currently unclear why this decrease in heart rate after exercise occurred. Possibly, the greater disposition of pyruvate, which activates the aerobic cellular metabolic pathways of the Krebs cycle, along with the greater oxygen consumption and increased levels of ATP, would result in a decrease in the heart’s workload, therefore lowering the heart rate after exercise.

In conclusion, TPP resulted in lower levels of serum lactate and heart rate compared with placebo and a higher VO_{2max} in athletes performing aerobic physical activity. Future studies could be expanded to include subjects with lactic acidosis.

Conflicts of interest

The authors had no conflicts of interest to declare in relation to this article.

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