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EFFECTS OF THIAMINE PYROPHOSPHATE ON BLOOD LACTATE LEVELS IN YOUNG, SEDENTARY ADULTS UNDERGOING MODERATE PHYSICAL ACTIVITY

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ABSTRACT

Bautista-Hernández Víctor Manuel, López-Ascencio Raúl, Trujillo-Hernández Benjamín, Vásquez Clemente. Effects Of Thiamine Pyrophosphate On Blood Lactate Levels In Young, Sedentary Adults Undergoing Moderate Physical Activity. ***JEP****online* 2005;8(2):24-29. To evaluate the effect of thiamine pyrophosphate (TPP) on blood lactate levels in young, sedentary adults during moderate physical activity. A randomized double blind crossover design was used. Blood lactate levels were compared in resting and post-exercise conditions after placebo or TPP administration. 29 healthy individuals participated in the study. Interventions were: 1) administration of a placebo with an isotonic solution of 0.9% NaCl and moderate physical activity; 2) administration of intravenous TPP at a dose of 1 mg/kg of body weight and moderate physical activity. Blood lactate levels were determined in all individuals in resting and post-exercise conditions, the latter after a workout on a treadmill at a speed of 10 Km/hr for 10 min. At rest, blood lactate levels with the placebo solution were 1.90±0.37 mmol/L and with TPP were 1.70±0.36 mmol/L (p=0.09). After exercise, blood lactate levels with the placebo solution were 4.30±1.20 mmol/L and with TPP were 2.90±0.91 mmol/L (p=0.00). Blood lactate levels decreased in the presence of TPP in sedentary individuals undergoing moderate physical activity. Through further studies these results could be extended to include high-impact (elite) athletes.

Key Words: Exercise, Cocarboxylase, Modified Pugh Protocol

INTRODUCTION

Thiamine (vitamin B_1) is an essential vitamin for glucose metabolism (1,2). After being absorbed (from) the intestine, it is phosphorylated into thiamine pyrophosphate (TPP). TPP is the co-factor of three important enzymes: pyruvate dehydrogenase, alpha-ketoglutarate dehydrogenase and transketolase. Pyruvate dehydrogenase is a multi-enzymatic complex which, under aerobic conditions, allows pyruvate to be decarboxylated into Acetyl-CoA. TPP is also necessary for the decarboxylation of alpha-ketoglutarate into succinyl-CoA within the citric acid cycle, thus favoring aerobic glucose oxidation to obtain ATP, while transketolase acts in the pentose phosphate pathway (3). It has been shown that lactic acidosis is favored in situations where there is thiamine and pyruvate dehydrogenase deficiency (4,5).

On the other hand, the regular practice of exercise increases oxygen availability to the skeletal muscle due to myoglobin formation, increased muscle capillarization, increase in the size and number of mitochondria, increase in aerobic enzyme levels and activity, etc. These adaptations increase an individual’s physical capacity increases, which are often detected by decreases in muscle and blood lactate concentrations (6-8).

There is evidence that thiamine administration (100 mg/.day during 3 days) improves exercise performance, reduces blood lactate and decrease exercise-induced fatigue (13-16). Although McNeill and Mooney (17) showed the efficacy of thiamine administration as an ergogenic aid, Webster (18) and Webster et al. (19) showed no effect of thiamin on exercise performance, including blood lactate levels.

Taking this into account, it is possible that TPP could have an effect on lactate levels, tentatively, upon improving carbohydrate oxidation through aerobic metabolism. Therefore, the objective of the present work is to study the effect of TPP supplementation in young, sedentary adults during moderate physical activity. It is pertinent to study in this population as a physiological condition, because previous reports were done on individuals with disease. Additionally, to the best of our knowledge, this is the first study that has administered TPP intravenously in young sedentary adults.

METHODS

A randomized, double blind crossover trial was carried out at the University of Colima’s Faculty of Medicine in Colima, Mexico. Twenty-nine healthy male university students between 18 and 25 years of age were included. Subjects having any physical or mental alteration, significant emotional anguish, psychiatric incapacity, arrhythmias, or electrolyte abnormality did not participate in the study. The University Ethics Committee approved the study and all participants signed a letter of informed consent, in accordance with the ethical standards formulated in the Helsinki Declaration of 1964 (revised in 2000).

Once the individuals were selected, they received either placebo or TPP in phase one (which lasted 48 hours), and the opposite in phase two (which lasted another 48 hours), as follows:
A) Phase 1: Placebo, 80 ml of isotonic solution 0.9% NaCl (Laboratorios PISA de México, S.A.) or treatment 80 ml of isotonic solution 0.9% NaCl plus TPP, 1 mg/kg of weight of TPP (Investigaciones Filosóficas y Científicas, S.A. de C.V. de Mexico) were administered intravenously at a 60 min interval for each subject. TPP was dissolved previously in sterile water (approximately 1.8 mL) from a

40 mg/mL stock solution and the same water volume used for this procedure without TPP was added to placebo solution. Twenty-four hours later, subjects underwent moderate physical exercise using the modified Pugh protocol (20). This was carried out using a treadmill at an inclination of 1% (to simulate wind resistance presents in field conditions) and a constant speed of 10 Km/hr for a duration of 10 min (the rationale for such a protocol is because the subjects are sedentary and they can not be forced to do a higher effort). Lactate levels were measured before (baseline) and after the exercise protocol. The subjects performed a 5 min warm-up period before the tests.

B) Phase 2 (crossover): This stage was carried out after completion of Phase 1. The subjects who had received placebo in Phase 1, now received TTP and vice versa. The exercise protocol and lactate measurements were repeated exactly as in Phase 1.

Lactate Measurement

Following asepsis, an ear-lobe was pierced allowing blood to flow until a drop of pure capillary blood was formed. The first drop of blood was discarded, with the second sample immediately applied to lactate reactive strips and analyzed using an Accusport Analyzer (21). This instrument takes approximately 60 s to measure by enzyme and photometric determination, using a wavelength of 660 nm and capillary blood samples, and has been previously reported to have high validity (22).

Statistical analyses

Averages, standard deviations and variance were used to obtain descriptive statistics. Paired Student t-test and 95% confidence intervals were used for the inferential statistics. Differences were considered significant when $p<0.05$.

RESULTS

General information about the 29 subjects participating in the study is shown in Table 1.

Table I. General characteristics of sample studied.

Variable	*Mean±SD*
Age (years)	21.5±2.4
Height (m)	1.7±0.06
Weight (Kg)	71.9±8.3
Body Mass Index (%)	21.1±2.3

Figure 1 shows baseline lactate level values and the similarity between the placebo and TPP treatment levels (1.9±0.37 mmol/L vs. 1.7±0.36 mmol/L; $p=0.09$).

Figure 2 shows the significant difference in the post-exercise lactate level values between the placebo and TPP treatments (4.3±1.2 mmol/L, versus 2.91 ±0.91 mmol/L; $p = 0.00$), indicating that lactate values were reduced in the presence of TPP.

Twenty-six of the 29 subjects reported a sensation of well-being after TPP administration and only 3 of the 29 subjects presented with localized complaints (burning, at injection zone) at the moment of TPP administration. No further adverse effects were observed.

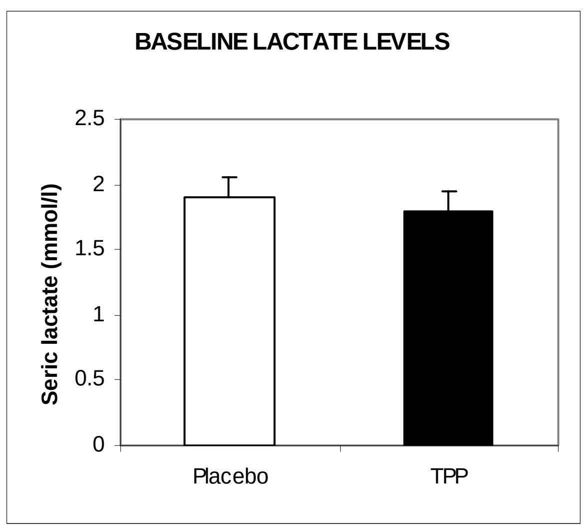

Figure 1. Baseline lactate values prior to exercise were: 1.9±0.37 mmol/L (placebo bar) for the placebo solution and 1.7±0.36 mmol/L (TPP bar) for the TPP solution, p=0.09. The bars correspond to a confidence level of 95%.

DISCUSSION

The objective of the present study was to determine the effect of TPP on the concentration of lactate in the blood in young, sedentary adults undergoing moderate physical activity (10 min of running at 10 km/h).

The selected design for the study was a randomized, double blind crossover trial in which each subject was his own control in order to determine if the intervention itself was responsible for the difference and to control extraneous factors that could have influenced the results. We observed that when the subjects received TPP there was a lowering of blood lactate levels after physical activity, compared when they received the placebo. On the other hand, there was no significant variation in the baseline lactate level among trials.

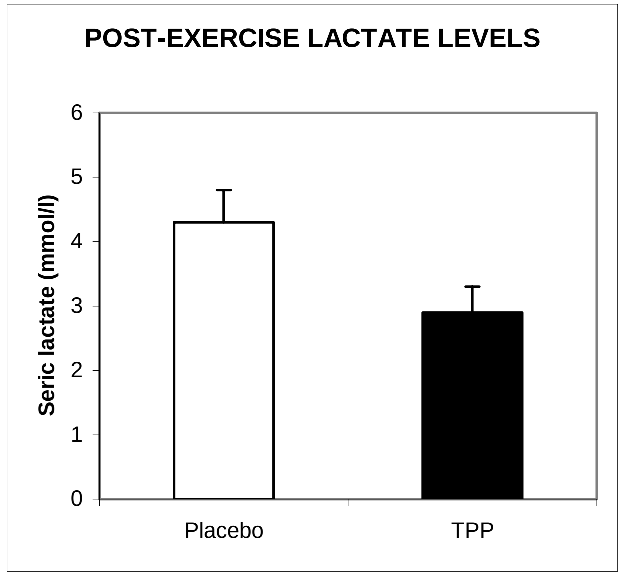

Figure 2. Post-exercise lactate values were: 4.3±1.2 mmol/L (placebo bar) for the placebo solution and 2.9±0.9 mmol/L (TPP bar) for the TPP solution, p = 0.00. The bars correspond to a confidence interval of 95%.

To the best of our knowledge, there are no existing publications reporting the effect of TPP in young, sedentary adults undergoing moderate physical activity. However, there have been publications reporting that because of its action in carbohydrate metabolism, TPP is especially important in pyruvate decarboxylation, averting diabetic acidosis and acute myocardial infarct and favoring the carrying of O_2 to the ischemic cell (15,16,23). Interestingly, thiamine supplementation can improve left ventricular function in some patients presenting with congestive cardiac insufficiency receiving long-term furosemide treatment (24) and significantly reduces fatigue after exercise (13). These thiamine effects can be explained as thiamine is converted to thiamine pyrophosphate to exert its cellular action (1), thus supporting the direct use of TPP as carried out in the present study.

Even though TPP levels of the subjects were not measured, we consider that a substantial amount of the TPP dose administered was still present during exercise period, because in adults, the minimal daily requirement is 1 mg, when intake exceeds the requirement, tissue stores are first saturated, as the intake of TPP is increased, the excess is excreted in urine several days after (1).

It is important to underline the fact that none of the subjects reported secondary effects following the placebo and TPP administration. The physical well-being (“without fatigue”, “still physically strong”, “can do more exercise”) described by the subjects at the time of taking the treadmill test after having received the TPP is noteworthy. We do not yet have an explanation for that phenomenon.
There are different compensating mechanisms that increase the organic capacity to aerobically metabolize carbohydrates, thus reducing the quantity of lactate produced during physical activity. This makes it possible for TPP to lower blood lactate by deceasing lactate production as follows:
a) The pyruvate dehydrogenase complex consists of three enzymes and five co-enzymes, among which TPP is included as one of the primordial co-enzymes. TPP could therefore increase pyruvate entry into the mitochondria for a give rate of glycolytic flux.
b) Within the Krebs cycle, the oxidative decarboxylation of α-ketoglutarate to succinyl-CoA with CO_2 liberation is catalyzed by a multi-enzymatic complex very similar in structure to that of pyruvate dehydrogenase. Once again TPP gives a stable carbanion to react with the α-carbon of α-ketoglutarate becoming indispensible for the decarboxylation of pyruvate to acetyl-CoA, as well as for the decarboxylation of α-ketoglutarate to succinyl-CoA.

On the other hand, the role of diet cannot be discarded. We did not control the diet of subjects prior to the trials, and it has been shown to have an influence on lactate accumulation (25). The influence of other factors such as physical state and type and length of exercise has been described and they were controlled in our study. Subjects were sedentary, but we controlled for the amount of physical activity that each subject performed before trials, asking them to refrain from exercising for 24 hours before the trials.

Our data show that TPP reduces the concentration of blood lactate in young, sedentary adults exposed to moderate physical activity. Through further studies these results could be extended to include high-impact (elite) athletes and so invaluably contribute to the scientific control of athletic training and the improvement of physical capacity.

CONCLUSIONS

The intravenous administration of TPP at a dose of 1 mg/kg of weight significantly reduced lactate levels in young, sedentary subjects at the end of 10 min of treadmill exercise at 10 km/h, compared with those receiving a placebo. There was no significant difference in baseline lactate levels. TPP produced no important adverse effects.

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