Clinical Study

Effect of Ribose Supplementation on Resynthesis of Adenine Nucleotides after Intermittent Training in Humans

Adapted from a study conducted by

Statement of Purpose

During intense exercise a fraction of the ATP pool in human skeletal muscle is degraded to inosine-5-monophosphate (IMP). While most IMP is retained in the cell for reamination to AMP at rest, a significant fraction of IMP is further degraded to inosine and hypoxanthine and enter the bloodstream lowering the adenine nucleotide pool. Lost nucleotides must be restored via the purine salvage pathway or the de novo pathway of adenine nucleotide metabolism. The limiting step in nucleotide synthesis de novo is the availability of phosphoribosylpyrophosphate (PRPP), which is formed from ribose-5-phosphate. The level of ribose in the muscle is limited; thus an increased availability of ribose may enhance the formation of PRPP and the rate of synthesis of adenine nucleotides. The aim of the present study was to assess the effect of oral intake of ribose after frequent, high-intensity training on adenine nucleotide resynthesis. Such information will not only be useful for people performing regular physical exercise but may also be important for patients having impaired skeletal muscle metabolism, such as those with congestive heart failure and peripheral arterial disease.

Methods

During intense exercise a fraction of the ATP pool in human skeletal muscle is degraded to inosine-5-monophosphate (IMP). While most IMP is retained in the cell for reamination to AMP at rest, a significant fraction of IMP is further degraded to inosine and hypoxanthine and enter the bloodstream lowering the adenine nucleotide pool. Lost nucleotides must be restored via the purine salvage pathway or the de novo pathway of adenine nucleotide metabolism. The limiting step in nucleotide synthesis de novo is the availability of phosphoribosylpyrophosphate (PRPP), which is formed from ribose-5-phosphate. The level of ribose in the muscle is limited; thus an increased availability of ribose may enhance the formation of PRPP and the rate of synthesis of adenine nucleotides. The aim of the present study was to assess the effect of oral intake of ribose after frequent, high-intensity training on adenine nucleotide resynthesis. Such information will not only be useful for people performing regular physical exercise but may also be important for patients having impaired skeletal muscle metabolism, such as those with congestive heart failure and peripheral arterial disease.

Protocol

The study was of a random double-blind crossover design. The subjects participated in two identical 7-d training protocols on two occasions, 5 - 9 weeks apart. The subjects performed two training sessions, separated by 5 - 7 h, per day and 14 training sessions in total. Each training session consisted of 10-min of warming up at an intensity of 65% followed by a 3-m rest period and then 15 10-s maximal exercise bouts separated by a 50-s rest period. The subjects repeated the exercise protocol 72-h after the last training session (72-h test).

In one study leg the last training session was followed by oral intake of nine supplementations, each containing 200 mg/kg body wt of ribose (mixed with sucrose) and in the second leg by oral intake of nine supplementations of 200 mg/kg body wt of malodextrin (mixed with sucrose). The first supplementation was ingested 10-min after the last training session and thereafter at each main meal for 3-days, with the last intake being approximately 60-hours after the last training session.

A muscle biopsy was taken from the vastus lateralis muscle of each leg at rest, 6 - 7 days before the first training session. Muscle biopsies were again taken immediately after the last training session as well as 5, 24, and 72-h after the training. To facilitate immediate sampling on cessation of exercise, a small incision was made before the experiment. The biopsies obtained after exercise were frozen in liquid nitrogen within 10-s of cessation of exercise, and in general, the muscle samples were frozen within 5-s of collection. The biopsies were stored at -80C until analyzed.

Before the last training session as well as before the test 72-h after the last training session, a venflon was inserted in an antecubial vein for collection of blood samples. In each test, blood (2 - 5 ml) was drawn in heparinized syringes, before the first sprint, before the last exercise bout (- 10-s), and immediately after the last exercise bout as well as 5, 10, 20, 30, 45, 60, and 120-min in recovery after exercise.

A part of the blood sample was immediately centrifuged for 30-s, and plasma was collected and stored at -80C. Another part was hemolyzed with Triton X-100 for analysis of blood lactate. The remaining part of the blood was stored on ice until analyzed.

Muscle samples were analyzed for adenine nucleotides with a reverse-phase HPLC method. Plasma hypoxanthine and urate were similarly analyzed by HPLC.
Results

Immediately after the last training session, muscle ATP was lowered (p<0.05) by 25 +/- 2 and 22 +/- 3% in Pla (placebo) and Rib (ribose), respectively. In both Pla and Rib, muscle ATP levels at 5 and 24 h after the exercise were still lower (p<0.05) than pretraining. After 72 h, muscle ATP was similar (p<0.05) to pretraining in Rib, but still lower (p<0.05) in Pla, and higher (p<0.05) in Rib than in Pla (Figure A).

Total adenine nucleotides (TAN) was lower than pretraining still at 72 h after exercise in Pla, but in Rib TAN at 74 h was similar (p<0.05) to pretraining level, and the level was higher than Pla (p<0.05). Muscle IMP levels increased (p<0.05) to 1.4 and 1.2 mmol/kg dry wt during the last training session in Pla and Rib, respectively, and were similar (p<0.05) to the pretraining level at 5 h after exercise. TAN + IMP after the last training session was lower (p<0.05) than pretraining in both Pla and Rib, and it was maintained lower (p<0.05) during the first 72 h after exercise in Pla, whereas in Rib, TAN + IMP at 24 h after exercise was higher (p<0.05) than immediately after exercise and was similar (p<0.05) to pretraining levels after 72 h (Figure B).

After repeated high-intensity exercise, muscle ATP levels remained depressed for more than 72 h in the placebo group, while ATP levels in the ribose group returned to normal.

Total adenine nucleotide (TAN) + inosine monophosphate (IMP) levels also remain depleted in the placebo group, but returned to baseline levels in the ribose group. Results suggest a depletion in the energy pool with high-intensity exercise that is attenuated with ribose supplementation.
Conclusion

The results of the present study support the findings of previous investigations that 1-week of frequent, intense training is sufficient to markedly lower the resting muscle adenine nucleotide level. The data moreover show that oral intake of ribose after training enhances the rate of adenine nucleotide resynthesis, probably by increasing the rate of phosphoribosyl pyrophosphate (PRPP) synthesis. The finding, therefore, suggests that PRPP availability is a rate-limiting factor for ATP resynthesis in human skeletal muscle.

References


