ADENOSINE PLAYS A ROLE IN THE REGULATION OF SKELETAL MUSCLE BLOOD FLOW HETEROGENEITY IN HUMANS

Heinonen Ilkka1, Nesterov Sergey V.2, Kemppainen Jukka3, Nuutila Pirjo2, Knuuti Juhani2, Laitio Ruut2, Kjaer Michael4, Boushel Robert5, Kalliokoski Kari2

(Turku PET Centre, University of Turku1, Finland, Turku PET Centre2, Finland, University of Turku3, Finland, Institute of Sports Medicine, Bispebjerg Hospital, Copenhagen4, Denmark, Department of Exercise Science, Concordia University, Montreal5, Canada)

INTRODUCTION
Adenosine is a potent single candidate for causing exercise hyperemia in skeletal muscle in humans since a non-selective adenosine receptor blockade with theophylline has been shown to induce 15-20% reduction in limb blood flow (BF) during exercise (1, 2). However, it is not known whether adenosine plays a role in the regulation of skeletal muscle BF heterogeneity within the muscle and the present study concentrated on that phenomenon.

METHODS
Skeletal muscle BF was measured during rest and exercise from m. quadriceps femoris (QF) and from its four different muscle compartments in six healthy women (age 23.7 ± 2.5 yrs) using positron emission tomography. BF was measured at baseline, during two doses (70 and 140 micro/g/min) of continuous IV infusion of adenosine at rest, and during three incremental work-loads (50, 100 and 150 N) with one-leg intermittent isometric contractions without and with theophylline-induced non-selective adenosine receptor blockade. Spatial BF heterogeneity was calculated as standard deviation divided by the mean BF value obtained from pooled voxel by voxel blood flow values from QF and its compartments.

RESULTS
Adenosine infusions did not induce any significant changes in mean BF at rest (p = 0.5), but BF heterogeneity increased during the higher dose of adenosine compared to baseline (p = 0.02) in the whole QF as well as in all four different muscles of QF. BF increased with increasing work-load (p < 0.001) both without theophylline (22 ± 4, 30 ± 4 and 38 ± 6 ml/100g/min, respectively) and with theophylline (23 ± 5, 28 ± 3 and 36 ± 5 ml/100g/min, respectively). Variability of mean BF between the four QF muscles decreased with incremental work-load (p < 0.001) and BF heterogeneity at the level of whole QF decreased with increasing exercise intensity (p = 0.02). Locally in four QF muscles, BF heterogeneity decreased only in m. vastus lateralis (p = 0.04), where the mean BF increased the most (124%) from the lowest to the highest exercise intensity. Theophylline had no effect on mean BF during exercise (p = 0.5), but it increased BF heterogeneity locally in four QF muscles (p = 0.03).

DISCUSSION
Blocking of adenosine receptors with theophylline increases skeletal muscle BF heterogeneity during exercise as well as intravenously infused exogenous adenosine at rest. These findings indicate that adenosine may play a more important role in local vasodilation and BF heterogeneity and thus potentially coordinating localized BF to muscle metabolic demands rather than in altering mean BF in contracting skeletal muscle in humans. In addition, this study also demonstrates for the first time that skeletal muscle BF heterogeneity decreases with increasing exercise intensity, which is due to newly activated muscle mass and decreased mean BF variability between muscles engaged in exercise.

REFERENCES

Keywords: Blood Flow, Physiology, Skeletal Muscle

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