Improved bioenergetic recovery during experimental ischemia and reperfusion by irradiation

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin
vid Göteborgs Universitet kommer att offentligen försvaras i hörsalen
Arvid Carlsson, Academicum, Medicinaregatan 3, Göteborg
fredagen den 7 december, kl. 13.00.

av

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Avhandlingen baseras på följande delarbeten:

I Lindgård A., Lundberg J., Rakotonirainy O., Elander A. and Soussi B.
Preservation of rat skeletal muscle energy metabolism by illumination.
Life Sciences 72 (23), 2649-2658, 2003.

II Lundberg J., Lindgård A., Elander A. and Soussi B.
Improved energetic recovery of skeletal muscle in response to ischemia and reperfusion injury followed by *in vivo* ^{31}P-Magnetic Resonance Spectroscopy.
Microsurgery 22 (4), 158-164, 2002.

III Lukes D., Lundgren A., Wilton J., Lindgård A., Omerovic E., Rakotonirainy O., Parra AK., Olausson M. and Soussi B.
Singlet Oxygen Energy illumination during ischemia preserves high energy phosphates in a concordant heart xenotransplantation model**.**
Laser Physics 13 (1), 84-90, 2003.

IV Lindgård A., Hultén LM., Svensson L. and Soussi B.
Irradiation at 634 nm releases nitric oxide from human monocytes.
Lasers in Medical Science 22 (1), 30-36, 2007.

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Improved bioenergetic recovery during experimental ischemia and reperfusion by irradiation

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Abstract

Prolonged ischemia and reperfusion frequently occur during clinical operations. The bioenergetic status decreases during ischemia and reactive oxygen species (ROS) are formed during reperfusion, which may lead to irreversible tissue injury. During prolonged ischemia, such as in complicated microsurgical operations, tissue injury should be minimized to improve the chance of full recovery and function. Irradiation has previously been shown to improve functional recovery of cold-stored rat hearts via conservation of ATP. In this thesis, we used photons at 634 nm produced from a singlet oxygen system to investigate whether irradiation improves the bioenergetic status in skeletal muscle and graft hearts and decreases ROS in monocytes, and thus decreases tissue injury.

The effect of irradiation on bioenergetic status was examined in rat rectus femoris muscle in vitro following 5 h ischemia. Phosphocreatine (PCr), ATP and inorganic phosphate (Pi) levels were measured using high resolution 11.75T ^{31}P magnetic resonance spectroscopy (MRS). PCr and ATP were significantly higher in the irradiated groups than in the non-irradiated group, but no difference in Pi was observed. The effect of irradiation on bioenergetic status was examined in rat rectus femoris muscle in vivo following 4 h ischemia and 1 reperfusion. ATP, PCr and Pi levels were measured using 2.35T ^{31}P MRS. After 4 h ischemia, ATP levels in the irradiated group were significantly higher than in the non- irradiated group, but no difference in PCr/(PCr+Pi) levels were observed. After 1 h reperfusion, ATP and PCr/(PCr+Pi) levels in the irradiated groups were significantly higher than in the non-irradiated groups. Blood-perfusion was measured using laser Doppler flowmetry and did not differ between the groups. The effect of irradiation on xenografts was examined in vivo following heart xenotransplantation from hamster to rat. PCr and ATP levels were measured daily using 2.35T ^{31}P MRS over 4 days. Irradiation of xenografts before reperfusion preserved the energetic status of hamster grafts, as demonstrated by a significantly higher PCr/ATP ratio in the irradiated group than in the non-irradiated group on the first postoperative day. However, irradiation did not delay the rejection process in this experimental model. Finally, the effect of irradiation was examined in human monocytes. Intracellular ROS, nitric oxide (NO) release and ATP were measured using chemiluminescence assays. iNOS and eNOS mRNA levels were measured using reverse transcription PCR. NO levels were significantly higher in the irradiated group than in the non-irradiated group, but no differences in iNOS or eNOS mRNA were observed. Intracellular ROS release was significantly lower in the irradiated group than in the non-irradiated group, and there was no difference in ATP levels. The salvaging effect of irradiation may have a wide range of clinical applications, for example in complex microsurgery and transplantation surgery.

Key words: energy metabolism, skeletal muscle, monocyte, ischemia, reperfusion, NMR, singlet oxygen energy, light, LED
ISBN 978-91-628-7294-6 Göteborg 2007