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Title : STEROIDS PREVENT MUSCLE HYPOXIA IN HEMORRHAGED RATS

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Introduction. Data from previous experiments indicate that glucocorticoids reduce the mortality associated with low blood flow conditions such as hemorrhagic or bowel ischemic shock.[1] However, the mechanism responsible for the protective effect of glucocorticoids in low flow states remains uncertain. The present study was designed to determine the influence of glucocorticoids on tissue oxygen tension and microvascular diameters during hemorrhage in rats.

Methods. 23 male Sprague-Dawley rats (99±4g body weight) were anesthetized with enflurane, 2.2 vol% in air, and allowed to breathe spontaneously. Prior to the experiment, rats were pretreated with either methylprednisolone sodium succinate (MP), 30 mg/kg IV (n=13), or an equal volume of saline (n=10). A cremaster muscle was prepared for television microscopy and a carotid artery was cannulated for pressure monitoring and for blood removal. The muscle was suffused with a warmed physiological salt solution equilibrated with nitrogen to prevent the diffusion of oxygen into the tissue from the surrounding environment. An oxygen microcathode (tip diameter approximately 1.5 μm) was placed in the muscle in an area devoid of major arteries and/or veins, and tissue oxygen tension was measured polarographically. Body temperature was maintained at 37-38°C. The protocol consisted of a 20 minute normovolemic control period, 30 minutes of controlled hemorrhage at a mean arterial pressure (MAP) of 40 torr, followed by return of the shed blood and a subsequent 20 minute normovolemic observation period. MAP, cremaster muscle oxygen tension (PtO_2), and hemorrhage volumes were recorded continuously and measured at one minute intervals. The diameters of fourth-order arterioles were measured every 30 sec from the microvascular image on the video monitor. Arterial blood gases were measured immediately before and after hemorrhage.

Results. Values for an MAP, PaO_2, $PaCO_2$, microvascular diameters, and shed blood volumes were similar in both treated (MP) and untreated (saline) rats. Data for these values were pooled for statistical analysis. The MAP averaged 76±1 torr during the normovolemic control period. PaO_2 was 83±3 torr before hemorrhage and 88±2 torr after 30 minutes of hypovolemia. $PaCO_2$ increased from 35±1 torr before hemorrhage to 39±1 torr ($p < 0.05$) after hemorrhage. Maximum hemorrhage volume was 2.3±0.1 ml/100 g, or approximately 36% of estimated blood volume. Fourth-order arteriolar diameters, which averaged 22±0.5 μm before hemorrhage, decreased to 18±0.7 μm ($p < 0.05$) during hypovolemia. Before hemorrhage, PtO_2 was 15.8±0.7 torr in treated animals and 15.4±0.9 torr in untreated rats. Cremaster muscle oxygen tension decreased ($p < 0.05$) during hemorrhage in untreated rats, but was unchanged from control in those which received MP. The PtO_2 values during hemorrhage are summarized in the following table:

Min. of Hemorrhage	PtO_2 (% of Control) Saline	vs	MP
10	86±4	*	103±5
20	85±4	*	98±8
30	76±8	*	96±9

*$p < 0.05$, group t-test

Discussion. The results indicate that MP pretreatment prevents the development of muscle tissue hypoxia in rats subjected to hemorrhage. The doses of MP employed here are comparable to those which are recommended for the management of shock in humans. The absence of muscle tissue hypoxia during hemorrhage in rats which received MP cannot be attributed to differences in arterial pressures, arterial blood gases, anesthetic techniques, or shed blood volumes, since these were similar in both groups. Further, the fourth-order arterioles responded similarly in both treated and untreated animals, suggesting that the differences in tissue oxygen tension cannot be explained by altered microvascular responses produced by MP. These data document the value of MP in preventing one of the major pathophysiological derangements associated with hemorrhage and they provide at least one possible explanation for the improved survival of hemorrhaged animals which are treated with glucocorticoids.

References.

1. Altura BM, Altura BT: Peripheral vascular actions of glucocorticoids and their relationship to protection in circulatory shock. J Pharmacol Exp Ther 190:300-315, 1974

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