A ROLE FOR RENAL PROSTAGLANDIN E IN HEMORRHAGIC SHOCK IN THE DOG

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Submitted to the Faculty of the Graduate School
in partial fulfillment of the requirements
for the Degree of Doctor of Physiology
in the Department of Physiology
Indiana University
December 1973

Accepted by the faculty of the Graduate School, Department of Physiology, Indiana University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Dec. 21, 1923

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SUMMARY

This study has attempted to define a role for the renal prostaglandins in an extremely important clinical condition, shock from hemorrhage. Much evidence exists in the literature that supports this idea. The kidney has been shown to possess the ability to synthesize and metabolize the prostaglandins. Various agents that affect changes in renal function also cause the release of prostaglandins into the renal venous blood. These same agents have been shown to be elevated in hypotension and normovolemic shock. Normal renal blood flow has been shown to depend, in part, on renal prostaglandin production. Studies involving the infusion of prostaglandins into the renal artery have described effects on renal function that are very similar to the changes occurring in renal function following periods of acute hypotension. Finally, endotoxic shock has been shown to increase the concentration of prostaglandin-like substances in renal venous blood.

PGE_1 was infused into the left renal artery of anesthetized, non-volume loaded dogs. The changes in renal hemodynamics and electroylte and water handling were assessed

using standard clearance methods, measurements of pressure, and electromagnetic flow measurements. Unique responses were demonstrated for fC_{Ca}, fC_{PO_4}, and negative free water clearance. Calcium and phosphate clearances were increased upon infusion of the drug, as was negative free water clearance. The increased phosphate clearance may be related to the natriuresis that occurred with PGE_1 infusion. Increased calcium clearance may be related to direct effects of PGE_1 on tubular transport mechanisms for calcium. The increased negative free water clearance most probably is related to osmolar clearance and ADH levels.

These data were compared to postreinfusion, normovolemic shock renal function. A distinct similarity was defined. To assess the role of prostaglandins in hemorrhagic shock, renal output and arterial concentration of PGE were quantitated. Output and arterial (PGE) were both elevated following reinfusion. Arterial (PGE) rose to significant levels of elevation toward the end of the postreinfusion, normovolemic shock observation period. Arterial (PGE) was also significantly elevated during hypotension, but renal output of PGE following reinfusion may be related to enhanced levels of circulating catecholamines, angio-

tensin, or renin.

Increases in arterial (PGE) during hypotension and late in normovolemic shock may be the result of impaired blood flow through the lung, or injury, from anoxia, to enzyme systems concerned with prostaglandin degradation. Some evidence from this study suggested that the lung may not be able to control arterial (PGE) as effectively as it did under non-shocked conditions.

Indomethacin, an inhibitor of prostaglandin synthesis was injected into one group of animals to ascertain whether or not PGE had any definitive role in psythypotension renal hemodynamics or function. Following the treatment, RVR rose significantly, and RBF fell significantly. Very little change was noted in arterial (PGE). In fact, the upward trend continued. The changes in RVR and RBF were similar in degree, to those changes in the non-shocked animal following identical treatment with the drug. The vasoconstrictor levels, although lower than during hypotension are enhanced over initial control following reinfusion. Increased PGE generation by the kidney may be necessary to maintain vital blood flow in the face of increased vasoconstrictor influence.

Small changes in fC_{Ca}, fC_{Na}, and fC_{PO_4} were noted

after the drug treatment. These may indicate a role for PGE in posthemorrhage renal function. However, the changes may be the result of a more direct effect of indomethacin on renal function. Indomethacin has been shown to be an inhibitor of phosphodiesterase activity, and by this mechanism can effectively increase tissue cyclic AMP. Since cyclic AMP plays some role in renal function, especially with regard to calcium and phosphate handling, indomethacin may be exerting an effect by this means rather than by inhibiting synthesis of PGE.

Most probably, the enhanced production of PGE has a substantial effect on postreinfusion renal hemodynamics. In effect, renal blood flow was probably preserved at a level greater than would have been expected without a vasodilator influence to counter the increased vasoconstrictor influence present following hemorrhage. In this sense, PGE production is favorable to the organism. However, it may be deleterious to the extent that an increase in vasodilator substance, released into the systemic circulation, can not be removed from mixed venous blood. Impaired blood flow through the lung or the destruction, by anoxia, of metabolic systems responsible for degradation of prostaglandins may allow

the accumulation of this vasodilator in the arterial circulation and ultimately support the fall in blood pressure characteristic of normovolemic shock. In this manner, PGE may be a contributing factor to the onset of the irreversible stage of shock.

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