

TITLE: NITRENDIPINE AND SUPEROXIDE DISMUTASE REDUCE ISCHEMIC RENAL INJURY

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Introduction: Calcium antagonists and free radical scavengers have independently been shown to ameliorate ischemia-induced renal failure.^{1,2} We evaluated the effect of the calcium antagonist nitrendipine, and the free radical scavenger superoxide dismutase on renal function following renal vascular occlusion in rats.

Methods: During 1.2 MAC isoflurane anesthesia, the renal pedicles were exposed in rats (n=12) which were randomly assigned one of the following pre-ischemia treatment protocols: 1) Control-vehicle only, or 2) Nit/SOD-nitrendipine 1mg·kg⁻¹ and superoxide dismutase 7mg·kg⁻¹. The renal pedicles were clamped for 60 minutes, and the animals allowed to recover. Renal function was evaluated by 24 hour creatinine clearance (CrCl) determinations 24 hours prior to ischemia; and 72 hours post-ischemia. The data were analyzed using t-tests.

Results: There were no differences between groups with respect to pre-ischemia CrCl. Post-ischemia CrCl was increased in the Nit/SOD group versus the control group (p<0.05).

Discussion: Renal ischemia initiates a number of events, which theoretically might be prevented by calcium antagonists and free radical scavengers. This study demonstrates that the combination of nitrendipine and superoxide dismutase, when given prior to renal vascular occlusion, has a salutary effect on post-ischemic renal function.

Group	Pre-ischemia CrCl	Post-ischemia CrCl
Control	2.550±0.986	0.026±0.006
Nit/SOD	2.986±0.877	0.074±0.036*

Table 1- 24 hour CrCl in ml·min⁻¹ (mean±SD).
*p<0.05 versus the control group.

References:

1. Rose H, et al: J Cardiovasc Pharm 9:S57-59, 1987.
2. Bayati A, et al: Acta Physiol Scand 130:367-372, 1987.

TITLE: TOTAL PARENTERAL NUTRITION (TPN) INCREASES MORTALITY FOLLOWING METHOTREXATE-INDUCED ENDOGENOUS SEPSIS

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INTRODUCTION: The gut is an important source of endotoxins and bacteria which are believed to be responsible for sepsis and multiple organ failure in critically ill patients. TPN results in gut atrophy and has been reported to predispose to bacterial translocation in animals. On the other hand, enteral nutrition maintains gut mass and prevents bacterial translocation. Methotrexate (MTX) interferes with cell replication, resulting in gut atrophy and bacterial translocation. We postulated that enteral feeding would minimize gut loss and prevent bacterial translocation in animals following MTX. In this study, we examined the effect of TPN and enteral feeding on survival following MTX administration.

METHODS: Following approval by our Animal Care and Use Committee, anesthetized male Sprague Dawley rats (250-300 g) had jugular vein catheters and gastro-duodenal feeding tubes placed one day prior to experiments. On the day of the experiment animals were randomized to TPN (n=6) or enteral feeding (n=7) and MTX was injected intraperitoneally at a dose of 30 mg/kg. TPN was composed of glucose and amino acids while enteral feeding was accomplished with a

peptide-based diet. Both diets contained 1 cal/ml and 0.5 g/dl protein and were fed at equal rates. Both diets contained maintenance amounts of minerals and vitamins. Following injection of MTX, animals were followed daily for survival. Five days was considered permanent survival. Survival was analyzed using Fisher's exact test. P<0.05 was considered significant (*).

RESULTS: All animals receiving TPN died before 5 days while only 2 of 7 enterally fed animals died (Figure). Preliminary data indicate that TPN animals had more bacteria translocating through the intestines (using mesenteric lymph node cultures) than enterally fed animals.

DISCUSSION: This study indicates that TPN results in higher mortality following MTX than does enteral feeding. These data suggest that TPN may predispose to infection in critically ill patients by impairing gut barrier function.

