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TITLE: SUBARACHNOID ADRENAL MEDULLARY TRANSPLANTATION

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A unique approach to the management of terminal cancer pain is that of Sagen et al(1) from the Department of Anatomy & Cell Biology at the University of Illinois at Chicago: These investigators have demonstrated that adrenal medullary tissue transplanted into the subarachnoid space of experimental animals, not only survives, but continues to produce adrenergic agonists and opioid peptides, and more importantly, produces analgesia. Following the transplantation, CSF levels of norepinephrine and met-enkaphalin are markedly increased, and the analgesia that results can be reversed by the administration of Naloxone and Phentolamine. The present report presents the preliminary results obtained in humans suffering from terminal cancer pain.

Approval for this preliminary study was obtained from the Institutional Review Board of the University of Illinois College of Medicine. Consenting patients were selected for study because they were suffering from terminal cancer pain which had become unresponsive to the narcotic analgesics. The patients had to have radiological or pathological evidence of an incurable organic lesion that limited their life expectancy, and they had to be mentally alert so that they could assess their pain following the adrenal medullary transplantation. The protocol was as follows: The patients were given Cyclosporine 10 mg/kg the day prior to and the day of the procedure. Intravenous Vancomycin and Gentamycin were given prophylactically immediately prior to the transplantation procedure. Then using sterile technic with the patient in the lateral decubitus position, lumbar puncture was performed using a 14-gauge Tuohy needle. After aspiration of sufficient CSF for culture, cytology, and biochemical assay, approximately 2 ml of suspended, human adrenal medullary tissue were injected. Patients were discharged home the following day on Cyclosporine 10 mg/kg/day. Patients were given visual analogue score sheets to monitor their pain relief at home, and they were instructed to return at 1 week, 1 month, 2 months, 4 months, and 6 months for additional lumbar puncture for CSF analysis.

All of the first four patients selected for study, two males and two females, three suffering from metastatic CA of the colon, and one from metastatic CA of the breast, demonstrated progressive, sequential decreases in their pain scores over time, with two of the patients becoming pain free within 2 weeks of the transplant, one patient at 8 weeks, and one patient at 10 weeks. One patient has had a recurrence of her pain, probably secondary to a neurological complication of her disease, but all of the others are currently off all analgesics, and all have exhibited marked increases in their activities of daily living.

In conclusion, while these obviously represent preliminary data, they would appear to indicate that this technic may provide new hope for patients suffering from terminal cancer pain.

Reference:
(1) Pain 42:69-79, 1990

A696

TITLE: THE ENDOCRINE RESPONSE TO SURGICAL STRESS: A COMPARISON OF EPIDURAL ANESTHESIA/ANALGESIA VS. GENERAL ANESTHESIA/PATIENT CONTROLLED ANALGESIA

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Introduction: Modification of the surgical stress response both intraoperatively and postoperatively may have effects upon clinical parameters of morbidity and mortality, particularly in high-risk patients. Considerable controversy exists regarding the use of regional or general anesthesia and in the techniques of postoperative pain control. Therefore, we examined the endocrine response to surgical stress in the perioperative period in patients undergoing lower extremity revascularization under epidural anesthesia with post-op continuous epidural fentanyl infusion (EPID/CEFI) or general anesthesia with post-op intravenous morphine patient controlled analgesia (GEN/PCA).

Methods: After institutional approval and informed consent, 42 patients scheduled for elective lower extremity revascularization procedures were randomized to receive EPI/CEFI (n = 22) or GEN/PCA (n = 20). Clinical decisions (premedication, hemodynamic monitoring, anesthetic agents and dosages, heart rate and blood pressure limits, and therapy) were rigorously controlled by protocol throughout the perioperative period. At specific time points (preinduction; postinduction/preincision; 15 and 60 minutes postincision; skin closure; 1, 6, 12, and 18 hours after arrival in the ICU) heart rate, mean arterial pressure, and pain scores (scale of 1 to 10, postoperative only) were recorded, and blood was obtained for subsequent measurement of plasma epinephrine (EPI) and norepinephrine (NOR) by HPLC. Intraoperative and postoperative urine was assayed for free cortisol by RIA. The data were analyzed with analysis of variance (ANOVA) for repeated measures and the unpaired t-test. Results are reported as mean ± SEM; $p < 0.05$ was considered significant.

Results: Plasma EPI and NOR were not elevated over preinduction levels during surgery for either anesthetic regimen, except during skin closure when both NOR and EPI increased significantly in the GEN group. Intraoperative heart rate, mean blood pressure, and cortisol excretion were similar in both groups. In the postoperative period plasma NOR and cortisol excretion were significantly higher in the PCA group than in the CEFI group (Figs. 1 and 2). Mean arterial pressure was elevated in the PCA group at one hour after arrival in the ICU. There were no differences at the other time points. Pain scores were low and comparable in both groups at all postoperative time points. Mean arterial blood pressures postoperatively correlated with plasma NOR levels in the PCA group.

Discussion: These data suggest that: 1) based on intraoperative suppression of EPI, NOR, and cortisol secretion, both epidural and general anesthesia are effective in suppressing stress hormone secretion in patients undergoing lower extremity revascularization procedures; 2) EPI and NOR increase during emergence from GA; 3) although PCA morphine is as effective as epidural fentanyl for control of postoperative pain following surgery, it does not suppress the NOR or cortisol response to the same degree. This latter finding suggests that epidural opiates may directly modulate the stress response to surgery.

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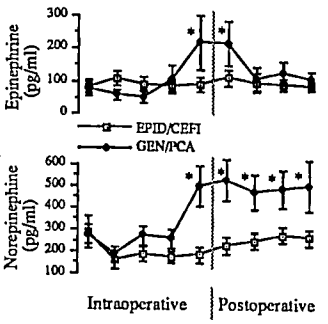
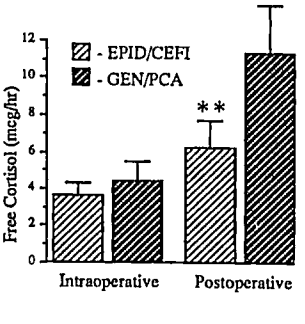
FIGURE 1



* $p < 0.05$ versus EPID/CEFI

FIGURE 2



** $p < 0.01$ versus GEN/PCA