TITLE: CLONIDINE DOES NOT CAUSE EPIDURAL INFLAMMATORY CHANGES

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Epidurally injected clonidine has been shown to be effective in the control of chronic pain in cancer patients[6] and for postoperative analgesia[1,2]. Several animal studies have shown no direct neurotoxic effects of intrathecal clonidine[3], but other work has revealed proliferation of dural connective tissue in sheep who received chronic epidural infusions of clonidine[4], which was felt to be secondary to the epidural catheter. In this study, we attempted to determine if clonidine provoked any acute inflammatory effect (< 20 days) when injected into the epidural space of rabbits.

After permission from the University of Tennessee Animal Use Committee 36 adult white rabbits were divided into six groups. Using a 20 gauge B bevel needle and the loss of resistance to air technique, an epidural injection was performed at the lumbo-sacral interspace. Groups A and B received injections of normal saline, 0.3 ml per kilogram of body mass to serve as a negative control. Groups C and D received 0.3 ml per kilogram of a normal saline solution containing talc 0.1 mg per ml, to serve as a positive control. Groups E and F received 30 ug of epidural clonidine in normal saline.

Animals in groups A, C, And E were killed on day 4 following the procedure, and those in groups B, D, and F were killed on postinjection day 10. Complete cross sections of meningeal membranes, spinal cord, and nerve roots were the made at L_{5-6} level. Specimens were processed for light microscopy and examined for cellular infiltrates, signs of inflammation and fibroblastic activity by an experienced histologic anatomist (J.E.), who was blinded to the agent injected and the time until sacrifice of each animal.

In all animals which received epidural injections of either saline or clonidine, microscopic examination revealed no white cell infiltrates and no fibroblastic activity. All animals that received epidural injections of saline containing talc had marked epidural infiltration of tissue macrophages. In group C an average of 74 (± 23) macrophages per slide were seen in the epidural space, and in group D , an average of 420 (±113) macrophages per slide in the epidural space. No polymorphonuclear cell or fibroblasts were identified. There was no thickening of the meningeal membranes or nerve roots in any animal.

Our findings of no white cells, tissue macrophage and/or meningeal thickening indicate that there is little if any chemical irritation or inflammatory reaction when clonidine is injected into the epidural space. These findings are consistent with clinical studies which report no neurologic side effects after epidural injection of clonidine. The lack of changes in this series does not preclude the possibility of inflammatory reactions in other species or individual sensitivity to this agent.

REFERENCES

1. Anesthesiology 71:647-652, 1989
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TITLE: A COMPARISON OF EPIDURAL AND INTRAVENOUS PCA AFTER GYNECOLOGICAL SURGERY

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This prospective, randomized study assessed the postoperative analgesia of epidural PCA (E) with intravenous PCA (IV). Recent studies have questioned the advantage of epidural narcotics compared to IV PCA.[1,2]

After approval by the IRB, post-randomization consent was obtained on 51 ASA status I-III patients undergoing major gynecological surgery. Group IV (28 patients) received morphine (M) 1 mg bolus with a 6 min lockout. Group E (23 patients) received M 0.4 mg/hr infusion with a 0.2 mg PCA bolus, and 10 minute lockout. Both groups had their M dose adjusted as needed for side effects or pain.

All patients received N_2O/ISF general anesthesia. Group E received intraoperative epidural lidocaine and M (2-3 mg). Group IV received iv M loading before abdominal closure; this was continued in the recovery room (2 mg M q 5 minutes until analgesic) until PCA was started. Evaluation of pain intensity was by Visual Analog Scales (VAS) for 96 hours postop. These were performed 3-4 times on the day of surgery (day 0) and on postop days 1-3, between 8 am and 11 pm. Pain at rest, on leg movement, and after coughing were measured and side effects (nausea, pruritus, sedation) assessed using VAS. Patient satisfaction, anxiety and overall pain were measured once daily using VAS. Values were analyzed by repeated measures ANOVA and are presented as mean ± SD (Table 1). Daily and total M consumption were assessed by Student's t-test.

TABLE 1		DAY 0	DAY 1	DAY 2	DAY 3
Pain at Rest	IV	6.1±2.0	4.3±2.3	3.9±2.2	3.5±2.3
	E	3.6±2.0	2.4±1.5	1.6±1.6	1.6±1.5
Pain on Movement	IV	7.2±2.0	6.7±1.8	6.2±2.0	5.3±2.2
	E	5.2±2.3	5.0±2.4	3.6±2.2	3.7±2.0
Pain on Coughing	IV	8.2±1.5	7.5±1.8	7.4±2.0	6.8±2.1
	E	6.6±2.4	6.0±2.5	4.9±2.4	4.6±2.2
Overall Pain	IV	7.5±2.4	6.1±1.7	5.2±2.1	4.8±2.2
	E	5.3±2.5	3.9±2.2	3.3±2.2	3.3±2.2

All pain scores were significantly lower in Group E compared to the IV group. Sedation scores were decreased in Group E on postop days 1, 2, and 3 ($p<.05$). There were no significant differences in other side effects, satisfaction or anxiety scores. Total M consumption was also dramatically reduced in Group E vs Group IV (34 ± 16 mg vs 124 ± 69 mg over 96 hr, respectively, $p<.001$).

References

1. Anesthesiology 71:A757, 1989.
2. Anesth Analg 70:72, 1990.