## A661

TITLE: THE SYSTEMIC EFFECTS OF EPIDURAL CLONIDINE AND BUPIVACAINE.

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INTRODUCTION. The alpha 2 adrenergic agonists are of increasing interest for their anxiolytic, analgesic and anesthetic sparing properties [1]. Epidural clonidine has been shown to produce analgesia of variable duration and marked hemodynamic effects [2]. The aim of this study was to examine the systemic effects of epidural clonidine and compare the effects to those of bupivacaine, and a combination of the drugs.

METHODS. With ethical committee approval and patient consent, healthy patients in the age range 30-75 years, and scheduled for hip replacement under a standardised general anesthesia, were included. Approximately 30 minutes prior to the end of surgery, patients were randomly allocated to receive either clonidine 150 mcg 1ml, diluted to 10 ml in 0.9% saline, bupivacaine 0.25% 10 ml or a combination of the drugs. Postoperatively, a blinded nurse observer recorded sedation and pain scores, blood pressure, heart rate and respiratory rate. Height, grade and duration of sensory and motor blockade were recorded. The incidence of urinary retention and emetic symptoms were also noted.

RESULTS. Demographic data was similar in the three groups. In all groups, mean arterial pressure (MAP) and HR (Table 1) decreased during the course of the study, but there was no significant differences between the groups. Although sedation is a prominent effect of oral clonidine, postoperative sedation scores were similar in all three groups. There were no episodes of respiratory depression in any of the patients studied. Pain scores were lower in both the clonidine groups, and analgesic requirements were significantly reduced ($p<0.05$). Clonidine alone produced no sensory or motor impairment. The addition of clonidine to bupivacaine resulted in an increased duration of both motor and sensory block, but this was not significant. Height and intensity of the block were not increased. Urinary retention and the incidence of catheterisation was similar in all three groups. There was no increase in emetic symptoms associated with the use of clonidine.

DISCUSSION. The analgesia produced by clonidine is of great interest. This study demonstrates that epidural clonidine produces analgesia in the absence of significant systemic effects, and its addition to low dose bupivacaine prolongs analgesia without significantly altering motor or sensory function.

TABLE 1. Mean (± S.E) max. changes in MAP and HR

| | CLONIDINE | BUPIVACAINE | COMBINATION |
|---|---|---|---|
| MAP (mmHg) | 19 ±4 | 20 ±3 | 20 ±3 |
| HR (bpm) | 6 ±2 | 5 ±2 | 9 ±3 |

REFERENCES:
1. Seminars in Anesthesia 1980; 7: 170-177.
2. British Journal of Anesthesia 1989; 63: 516-519.

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TITLE: PHARMACOKINETIC AND DYNAMIC STUDIES OF INTRATHECAL, EPIDURAL, AND INTRAVENOUS DEXMEDETOMIDINE

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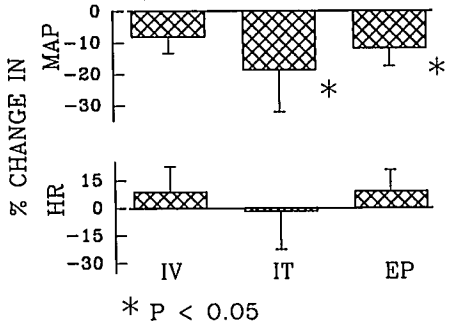
**Introduction.** Epidurally administered clonidine produces analgesia, but may also decrease BP. Although clonidine has been effective in treating chronic pain syndromes, its use in acute pain is less certain, due to large dose requirements and hemodynamic side effects. Dexmedetomidine, a more potent and specific $\alpha_2$-adrenergic agonist, may produce analgesia with fewer side effects. Although dexmedetomidine is now being evaluated for potential clinical use, dural transfer and elimination from cerebrospinal fluid (CSF) have not been evaluated. We examined the pharmacokinetics and pharmacodynamics of intrathecal (IT), epidural (EP), and IV dexmedetomidine in sheep CSF and plasma.

**Methods.** Following approval by the Animal Care and Use Committee, 6 non-pregnant ewes were anesthetized and arterial, venous, lumbar epidural and intrathecal catheters inserted. Two days later, each ewe received, on separate days and in random order, dexmedetomidine 100 $\mu$g by IT, EP, or IV injection. Plasma and CSF samples were obtained at specified intervals for pharmacokinetic analysis. Mean arterial pressure (MAP) and heart rate (HR) were recorded at each sampling time and blood was obtained for blood gas analysis. Plasma and CSF concentrations will be determined by mass spectrometry.

**Results.** Maximal hemodynamic effects were observed within 30 min of injection. IT and EP administration decreased MAP, whereas there were no statistically significant changes in HR (Fig. 1). Pharmacokinetic data are pending.




**Discussion.** These data agree with the clonidine pharmacodynamic data obtained in sheep: the BP lowering effect is greater following intraspinal than systemic administration, reflecting a local action on spinal sympathetic outflow. However, the lack of significant changes in HR in this study may relate to pharmacokinetic differences between dexmedetomidine and clonidine. Although these pharmacodynamic data support the use of epidural dexmedetomidine, neurotoxicity studies are needed to determine the safety of spinal administration.

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