TITLE: MICRODOSE INTRATHECAL CLONIDINE AND MORPHINE FOR POSTOPERATIVE ANALGESIA

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Introduction. Alpha$_2$ adrenergic agonists are analgesic when given intrathecally in animal and man.[1,2] Further, these agents may be synergistic when given intrathecally in combination with morphine, potentially reducing respiratory complications with higher doses of spinal morphine. The analgesic impact of intrathecal clonidine, a partial alpha$_2$ adrenergic agonist, was studied in patients having lumbar laminectomy utilizing two techniques of assessment, serial visual pain analogue scores (VPAS) and cumulative intravenous patient controlled morphine analgesia (PCA).

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Methods. All patients gave their written and oral informed consent. Thirty two patients, ages 23-71, 23 male, 7 female, scheduled for laminectomy were randomized to receive double blind an intrathecal analgesic at dural closure. Group A, control (C), received intrathecal saline (2 ml), Group B, (CL), 100 mcg of preservative free clonidine in 2cc saline, Group C, (CL-M), 100 mcg of clonidine Hcl and 100 mcg morphine sulfate, both preservative free, in 2 ml saline. All patients received balanced N_2O/O_2, fentanyl anesthesia with additional inhalational forane or enflurane at anesthesiologist's discretion. Each patient was instructed in the use of PCA delivered morphine; general postoperative parameters were: 2 mg loading dose followed by unit dose 1 mg, lockout 6 minutes with initial upper limit of 20 mg per 4 hours increased as needed. A pain observation nurse recorded blood pressure, pulse, respiration, and serial PCA morphine use for 24 hours. Serial visual pain analogue scales (0-no pain to 10-worst pain ever) were recorded at 1,1.5,2,3,4,5,6,7,8,12,16, and 24 hours. The scores are summarized in Table I along with cumulative PCA morphine use. Analysis included one way analysis of variance with Students-T or Krauskal Wallace nonparametric tests where appropriate.

Results and Discussion. As shown in Table I, neither intrathecal clonidine or its combination with intrathecal morphine, decreased pain intensity significantly compared to PCA morphine. Variability in pain report may eclipse real differences since clonidine alone and combination initially decreased intensity relative to control. Beyond 24 hours PCA patients generally reported less pain intensity (not significant). These results are supported by the cumulative PCA morphine doses. During the first 8 hours, combination clonidine and morphine patients required significantly less PCA morphine than control or CL alone. This trend persisted through 16 hours for the clonidine alone and combination groups; though combination patients required on average less MS than control, this was not significant. Paralleling VPAS data during the last 12 hours, over the last 16 hours, PCA intake for clonidine patients showed a trended to more; the combination group took significantly more PCA morphine. These data suggest 1. A larger intrathecal dose of clonidine is needed to show differences (if they exist), 2. The clonidine-morphine combination reduces the PCA morphine requirement for at least 8 hours in this setting, and 3. A rebound pain phenomenon may occur with intrathecal clonidine perhaps acutely influencing the potential utility of such spinal agonists. The authors speculate that bulbospinal adrenergic inhibitory pathways may be blocked by clonidine ascending in the CSF, inhibiting morphine analgesia mediated at a higher level.

References.
1. Yaksh TL, Reddy SVR: Anesthesiology 54:451-467, 1981
2. Coombs DW, Saunders RL, Lachance D, et al: Anesthesiology 62:358-363, 1985.

Table I. Mean ± SD of Serial VPAS and PCA Morphine

Groups (n)	Cumulative 1-8 hr VPAS	12 hr VPAS	24 hr VPAS
C (14)	272 ± 200	27.5 ± 23.6	20.5 ± 17.0
CL (9)	244 ± 153	32.6 ± 28.0	32.1 ± 34.6
CL-M (9)	211 ± 128	41.3 ± 25.1	28.8 ± 20.9

	Cumulative PCA MS			
	0-8 hr	0-12 hr	0-16 hr	24-8 hr
C (14)	11.6 ± 8.1	15.4 ± 9.8	18.4 ± 9.2	15.9 ± 10.7
CL (9)	12.2 ± 6.7**	20.4 ± 13.4	26.9 ± 17.9	26.2 ± 19.1 (tc)
CL-M (9)	6.1 ± 6.2*	11.0 ± 8.4 (tCL)	16.4 ± 9.2 (tCL)	25.0 ± 12.1*

*P ≤ 0.05 Control versus treatment
**P ≤ 0.05 Group B versus C
T_x = Trend (P ≤ 0.10) and reference group (x)