Title: INTRATHECAL MORPHINE *DOES NOT* REDUCE THE MAC OF HALOTHANE IN HUMANS: RESULTS OF A DOUBLE BLIND STUDY

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Introduction: Peridural narcotics are frequently used in the treatment of postoperative pain. Clinical observations as well as animal work suggest that anesthetic potency is augmented by intrathecal morphine (ITMS)[1]. This study was designed to investigate whether preoperative ITMS reduces halothane MAC in patients undergoing abdominal surgery.

Methods: With institutional approval and informed consent, we studied 24 adult unpremedicated ASA I or II patients scheduled for lower abdominal surgery. Patients taking medication known to affect MAC were excluded. They were randomly assigned to control (CTRL) or ITMS groups. ITMS patients received 15 µg/kg preservative free morphine sulfate (Duramorph®) intrathecally via lumbar puncture at L4/5 (after infiltration with 1% lidocaine) in the right lateral decubitus position at least 2.5 hours prior to surgical incision to ensure onset of clinical effect[2]. With the exception of subarachnoid puncture, CTRL patients underwent an identical procedure, including initial skin infiltration and placement of the introducer needle. Care was taken to blind all patients to the administration of ITMS. At least two hours thereafter, anesthesia was induced with halothane and oxygen. Tracheal intubation was facilitated by intravenous succinylcholine. After tracheal intubation end-tidal halothane concentration (ETHal) was selected according to the modified up-down method of Dixon[3] and adjusted for age[4]. Mechanical ventilation was adjusted to maintain end-tidal carbon dioxide tension (ETCO2) between 27 and 34 mmHg. ETHal and ETCO2 were measured using a Puritan-Bennett model 254 airway gas monitor. The instrument was calibrated immediately prior to each study according to manufacturer's recommendations, using a standardized calibration gas mixture. The preselected ETHal was maintained at a constant level for a minimum of 20 minutes (Tequ) prior to skin incision to allow for adequate equilibration between alveolar and brain anesthetic concentrations. Neuromuscular blockade, mean blood pressure (MBP), heart rate (HR), ETCO2, finger pulse oxygen saturation (SaO2) and pharyngeal temperature were monitored at 5 minute intervals throughout the study period. Complete return of neuromuscular transmission was always present prior to skin incision. An observer blinded to the patient's assignment (ITMS vs. CTRL) determined whether movement occured with skin incision. Purposeful extremity or head motions but not coughing was considered movement. The data were analyzed using a modification of Dixon's method for sequential sampling of quantal response data[3], as well as Student's t-test where appropriate.

Results: The responses to incision of CTRL and ITMS patients are shown in the figure. MAC (±SEM) after ITMS was 0.79 ± 0.02 compared to a CTRL MAC of 0.85 ± 0.08 (n.s.). There were no significant differences among the groups with respect to age, preincision temperature, MBP, HR, SaO2 or ETCO2. Likewise, Tequ and times from injection and induction to incision (Tms-in and Tind, respectively) were not different (see Table).

Discussion: Our results differ from those of another group who recently reported a 40% reduction of human halothane MAC with preoperative ITMS[1]. Differences in study design may account for this discrepancy. Failure to blind patients in the previous study may have resulted in a tendency for patients knowingly receiving intrathecal morphine to be more at ease preoperatively than controls, biasing the results toward a reduction in MAC[5].

The present data suggest that the anesthetic potency of halothane is not significantly affected by ITMS administered at least 2.5 hours prior to surgical incision. Further investigation of the effect of preoperatively administered peridural narcotics on later intraoperative anesthetic requirements and emergence is needed to delineate their characteristics and utility as adjuncts to general anesthesia .

References:

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Fig.: Responses to surgical incision:

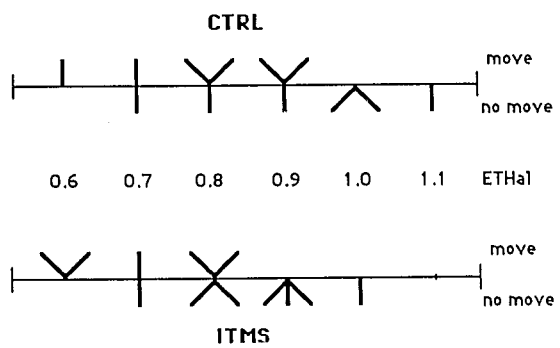

TABLE: PHYSIOLOGIC VARIABLES AND TIME INTERVALS (Mean±S.D.)

	Age (yrs)	MBP (mmHg)	HR (bpm)	ETCO2 (mmHg)	Temp (°C)	Tequ (min)	Tind (min)	Tms-in (min)
CTRL	31.2±8.9	77.5±9.6	74.4±15.9	31.0±3.4	36.1±0.2	22±3	41±6	203±65
ITMS	31.4±7.9	73.2±8.8	66.4±9.5	29.8±2.6	35.7±0.6	22±4	37±8	189±56