POSTER SESSION VIII

A769

TITLE: KETOROLAC DOES NOT DECREASE THE MAC OF HALOTHANE OR DEPRESS VENTILATION IN RATS

AUTHORS: GF Rich, M.D., Ph.D., R Schacterle, M.S., JC Moscicki, M.S., CA DiFazio, M.D., Ph.D., JM Adams, Ph.D.

AFFILIATION: Univ of Virginia Health Sciences Center, Departments of Anesthesiology and Biomedical Engineering, Charlottesville, Virginia 22908

INTRODUCTION: Ketorolac is a non-steroidal antiinflammatory drug which is useful for perioperative analgesia. However, it is unknown if I.V. doses of ketorolac have significant CNS effects that would decrease MAC or cause respiratory depression. Therefore, we evaluated MAC reduction and CO_2 response curves in rats administered IV ketorolac (0.2, 2.0, 20 and 40 mg/kg).

METHODS: Institutional approval was given for our study. Eighteen male Sprague-Dawley rats were anesthetized with halothane and a tracheostomy was performed for airway control. The femoral vessels were cannulated for IV administration of ketorolac and mean arterial pressure(MAP) and blood gas sampling. The temperature (37.0 ± 0.1°C) was maintained constant throughout the study.

Group I MAC reduction (6 rats) - Ventilation was controlled ($PaCO_2$ = 39 ± 1mmHg) with a rodent volume ventilator. Control MAC, determined by the tail clamp technique, was compared to the MAC after the 4 successive doses of IV ketorolac.

Group II CO_2 response curves (12 rats) - Spontaneous ventilation using 1% halothane and 99% O_2 (to minimize peripheral chemoreceptor contribution) was used to generate CO_2 response curves. A small closed circle system with attached balloon allowed rebreathing as the end-tidal CO_2 ($ETCO_2$) increased from 5.5% to 9.5% over 3 to 5 minutes. A pneumotachometer and circuit integrator were used to calculate minute ventilation. An Engstrom Eliza CO_2 analyzer sampled CO_2 from within the tracheostomy tube. The CO_2 response curves were generated prior to and after the 4 successive doses of IV ketorolac (n = 6) or 4 IV placebo doses (n = 6) allowing 20 minutes between runs for equilibration. All results were compared by ANOVA.

RESULTS:

Group I. There was no significant reduction in the halothane MAC by any of the 4 doses of ketorolac (Table I). The MAP (103 ± 2 mmHg) did not change throughout the study.

Group II. The MAP (80 ± 3 mmHg) remained unchanged after 0.2, 2.0, and 20 mg/kg IV ketorolac but decreased ($p < .05$) by 8% after 40 mg/kg. Ketorolac did not effect the resting $ETCO_2$ (5.3 ± 0.1%). Likewise, ketorolac did not effect the slope of the CO_2 response curves compared to control or to placebo doses (Table II).

CONCLUSION: Despite potent analgesic effects, ketorolac appears to have minimal CNS effects as MAC is not decreased even at extremely large (40 mg/kg) I.V. doses. Other investigators have demonstrated in adult patients that ketorolac up to 90 mg has minimal cardiovascular effects[1]. This study demonstrates that larger I.V. doses of ketorolac produce clinically insignificant effects on MAP. Lack of respiratory depression has been previously shown in unanesthetized human volunteers receiving up to 90 mg IM ketorolac[2]. This study demonstrates that large IV doses do not depress ventilation under halothane anesthesia.

In conclusion, I.V. ketorolac may be administered with a large margin of safety without central effects including anesthetic MAC reduction, MAP changes, or respiratory depression.

REFERENCES:

1. Murray, Br J Anaesth (1989) 63:601-603
2. Bravo, Eur J Clin Pharmacol (1988) 35:491-494

Table I. MAC (x ± SEM)

Ketorolac (mg/Kg)	MAC %
0	0.82 ± .02
0.2	0.89 ± .05
2.0	0.86 ± .03
20	0.80 ± .02
40	0.80 ± .03

Table II. CO_2 Response Curves (x ± SEM)

Ketorolac (mg/kg)	slope ml/min/%CO_2	placebo	slope ml/min/%CO_2
0	76±5	0	66±11
0.2	72±10	0	69±8
2.0	77±9	0	59±11
20	71±9	0	51±8
40	61±9	0	55±9

A770

TITLE: NALBUPHINE AMELIORATES THE PRURITUS CAUSED BY CONTINUOUS EPIDURAL BUPIVICAINE-FENTANYL IN POST-OPERATIVE PATIENTS.

AUTHORS; LM Newman, PhD, MD, PB Dragisic, MD, TR Lubenow MD, RJ McCarthy, PharmD, AD Ivankovich, MD

AFFILIATION: Department of Anesthesiology Rush-Presbyterian-St. Luke's Medical Center, Chicago IL 60612

Continuous epidural infusions of fentanyl/bupivicaine [F/B] provide excellent pain relief for post-operative patients. Pruritus is a common side effect[1]. Small intravenous doses of nalbuphine [N] have been administered to treat the epidural narcotic induced pruritus[2]. The present study investigated whether adding N to the epidural F/B mixture would reduce the pruritus seen with F/B in post-operative patients.

After institutional approval 297 consecutive patients were randomly allocated to one of four groups. All patients received the F/B [.001%/.1%] mixture. 101 received epidural F/B only. In the three remaining groups nalbuphine was added to the epidural solution to a final concentration of: .0066% (N=59)[$F/B/N_{10}$], .0132% (N=76) [$F/B/N_{20}$], and .0264% (N=61)[$F/B/N_{40}$]. All infusion rates were between 7 and 10 cc per hour. The patients were evaluated at 24 hours post delivery for analgesia, using the visual analogue scores [VAS], and monitored for the occurrence of nausea/vomiting [N/V], pruritus [PR], and sedation [SED]. The data were analyzed by use of the ANOVA and the χ^2 statistic. A $p<.05$ was considered statistically significant.

All patients received similar amounts of the epidural mixtures and no patients exhibited a significant decrease in respiratory rate. Postoperative evaluation of pain and the occurrence of side effects data are presented in the table. There was a statistically significant reduction in the occurrence of pruritus with the addition of nalbuphine .0264% There were no significant differences in N/V, PR, or SED.

	F/B	$F/B/N_{10}$	$F/B/N_{20}$	$F/B/N_{40}$
VAS	2.9	2.7	3.7	3.0
N/V [%]	18.8	20.3	19.7	8.2
PR [%]	10.9	13.6	6.6	1.6*
SED [%]	7.9	13.6	5.3	9.8

*$p<.05$ when compared to F/B and $F/B/N_{10}$

These data support the notion that by mixing agonists with agonist-antagonist narcotics for epidural administration the side effects of agonists alone may be ameliorated. Additional support comes from recently published data demonstrating that the addition of 10 mg nalbuphine to 5 mg morphine, administered epidurally, significantly decreases the incidence of pruritus, nausea and vomiting, and urinary retention[3]. An additional advantage of nalbuphine is that unlike butorphanol it does not cause an increase in sedation[4].Thus it is possible to provide superb post-operative analgesia with minimal or no side effects.

References: 1. Anest Analg 67:559,1988.
2. Anesthesiology 65:216, 1986.
3. Anesthesiology 71:A703, 1989.
4. Anesthesiology 73:A800, 1990