POSTER SESSION VIII

A745

TITLE: COMBINATION OF LOW DOSE EPIDURAL MORPHINE AND INTRAMUSCULAR DICLOFENAC SODIUM FOR POSTCESAREAN ANALGESIA

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Introduction: Epidural morphine (EM) produces profound analgesia but also causes many adverse effects in a dose dependent manner. Non-steroidal anti-inflammatory drugs have been shown to provide postoperative analgesia[1] and relieve postpartum uterine cramps.[2,3] Parturients suffered from two different kinds of pain after cesarean section, namely wound pain (WP) and uterine contraction pain (UP).[2] We conducted the following study to evaluate the analgesic efficacy, in terms of relieving either WP or UP, of the combination of low dose EM and intramuscular (IM) diclofenac sodium in comparison with either of the two managements alone after cesarean delivery.

Methods: After informed consent and with institutional approval, 120 parturients under epidural anesthesia were allocated at random with double-blind design into 4 treatment groups. Group A: received 10 ml normal saline (NS) epidurally and 3 ml NS IM; Group B: the same epidural NS and 75 mg diclofenac IM; Group C: 2 mg EM in 10 ml NS and 3 ml NS IM; Group D: 2 mg EM in 10 ml NS and 75 mg diclofenac IM. Epidural injections were given after placenta delivery and the IM injections were given upon arrival at postanesthesia recovery room. Pain scores (verbal analog score) of WP and UP were recorded at 2, 4, 8, 12, 18, and 24 hours after epidural injection. Vital signs and adverse effects were also closely observed for 24 hours. Meperidine 50 mg IM as needed was used as the "rescue analgesic" for all parturients. Nonparametric one way analyses of variance (Kruskall-Wallis) were used for pain scores at each specific time interval. Mann-Whitney rank sum tests were used to do pairwise comparison when intended. A p value < 0.05 was considered statistically significant.

Results: Group D was superior to the other three groups in analgesic effect for both WP and UP from 4 to 18 hour ($p < 0.05$). Diclofenac (Group B) alone was not effective for postcesarean analgesia and 2 mg EM (Group C) was not as effective in the relief of both WP and UP as compared to Group D (Fig. 1). Group A and B required more rescue meperidine than Group C and D, and none in the Group D requested supplemental analgesia. Both Group C and D showed similarly higher incidence of nausea, vomiting and pruritus than that of Group A and B. No clinically significant respiratory depression was observed in any of the parturients who were monitored continuously with pulse oximeter.

Discussion: Our results demonstrate that diclofenac sodium alone is not effective for postcesarean analgesia. The addition of diclofenac sodium, a non-opiate prostaglandin synthetase inhibitor, enhances the analgesic effect of low dose (2 mg) epidural morphine, especially in the control of postcesarean uterine cramps, without potentiating its adverse effects.

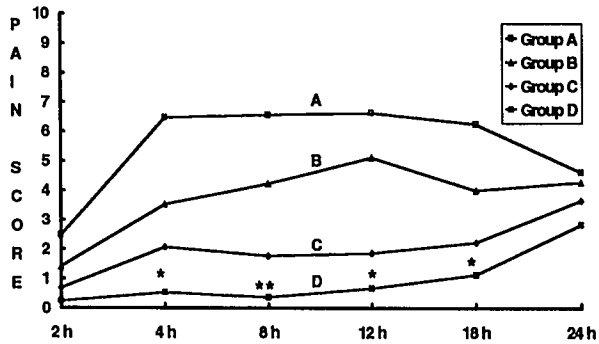

Figure 1. Trends of mean uterine contraction pain score among the four treatment groups. *$p < 0.05$, **$p < 0.005$, Group C *vs.* D

References:
1. Hodsman NBA et al. Anaesthesia 42:1005-8, 1987
2. Bloomfield SS et al. Pain 27:171-179, 1986
3. Sunshine A et al. J Clin Pharmacol 25:374-380, 1985

A746

TITLE: STABILITY OF EPIDURAL FENTANYL AND BUPIVACAINE MIXTURE.

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Stability data has not been reported for commonly used epidural mixtures. The aim of this study was to investigate the stability of fentanyl 4ug/ml, bupivacaine 0.1% and adrenaline 1/200000 in 0.9% saline 100ml PVC containers, when exposed to varying environmental conditions. The antimicrobial activity of the combined solution was also tested.

METHOD. Nine groups of six 100ml PVC saline bags were mixed to contain either bupivacaine(B), fentanyl(F), fentanyl and bupivacaine(FB) or fentanyl bupivacaine and adrenaline(FAB). Samples were taken from each group and analysed by HPLC over 56 days to detect adsorption, drug degradation, precipitation and stability in darkness, temperatures of 4°C and 35°C, after freezing and autoclaving (121°C for 30 minutes). Staph aureas(ATCC 29213) was incubated in BHI broth, standardized and diluted to obtain 10^4 colony forming units (cfu)/ml. One ml inoculums were added to 9ml portions of solution and test broth. These were incubated at 35°C, 22°C and 4°C and sampled for colony counts.

RESULTS.Fentanyl and bupivacaine undergo adsorption onto PVC bags to day 3 (table) but remain stable thereafter to day 56 under all environmental conditions. Fentanyl exhibits greater and earlier adsorption under high temperatures. Adrenaline is stable at room temperature and 4°C, but is adsorbed at higher temperature. It is progressively degraded to day 56 under all conditions except when kept at 4°C. Freezing conferred no advantage for drug stability. Autoclaving resulted in significant reduction for all 3 drugs. The tested solution returned less than 10cfu/ml within 4hrs at 35°C and 8 hrs at 22°C. At 4°C counts remained the same as the starting inoculum.

CONCLUSIONS. The epidural mixtures tested are stable at room temperature for 3 days. If adrenaline is used storage should be at 4°C. The solution is capable of sustaining Staph aureas for 8 hrs at 22°C. Mixtures must be established under sterile conditions as autoclaving is not possible.

TABLE : Percentage of initial concentration

	Room temperature		35°C	
Drug	Day 3	56	3	56
Bupivacaine	90.7*	88.5	92.1*	89.1
Fentanyl	87.4*	87.1	81.2*#	81.9
Adrenaline	94.9	88.9*	88.0*#	62.7"

Student t test (Bonferroni correction) $p<0.05$

* compared with day 0; # Day 3(35°C) vs Day 3 (Room temperature); " compared with D56 (Room temperature)