Title: TRANSNASAL ANALGESICS: A NEW METHOD FOR PAIN RELIEF IN POST-CESAREAN SECTION PATIENTS

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Introduction: Butorphanol tartrate is a synthetic agonist-antagonist analgesic which is currently used as an intramuscular or intravenous injection for pain relief. Rapid uptake and delivery to the central nervous system of this relatively lipophilic drug can be expected from the highly vascular nasal mucosa. This study is a double blind, double dummy, placebo controlled study evaluating the analgesic efficacy and side effects of three dosage regimens of transnasal butorphanol as compared to intravenous butorphanol in post-cesarean section patients.

Methods: Approval of the Institutional Review Board and informed consents were obtained. A total of 183 healthy post-cesarean section patients experiencing moderate to severe pain were enrolled in the study. Patients were randomly assigned to receive one of five drug regimens in a double blind fashion: Group I: 2mg butorphanol (B) intravenously; Group II: 2mg B transnasally (TN); Group III: 1mg B TN followed by a repeat dose of 1mg at 60 min; Group IV: 0.5mg B TN followed by a repeat dose of 0.5mg at 60 min; Group V: placebo. Intranasal administration was done using a Valois Metered Pump. After administration of medications, patients were evaluated at 5, 15, 30, 60 and 90 min and hourly throughout the eight hours after the initial dose. Remedication with study drugs as required was allowed up to a maximum of 3 days. Pain intensity (PI) was evaluated by the patient on a scale of 0-3 as none, slight, moderate, or severe. Pain relief (PAR) was noted on a scale from 0-4 as none, little, some, a lot, or complete. The following were derived from the clinical measurement of pain and pain relief for each patient as follows: 1. sum of pain intensity difference (SPID); 2. total pain relief (TOTPAR). Nasal mucosa was examined pre and post study for any signs of irritation and side effects were also noted.

Results: are presented in the table. Onset of analgesia was within 15 min for all active drug groups. The average duration of analgesia was approximately 4 hours for all the transnasal groups, which was significantly longer than the IV group, which was approximately 3 hours (P<0.05). Mean duration of analgesia for all active groups was significantly longer than the placebo. The average TOTPAR and SPID were also higher for all the TN groups compared to the IV group and all active groups were significantly higher than placebo. Somnolence was the most frequent side effect but patients were easily arousable. There were no incidences of nasal mucosa irritation, cardiovascular or respiratory depression.

Discussion: It is concluded that transnasal butorphanol represents a safe and effective alternative to injectable analgesics for post cesarean section pain and offers better and longer duration of analgesia compared to IV butorphanol.

Table

Group	Duration Analgesia	TOTPAR	SPID	Pt's Global Assessment
I n=37	**3.05 ± 0.28	**6.96 ± 1.09	**2.62± 0.73	3.19 ± 0.18
II n=36	4.19 ± 0.28	10.93± 1.10	4.89± 0.74	3.20 ± 0.16
III n=35	4.31 ± 0.29	11.19± 1.12	4.77± 0.75	3.00 ± 0.17
IV n=38	3.65 ± 0.27	8.40 ± 1.07	3.40± 0.72	2.65 ± 0.17
V n=37	*2.07 ± 0.28	*3.21 ± 1.09	*0.00± 0.73	*2.04 ± 0.20

* P<0.05 vs other groups
** P<0.05 vs groups II or III
Values are mean ± SEM