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TITLE: Failure of Ketorolac to Prevent Severe Postoperative Pain Following Outpatient Laparoscopy

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Ketorolac tromethamine (Toradol®, Syntax) is a recently approved injectable nonsteroidal anti-inflammatory analgesic. Ketorolac 10-30 mg has been found to be equipotent to the analgesic effect of morphine 6 mg¹. Our hypothesis was that intraoperative ketorolac would reduce the requirement for fentanyl in the immediate postoperative period and the side effects associated with the narcotic analgesics.

Method: Institutional Review Board (IRB) approved this ongoing study and each patient gave written informed consent. Fifty-four ASA 1 or 2 female patients, scheduled for outpatient laparoscopy participated in this study. After premedication with midazolam 1-2 mg IV, anesthesia was induced with propofol 2.5 mg.kg⁻¹, and maintained with a propofol infusion (200-50 µg.kg⁻¹.m⁻¹) and 70% nitrous oxide, oxygen, and vecuronium. Each patient received metoclopramide 10 mg IV at the end of the operation as a prophylactic antiemetic. At the time of induction of anesthesia, patients received the following analgesics in a randomized double blind fashion:

- Group 1: Fentanyl 1 µg.kg⁻¹ IV, plus saline IM
- Group 2: Fentanyl 1 µg.kg⁻¹ IV, plus ketorolac 30 mg IM
- Group 3: Fentanyl 1 µg.kg⁻¹ IV, plus ketorolac 60 mg IM
- Group 4: Saline IV, plus ketorolac 30 mg IM
- Group 5: Saline IV plus ketorolac 60 mg IM

All test medications were supplied in 2 ml volumes. Intramuscular injections were given in the deltoid muscle. Severe pain in the postoperative period was treated with incremental doses of IV fentanyl 25 µg. Later, when the patient could tolerate oral fluid, either ibuprofen or acetaminophen with codeine was used for pain relief. Once alert, patients assessed their pain on a 100 mm Visual Analogue Scale (VAS) every 30 minutes in the recovery room. Fentanyl requirements in the recovery room, analgesic requirements during the first 24 hours after the operation, incidence of nausea and vomiting, time to ambulate, and time to discharge were recorded. ANOVA or chi square test (contingency table) were used for statistical analysis.

Results: The demographic variables and the duration of anesthesia were comparable among the groups. There were no differences in fentanyl requirements in the postoperative period among the five groups nor were there any differences in the time to discharge or the incidence of nausea and vomiting in PACU or at home.

Postoperative Narcotic Requirements and Pain Scores

Group	n	Total Fent Req in PACU		VAS (30 min)	
		µg mean (SD)	mm mean (SD)	µg mean (SD)	mm mean (SD)
1	10	47.5 (49.2)	51 (20.3)		
2	10	50 (58.9)	37 (25.7)		
3	8	53.1 (52.5)	43 (15.3)		
4	13	46.2 (50.8)	55 (24.2)		
5	13	65.3 (50.5)	55 (19.2)		

No significant differences (ANOVA)

Discussion: The onset of action of ketorolac after an IM injection is reported¹ to be about 30-45 minutes, with a duration of action of 4-6 hours. Thus, a 30-60 mg dose given at the time of induction of anesthesia for a 60 minute procedure should have its near peak effect at the end of the operation and should last for several more hours. However, we found ketorolac by itself failed to reduce the fentanyl requirement in the recovery room after a laparoscopic procedure. It is possible that pain after laparoscopy is different than the other types of pain reportedly alleviated by ketorolac (an inhibitor of prostaglandin synthesis) or that a different combination of ketorolac with a narcotic may be necessary to prevent severe post-laparoscopy pain.

References:

1. Litvak KM, and McEvoy GK: Ketorolac, an injectable nonnarcotic analgesic. Clin Pharmacy, 9:921-933, 1990.

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TITLE: ESMOLOL BLUNTS TACHYCARDIA DUE TO TOPICAL COCAINE AND LIDOCAINE WITH EPINEPHRINE INFILTRATION

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Introduction. Topical cocaine combined with local injections of lidocaine (LIDO) with epinephrine (EPI) IS used for anesthesia during transnasal surgery (1). The short-acting cardioselective β-adrenergic blocker, esmolol, has been used to treat EPI- and cocaine-induced cardiovascular side effects (2). This study was conducted to evaluate minute-to-minute changes in heart rate (HR) and mean arterial pressure (MAP) following intranasal topical cocaine combined with LIDO-EPI infiltration, and the ability of esmolol to blunt these effects.

Methods. With informed consent and institutional approval, 24 patients scheduled for same-day surgery were randomized using double-blind design to receive study solution of placebo, or either of 2 doses of esmolol, 100 mg (ES-100) or 200 mg (ES-200). Cocaine (200 mg) in solution was topically applied intranasally for 5 min, after which baseline values for HR and MAP were obtained. Study solution was then injected as iv bolus. After 90 sec (Fig 1; min 0), HR and MAP were again recorded. 1% LIDO with EPI (1:100,000) was then injected by surgeon intranasally (13±2 ml). HR and MAP were recorded at 1-min intervals for subsequent 7 minutes. Data were analyzed using ANOVA and Student-Newman-Keuls test.

Results. Baseline HR and MAP were similar for three groups. In placebo group, LIDO-EPI increased HR abruptly by 35% (Fig 1: min 1). Increased HR waned in min 2 and 3, stabilizing at 10% above baseline by min 4. The two doses of ES caused immediate equivalent decreases in HR (Fig 1; min 0). ES-200 prevented increased HR observed in placebo group during min 1-3, whereas ES-100 had this effect only during min 1. By min 4, HR in both esmolol groups had increased to level similar to placebo group. In placebo group, LIDO-EPI increased MAP to 10% above baseline at min 2 and gradually recovered over the next 5 min. Values for MAP in esmolol groups did not differ from those in placebo group.

Conclusion. 1) LIDO-EPI following topical cocaine caused significant increases in HR and moderate increases in MAP 2) Bolus injections of esmolol had no influence on the increases in MAP, but it prevented increases in HR in a dose-related fashion. This latter findings suggests that esmolol may be useful adjuvant in patients vulnerable to tachycardia-induced myocardial ischemia who are receiving topical cocaine and LIDO-EPI infiltration for intranasal surgery.

References.

1. Ann Plast Surg 10:452-457, 1983.
2. Anesth Analg 69:663, 1989.

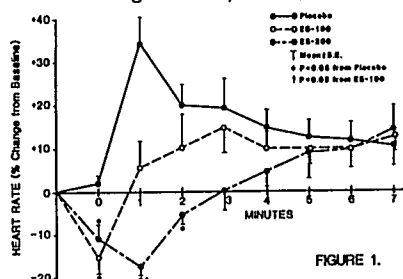


FIGURE 1.