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Title: ADDING FENTANYL AND CLONIDINE TO MEPIVACAINE RESULTS IN A RAPID IN ONSET AND PROLONGED ANESTHESIA AND ANALGESIA AFTER BRACHIAL PLEXUS BLOCKADE.

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Added to bupivacaine, epidural fentanyl (F) provides a more complete and prolonged analgesia with a faster onset.[1] Clonidine (Cl) added to mepivacaine 1% with epinephrine 1/200000 (M) prolongs the duration of both anesthesia and analgesia after brachial plexus blockade.[2] This study evaluates the effects of adding F and Cl to M on the onset time, the duration of anesthesia and analgesia after brachial plexus blockade.

Methods: After informed consent and institutional approval, 80 patients scheduled for elective orthopedic surgery under brachial plexus anesthesia were included in this study. Axillary brachial plexus block was performed following Winnie's approach.[3] A peripheral nerve stimulator was used to locate the brachial plexus sheath. The patients were randomly divided into 4 groups of 20 and received into the plexus sheath 40 ml of M without F nor Cl in group A, with 0.5 mcg/kg of Cl in group B, with 100 mcg of F in group C and with 0.5 mcg/kg of Cl and 100 mcg of F in group D. Block was assessed in each nerve territory by cold testing at 5-min interval until a complete thermoanesthesia was obtained (onset time). The duration of both anesthesia and analgesia (time between injection and, respectively, return of sensation and onset of pain) were recorded. Statistical analysis was done with ANOVA and Student t-test when appropriated. Results are expressed as means ± SEM.

Results: The onset time in each nerve territory and the duration of both anesthesia and analgesia in each group are presented respectively in tables 1 and 2. When compared with group A, a more rapid onset time in each nerve territory was noted in groups C and D. The duration of both anesthesia and analgesia were significantly increased only in groups B and D. No side effects were noted during the observation period.

Table 1: Onset time in each nerve territory (min).

	Group A (Control)	Group B (Cl)	Group C (F)	Group D (Cl + F)
Median N.	15 ± 3	15 ± 3	7 ± 1*	7 ± 1*
Cubital N.	14 ± 3	14 ± 3	7 ± 1*	7 ± 1*
Radial N.	21 ± 4	16 ± 3	10 ± 1*	14 ± 2
Musc. Cut. N.	22 ± 4	17 ± 2	14 ± 2	9 ± 1*

* p < 0.05 (ANOVA and Student t-test) when compared with A.

Table 2: Duration of both anesthesia and analgesia (min).

	Group A	Group B	Group C	Group D
Anesthesia	228 ± 8	301 ± 11*$	251 ± 7	311 ± 9*$
Analgesia	270 ± 10	438 ± 41*$	324 ± 14	456 ± 30*$

* p < 0.0005 (ANOVA and Student t-test) when compared with group A.
$ p < 0.05 (ANOVA and Student t-test) when compared with group C.

Conclusions: This randomized, double blind study shows that adding 100 mcg of F and 0.5 mcg/kg of Cl to M results in a faster and prolonged anesthesia and analgesia after brachial plexus blockade. When added to M, the specific effects of F (rapid onset time) and of Cl (prolonged anesthesia and analgesia) are additive.

References: 1. Br. J. Anaesth. 54: 409-414, 1982.
2. Anesthesiology 73: A797, 1990.
3. Anesthesiology 25: 353-363, 1964.

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TITLE: *INTRAOPERATIVE CLONIDINE ENHANCES POSTOPERATIVE MORPHINE PATIENT CONTROLLED ANALGESIA*

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The benefits of adequate postoperative analgesia (POA) are demonstrated (1). An exclusive opioid-based management is often limited and there is now a quest for "balanced" POA. In this prospective study, the postoperative analgesic effects of intraoperative iv clonidine (CL) were evalued by measuring the analgesic requirements of patients using PCA.

Methods: With institutional approval and after informed consent, 200 consecutive patients (ASA I-III) undergoing major abdominal surgery were studied. Exclusion criteria were cardiac conduction disturbances, chronic use of CL and unability to understand PCA pain control. Patients were randomly assigned to receive either balanced anesthesia with iv CL (a loading dose of 4 µg/kg before incision followed by an infusion of 2 µg/kg/h till closure of the peritoneum) (group I n=97) or balanced anesthesia alone (group II n=91). A PCA infuser Abbott 4200 was connected in the recovery room. It was programmed to deliver morphine "on demand" as iv boluses at the doses of 1mg for patients over 65 years, 1.5mg for females and 2mg for males with a 7 min lockout interval. A blinded observer assessed POA by recording morphine requirements (MR) (mg/12-24-36 h), unsatisfied analgesic demands (UD) (n/12-24-36 h), sedation analog scale and side effects (q2h). Statistical analysis was done by parametric (t test, Fisher exact t test, MANOVA) and non parametric (Medians tests) methods where appropriate.

Results: Thirteen patients were excluded because of intraoperative events unrelated to the protocol. Both groups were comparable for population, duration of surgery, intraoperative fentanyl requirements, allocation of bolus morphine doses. MR and UD are presented in table 1. Intraoperative iv CL reduced the total MR (55.4 mg/G1 vs 67 mg/G2 - p=.038) mainly by reducing consumption during the first 12 hours and decreased UD at any interval considered. Both groups were comparable for sedation score or side effects. The analgesic effect of CL was more prominent in males than in females and patients over 65.

Discussion: Intraoperative iv CL enhances morphine POA. This effect extends far beyond the reported elimination half live of Cl (2). A preventive action on postop pain of CL e.g. by blocking spinal hyperexcitability (3), if administered before incision or by reducing the emotional component of pain (4), is therefore suspected.

References: 1. Can J Anaesth 37:719-21,1990 2. Clin Pharmacokinetics 14:287-310, 1988
3. Brain Res. 334:243-254,1985 4. Anesthesiology 74:3-8, 1991

	N	0-12h POA Mean	SD	12-24 h Mean	SD	24-36 h Mean	SD
Morphine group1	96	19.7	11.0	20.9	13.6	14.9	12.5
group2	91	27.6	18.1	24.3	18.2	16.4	15.9
		p<.001		p=.33		p=.48	
U.D group1	96	5.0	8.9	4.1	5.9	1.7	3.3
group2	91	21.1	26.4	12.2	16.9	5.3	8.6
		p<.00001		p<.0001		p<.001	

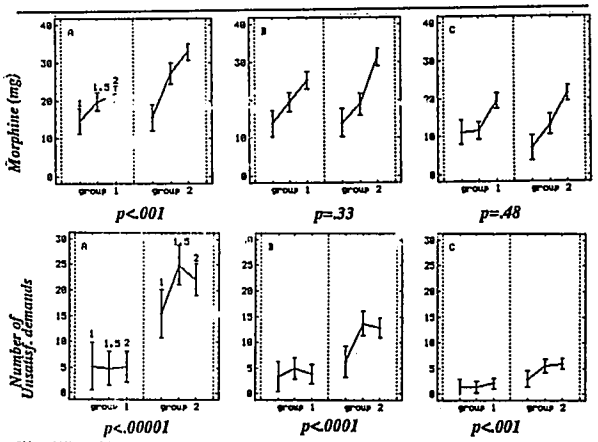

Fig.: UD and MR for each iv bolus doses and for A=0-12h, B=12-24h & C=24-36 h POA. Mean +/- SEM. Groupe 1= clonidine / group 2= no clonidine.