Title: DURATION OF BLOCK AND ANALGESIA AFTER BRACHIAL PLEXUS ANESTHESIA WITH MEPIVACAINE: EFFECT OF CLONIDINE ADDED TO THE ANESTHETIC SOLUTION.

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In man, adding clonidine to the anesthetic solution results in an increased duration of analgesia after femoral nerve block[1], spinal and epidural anesthesia.[2,3] The purpose of this study was to evaluate the effects of adding clonidine to mepivacaine on the duration of block and analgesia after brachial plexus anesthesia.

Methods: After informed consent and institutional approval, 30 patients (ASA I-II) scheduled for elective orthopedic surgery under brachial plexus anesthesia were included in this study. Axillary brachial plexus block was performed following the Winnie's technique.[4] A peripheral nerve stimulator was used to locate the brachial plexus sheath. The patients were randomly divided into 3 groups: group A (n=10) received 40 ml of mepivacaine 1% (M) with epinephrine 1/200000 (E), group B (n=10) received 40 ml of M + E and clonidine 150 μg subcutaneously (SC) and group C (n=10) received 40 ml of M + E and clonidine 150 μg in the sheath. The duration of the block (time between injection and return of sensation) and of analgesia (time between injection and onset of pain) were assessed by attending anesthesiologists unaware of the solution used. Statistical analysis was done with ANOVA and Student t test when appropriated. Results are expressed as means ± SEM.

Results: Adequate surgical anesthesia was obtained in all patients. The onset time was similar in each group. Duration of block and analgesia in each group are presented in Table 1.

No statistical differences were noted between group A and B. As compared with control group, duration of block and analgesia in group C were increased by 38% and 103% respectively. No side effects were noted during the observation period.

Table 1.

	Group A (n=10)	Group B (n=10)	Group C (n=10)
Duration of block (min.)*	226 ± 10	234 ± 12	311 ± 10**
Duration of analgesia (min.)*	260 ± 13	279 ± 10	528 ± 39**

* $p < 0.0001$ (ANOVA) ** $p < 0.0001$ (Student t test)

Conclusion: This randomized double-blind study shows that adding clonidine to mepivacaine for brachial plexus block results in a significant increase in duration of block and analgesia. Our results also seem to prove that clonidine does not act through systemic resorption. Further studies are needed to determine its local mechanism of action: anesthetic-like effect, receptor interaction or axonal transport ?

References:

1. Anesthesiology 71: A643, 1989.
2. Anesth. Analg. 68: S298, 1989.
3. Anesth. Analg. 66: 442-446, 1987.
4. Anesthesiology 25: 353-363,1964.

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TITLE: PROLONGATION OF ANESTHETIC EFFECT BY EPIDURAL ADMINISTRATION OF LIPOSOMAL-ENCAPSULATED LIDOCAINE IN DOGS

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A need for the development of long-acting local anesthetics has been existing for control of acute and chronic pain. The present study was planed to attempt to produce a long-acting local anesthetic by use of liposome which would entrap the drug. Egg yolk phosphatidylcholine and cholesterol were used as materials of large unilamellar liposome of lipid bilayers which lidocaine was intercalated. The liposomal lidocaine sample showed a large decrease in dialysis speed compared to control free lidocaine. The 50% permiability time for lidocaine encapsulated with liposome was 90 min, while that for free lidocaine was 37 min. The decreased dialysis speed appears to result from the ability of liposome to entrap the drug.

Pharmacodynamics and pharmacokinetics of liposomal and free lidocaine following epidural administration were studied in 17 dogs. Two milliliter of 2% liposomal or free lidocaine was administered into lumbar epidural space. Nerve blocking effect of the drug was estimated by measurement of the somatosensory evoked potentials (SEP). Liposomal lidocaine produced long-lasting blocking effect as measured by latency and amplitude of the early component in SEP, when it was epidullaly administered. The recovery time from the epidural block in liposomal lidocaine group (170± 49.5 min) was about three times longer than that in the free lidocaine group (61± 18.1 min). Plasma lidocaine data following epidural administration were subjected to pharmacokinetic analysis using model-independent techniques. Table summarizes the obtained pharmacokinetic parameters. The data about the in vivo block study were coincident with that of the in vitro equilibrium dialysis study. This result suggests that the prolongation of epidural blockade by liposomal lidocaine may be due to a slow release of lidocaine from multilamellar liposomes. The present study suggests that liposomal lidocaine can be used as a long-lasting local anesthetic.

Table. Pharmacokinetic data characterizing the absorption of lidocaine following epidural administration

	C_{max} (μg/ml)	T_{max} (min)	AUC_{0-t} (μg.min/ml)	$AUC_{0-\infty}$	$T_{1/2}$ (min)	Cl/F (ml/min)	MRT (min)
2% Free Lidocaine (n=7)							
Mean	1.64	11.4	119.5	197.0	99.8	424.7	141.2
± S.D.	0.64	3.8	77.5	146.8	43.0	233.1	58.5
2% Liposomal Lidocaine (n=10)							
Mean	1.93	17.0*	214.4*	330.3*	157.6	206.8	226.4
± S.D.	0.63	4.8	76.1	104.4	100.4	97.6	139.4

* Significant difference with free lidocaine, $p<0.05$