LOCAL ANESTHESIA AND PAIN III

A677

TITLE: NIMODIPINE REDUCES THE CARDIO-RESPIRATORY TOXICITY OF INTRAVENOUS BUPIVACAINE IN RATS

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We have previously shown that other calcium channel blockers protect against fatal bupivacaine (BUP) cardio-respiratory toxicity in Sprague-Dawley rats[1,2]. Nimodipine is a dihydropyridine calcium channel blocker, which is effective in the treatment of neurologic deficit following subarachnoid hemorrhage[3]. This study examines the protective effect of nimodipine (NIM). Animals received either saline placebo or NIM (i.v.) three minutes before receiving i.v. BUP.

METHODS: Four groups received intraperitoneal pentobarbital (approximately 50 $mg \bullet kg^{-1}$). Groups 1 (n=10) and 2 (n=12) received 4 $mg \bullet kg^{-1}$ of 0.5% BUP (LD_{50}) and groups 3 (n=12) and 4 (n=11) received 4.5 $mg \bullet kg^{-1}$ (LD_{90}). Groups 2 and 3 were pretreated with 300 $\mu g \bullet kg$-1 NIM and groups 1 and 4 with equivalent volumes of saline. In a separate experiment, additional toxicity studies showed that 4.5 and 4.75 $mg \bullet kg$-1 of BUP were the LD_{50} and LD_{90} respectively. Four similar groups (denoted 1a, 2a, 3a, and 4a) were studied. In this experiment, group 2a and 3a animals received 500 $\mu g \bullet kg^{-1}$ NIM pretreatment. Group sizes in the latter experiment were comparable (1a (n=10), 2a (n=9), 3a (n=9), and 4a (n=8)).

Survival data were analyzed by Chi-square analysis with Yates' correction and demographic data by ANOVA. Data using two doses of NIM were analyzed separately. Differences were considered significant if $p<0.05$.

RESULTS: There were no differences among groups 1-4 in weight, fluid administration, dose of nembutal, dose of NIM. Similarly there were no differences among groups 1a-4a.

More animals survived BUP toxicity following 300 $\mu g \bullet kg$-1 NIM ($p<0.05$) than did their respective controls (group 2 7/12 [58.3%] versus group 1 1/10 [11.1%] and group 3 9/12 [75%] versus group 4 2/11 [18.2%]). Survival was not improved with 500 $\mu g \bullet kg$-1 NIM pretreatment (group 2a 2/9 [22.2%] versus group 1a 4/10 [40%] and group 3a 4/9 [44.4%] versus group 4a 2/8 [25%]).

CONCLUSION: Our data demonstrates that prophylactic administration of nimodipine (300μg/kg) protects against bupivacaine induced CRT. Pretreatment with 500 $\mu g \bullet kg^{-1}$ was not protective. A possible explanation for the non-protection of the larger NIM dose is the toxicity of the drug.

REFERENCES:
1. Can J Anaesth 37: 920-3, 1990.
2. Anesthesiology 71: A1145, 1989.
3. NEJM 308: 619-624, 1983.

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TITLE: REDUCTION OF PAIN FROM INITIAL APPLICATION OF PROPARACAINE FOR TOPICAL EYE ANESTHESIA

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Commercially prepared proparacaine (OpthaineR) 0.5% is commonly used for topical anesthesia prior to injections of local anesthetics for eye surgery. Generally proparacaine (P) causes stinging and burning when first applied. This study was designed to determine if P diluted in balanced salt solution (BSS) with a physiologic pH (Alcon R) would mitigate the pain of instilling P into the eye.

Following institutional approval and signed informed consent, a double blind study was performed in 42 consecutive adults undergoing cataract surgery. All subjects were ASA I-III physical status with the number of males, females, and ages comparable as analyzed by ANOVA and Chi Square testing. All subjects served as their own controls.

Two anesthetic solutions, prepared by a non-investigator and warmed to 37 ^{o}C, were assigned randomly as either solution A (A) or solution B (B). One solution was P 0.5%; the other P 0.03% in BSS (1:15 dilution). Each subject received a drop of A in one eye and B in the other. Subjects then rated the degree of discomfort on a scale of 1-10. Thirty seconds later the process was repeated. Ten minutes later, 2 drops of P 0.5% was instilled in both eyes and the degree of pain again elicited.

Non-parametric ordinal data (pain scores) were analyzed by Mann-Whitney U test for unmatched two group comparisons and the Kruskal-Wallis one way analysis of variance for unmatched multiple group comparisons.

Subjects receiving P 0.5% as the first drop had a mean pain score (MPS) of 1.28; those with P 0.03% as the first drop had a MPS of 0.09 ($P<0.01$). No subject had pain with either solution at thirty seconds. At the ten minute interval when P 0.5% was instilled into each eye, the eye with P 0.03% as the first drops had a MPS of 0.76; the eye with P 0.5% as the first drops, a MPS of 0.10 ($P<0.003$).

The exact cause of this pain on application is unknown[1,2]. Commercial P has a pH of 5.3 but raising this pH to 7.3 does not eliminate pain. BSS (Alcon R) is a painless ophthalmic irrigating solution with a pH of 7.4 to 7.8 and a nearly physiologic electrolyte composition. P 0.03% in BSS has a pH of 7.3. Thus the near physiologic electrolyte composition of dilute P in BSS is probably just as important as the pH is producing painless application.

In conclusion, proparacaine diluted to 0.03% with BSS is an effective and painless method of anesthetizing the eye prior to the instillation of stronger solutions of local anesthetics.

TABLE 1: MEAN PAIN SCORES (MPS) WITH DILUTE AND FULL STRENGTH PROPARACAINE

Time	Solution	MPS	P value	Solution	MPS
Initial	P 0.03%	0.09	<0.01	P 0.5%	1.28
P value	<0.001			<0.001	
10 min	P 0.5%	0.76	<0.003	P 0.5%	0.09

References:
1. Anesth. Analg 66:1180-82, 1987
2. Anesthesiology 45:687-689, 1976