POSTER SESSION III

A967

TITLE: CLINICAL EFFECTS AND PHARMACOKINETICS OF INTRANASAL PHENYLEPHRINE IN CHILDREN

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Introduction: Intranasal phenylephrine (IPE) is often used to reduce bleeding during nasotracheal intubation. There is no scientific evidence on the effects of IPE in children. The purpose of this study was to determine the hemodynamic effects and disposition of IPE in children undergoing procedures that included routine nasotracheal intubation.
Methods: After IRB and parental approval, 72 ASA I or II children were studied in a prospective, double blind, randomized manner. Group I received intranasal water while groups II and III received 0.25% and 0.5% IPE respectively. Anesthesia was induced via inhalation and end-tidal halothane and CO_2 were maintained at 1.5% and 35mmHg respectively. Immediately after induction and before instillation of study substance, baseline heart rate (HR) and rhythm, systolic, diastolic, and mean arterial blood pressures (SBP, DBP, and MAP) were recorded. Venous blood was obtained for serum phenylephrine (PE) level, blood gas and serum potassium (K+) at the same time. This same group of data was collected at 0,2,5, and 10 minutes. Bleeding (none, mild, moderate, and severe) was assessed after instrumentation of the airway. Bleeding and dysrythymia incidence was analyzed using a coded chi-square test. PE levels were measured by high performance liquid chromatography (HPLC).
Results: The results are summarized in the following table. 52 patients (72%) recived 0.1mL/kg of 0.25% or 0.5% IPE. There was no significant dysrhythmia incidence any group or difference among groups of serum K+,blood gases or bleeding.
Regression analysis of hemodynamic data and PE levels demonstrated positive correlation except for HR with r = .432, .482, and .406 for SBP, DBP, and MAP.
Discussion: Our data indicate that IPE causes significant systemic absorption resulting in increases of blood pressure which are statistically but not clinically significant. Although bleeding was less severe with 0.5% IPE, there was no difference in incidence of bleeding among groups. The lack of clinically significant hemodynamic changes contrasts the experience with (PE) concentrations of 2.5% or more for ophthalmic use in neonates. Pharmacokinetic analysis revealed an overall increase in IPE concentration with decline after 5 minutes. We conclude that 0.5% IPE in the above dose causes no hemodynamic danger to children and results in better reduction of bleeding than 0.25% IPE or placebo.

time	SBP (mmHg)			DBP (mmHg)			MAP (mmHg)			HR			PE (ng/ml)	
(min)	I	II	III	I	II	III	I	II	III	I	II	III	II	III
0	91±3	93±2	88±2	49±2	46±1	49±2	65±2	64±1	62±2	90±3	87±3	93±3	0.8±0.8	2.8±2.3
2	94±3	98±2†	88±2	49±2	49±2	48±1	66±2	68±2	62±2	92±3	89±3	94±2	5.5±3.7	16.5±9.9
5	94±3	97±2†	91±2	48±2	49±2†	48±2	65±2	65±2	64±2	92±3	83±3	91±2	21.7±7.6†	39.4±18.8†
10	97±3†	99±3†	94±2†	49±2	51±2†	52±2†	67±2	71±3†	68±2†	97±4†	87±3	93±3	15.2±5.2†	29.9±12.5†

†p<0.05 vs. 0 min. (ANOVA for repeated measures); N = 26 (I, Placebo), 24 (II, 0.25% IPE) and 27 (III, 0.50% IPE).

References:
1.Myers MG, Iazzeta JJ: Intranasally administered phenylephrine and blood pressure. CMA Journal 12:365-68,1982.
2.Martinsson A, Beregard S, Hjemdah P: Analysis of phenylephrine in plasma: initial data about the concentration-effect relationship. Eur J Clin Pharmacol 30:427-438,1986.

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TITLE SPINAL ANESTHESIA IN NEWBORNS : BUPIVACAINE PLASMA CONCENTRATIONS.

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Spinal anesthesia (SA) is reported as very suitable for minor surgery in newborns (1). In these patients it may result in a deep sedation without any evident explanation. This study was designed to investigate a possible blood absorption of bupivacaine (B) from CSF.

Ten infants, 45.8±4.8 weeks old (post-conceptual age), weighing 3.99±1.24 kg, scheduled for inguinal herniorraphy, entered this study, after institutional and parental approval. After a 4-hours fast, a 5% dextrose infusion was started. SA was performed with .5% plain B injected over 20s in the L_4-L_5 interspace through a 22 g spinal needle. The dose given was calculated on a body weight basis (2) : 3.75mg (0.75ml) under 5kgs and 5mg (1ml) above 5kgs. The occurence of sedation was recorded : infants were found sleeping but arousable with noxious stimulation applicated above T_{10}, or awake. B. plasma concentrations (BPC) were measured by HPLC (3) from a single blood sample collected within 10 minutes after SA. Results were expressed as mean ± SD and correlation coefficients were calculated.

8/10 infants were sedated at the time of sample withdrawal. No deleterious effect was noted during or after the procedure. Individuals BPC are presented in the table 1. Mean BPC was 0.259±0.09 $\mu g.ml^{-1}$. No significant correlation was found between age, weight and BPC.

Neither sedation nor systemic absorption of local anesthetics have been precisely documented after SA in infants. This study evidences that B absorption from CSF is constant. That may account for sedation. The importance of spinal vasculature as well as the relatively large dose of B related to body weight may partly explain this findings. No toxic effect was observed ; thus systemic absorption should not preclude interest of SA in newborns.

TABLE 1

	AGE (weeks)	WEIGHT (kg)	SEDATION (+ / -)	BPC $\mu g.ml^{-1}$
1	40	2.1	-	.43
2	54	5.6	-	.23
3	45	3.0	+	.34
4	52	4.4	+	.30
5	50	6.0	+	.18
6	42	3.3	+	.15
7	47	5.1	+	.26
8	40	3.4	+	.31
9	44	3.5	+	.24
10	44	3.5	+	.14

REFERENCES

1 - Anesth. Analg, 63 : 359-62, 1984
2 - Anesthesiology, 68 : 601-03, 1988
3 - Clin. Chem., 36 : 1041-1042, 1990