Title: Oral Atropine Premedication in Infants

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Introduction. Premedication with intramuscular (IM) atropine prior to induction of general anesthesia can attenuate cardiovascular depression in infants[1]. Oral atropine has been used in combination with other premedications[2], but its ability to preserve heart rate (HR) and blood pressure (BP) during induction of general anesthesia has not been evaluated. The purpose of this prospective, blinded, randomized study was to evaluate the efficacy of oral atropine premedication in modifying the cardiovascular depression associated with halothane (HALO) general anesthesia in infants.

Methods. Following approval by the IRB and after informed parental consent was obtained, 47 patients aged 1-11 mos (5.6 ± 3.0) weighing between 4.5-10.6 kg (7.1 ±1.7) were studied. All were >44 wks conceptual age, ASA I or II, NPO a minimum of 4 hrs (7.9 ± 3.3), and scheduled for elective surgery. The patients were randomly placed into 3 groups: 15 received oral atropine 0.04mg/kg (HI), 15 received oral atropine 0.02mg/kg (LO), and 17 received a placebo (NO). The premedication was administered 30-90 min (55.9 ± 16.2) prior to induction and the anesthesia team was unaware of the type of solution the patients received. In the OR, data aquisition included HR, systolic BP (SBP), and mean arterial pressure (MAP) measured by a Dinamap monitor and recorder. Measurements were obtained at 1 min intervals from preinduction until surgical stimulation which ranged in duration from 8-42 min (17.9 ± 5.9). Anesthesia was induced using HALO (up to 3%) in a N_2O (60%) and O_2 (40%) mixture at a 5 L/min flow rate via a semiclosed circle system with assisted ventilation. Immediately after induction, IV access was secured and D5LR 8-15ml/kg (11.3 ± 2.7) was infused prior to surgical stimulation. Intubation was performed under deep HALO (3%) anesthesia, after which the inspired HALO concentration was decreased to 1.25% and maintained until surgical stimulation. IV atropine was administered if HR<100bpm or the percentage decrease in SBP was greater than 50% (SBP%Δ>50%) from preinduction values. The results were evaluated to compare the preinduction HR, SBP, and MAP to the lowest values obtained along with the percentage change (%CH), the duration of time from induction to lowest HR and lowest SBP, and the incidence of HR<100bpm and SBP%Δ>50%. Side effects such as flushing or increased irritability were documented. The data was analyzed using analysis of variance (ANOVA) for the 3 groups and further analysis of HI vs LO was accomplished using a two tailed unpaired student t-test. A CHI Square test was used to compare the incidence of HR<100bpm and SBP%Δ>50% in the oral atropine (HI & LO) vs placebo groups. A $p<.05$ was considered significant for all tests.

Results. There were no significant differences between groups in age, weight, NPO time, IV fluids, preinduction HR, SBP, MAP and the duration of time between induction and surgical stimulation. Significant differences in lowest HR and % CH ($p<.0001$) were noted between HI vs NO and LO vs NO (Table 1) but not between HI vs LO ($p<NS$). Differences in the time to the lowest HR and lowest SBP was noted between HI vs NO and LO vs NO ($p<.02$) with a significant difference between HI vs LO from the time of induction to the lowest HR ($p<.04$). There were no significant differences between groups for lowest SBP, %SBP CH, lowest MAP, %MAP CH (Table 1). 13/17 patients receiving placebo and 3/30 patients receiving oral atropine met criteria for IV atropine administration (HR<100bpm, SBP%Δ>50%) as depicted in Table 2. Flushing was noted in 3/30 patients (2 HI, 1 LO) which resolved in <2 hr. All patients tolerated the oral solution except 1 patient who spit out a portion of the medication and was then excluded from the study.

Discussion. Oral atropine premedication was easy to administer and well tolerated. It effectively preserved HR in both HI and LO groups during induction and maintenance of general anesthesia. SBP and MAP was not preserved in either the HI or LO groups, however, the time to the lowest SBP was significantly increased and the number of patients with SBP%Δ>50% was lower suggesting some protection from hypotension with oral atropine. We conclude that in this population either oral atropine dosage effectively decreases the incidence and magnitude of bradycardia, but not hypotension, with minimal side effects.

TABLE 1	HI(.04mg/kg)	LO(.02mg/kg)	NO(placebo)	ANOVA
HR (bpm)	(n=15)	(n=15)	(n=17)	
Preinduction	187.5±25.0	179.6±24.0	175.0±26.0	NS
Lowest	151.0±19.0	148.5±16.0	99.7±16.0	p<.0001
% Change	20.5+6.0	16.8±9.9	41.8±11.7	p<.0001
SBP (mmHg)				
Preinduction	101.3±14.2	104.3±13.0	110.0±14.1	NS
Lowest	68.0±20.0	70.7±12.4	62.8±16.0	NS
% Change	32.7±19.3	32.0±14.5	42.0±16.0	NS
MAP (mmHg)				
Preinduction	82.5±15.7	88.0±13.0	93.2±17.6	NS
Lowest	53.5±15.7	56.7±10.9	47.4±10.9	NS
% Change	35.5±16.5	34.0±14.6	48.1±15.4	NS
Induction (min)				
To Lowest HR	9.1±7.2	4.7±2.5	4.8±2.5	p<.011
To Lowest SBP	9.8±5.8	11.7±7.1	5.7±2.6	p<.016

Values are expressed as Mean ± Standard Deviation

TABLE 2	Oral Atropine	NO	CHI^2
HR<100bpm	1/30	11/17	p<.01
SBP%Δ>50%	3/30	7/17	p<.02
Either Criterion	3/30	13/17	p<.01

References

1. Friesen RH and Lichtor JL: Cardiovascular depression during halothane anesthesia in infants. Anesth Analg 61: 42, 1982.
2. Brzustowicz RM et al: Efficacy of oral premedication for pediatric outpatient surgery. Anesthesiology 60: 475, 1984