Research Article

The effect of atropine on heart rate with rapid sequence induction in neonates

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Date Submitted:21.5.2012

Date Accepted:28.6.2012

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Abstract

Background: neonates experience physiological responses to endotracheal intubation, including bradycardia and oxygen desaturation. The bradycardia may be associated with severe hemodynamic disturbances like significant hypotension which may threaten patient's safety.

Aims: To determine the effectiveness of single dose IV atropine, 5 minutes before induction of anesthesia on reflex bradycardia to laryngoscopy in sick neonate baby.

Patients and Methods: In a randomized double blinded, placebo controlled clinical trial, thirty neonates aged 1-10 days, term, 2.5-3.5kg and from both sexes, were enrolled to receive 0.02mg/kg IV atropine (n=15), as study group and placebo group had received equivalent volume of normal saline five minutes before induction of anaesthesia (n=15), as control group. The induction technique was the same in all patients. The incidence of bradycardia just after intubation was recorded.

Results: data analyses showed that the overall incidence of bradycardia just after intubation in the study group was significantly lower than the control group.

Conclusions: A single dose IV atropine five minutes before induction of anaesthesia in neonate baby significantly decreases the incidence of bradycardia after intubation.

Keywords: Neonates, Bradycardia, Atropine, Rapid sequence induction, Endotracheal intubation

INTRODUCTION

Endotracheal intubation is not without risks, neonates experience physiologic responses to endotracheal intubation, and endotracheal intubation is a painful procedure.[1]

Although unable to demonstrate full behavioral responses to pain in the same way as an adult or child would, both preterm and term infants experience pain.[1] Physiologic changes that occur during times of pain may be linked to intraventricular hemorrhage or periventricular leukomalacia.[1, 2] The physical procedure of endotracheal intubation can also cause mechanical side effects, infants undergoing endotracheal intubation can experience apnea and cardiac arrhythmias, decreased or obstructed nasal airflow, increased systolic blood pressure, and decreased heart rate and transcutaneous oxygen.[2] According to the Neonatal Resuscitation Guidelines, endotracheal

intubation attempts in the neonate should be limited to 20 seconds.[3] However, intubation attempts are frequently unsuccessful and those that are successful frequently take longer than 20 seconds. Despite duration of endotracheal intubation attempts, adverse side effects including bradycardia and oxygen desaturations occurred as quickly as between 2 and 55 seconds.[1-4]

Glycopyrrolate and atropine are both effective and have not been directly compared. Dose requirements of glycopyrrolate in small preterm infants are not known.[5] Atropine has not been associated with significant adverse effects when given once in the correct dosage.[6]

The most frequent cause of bradycardia is activation of the vagal afferent-efferent 'reflex' loop, either by hypoxia and/or laryngoscopy, such bradycardia can be described as 'stable' because they can be corrected by a pause in laryngoscopy and re-oxygenation.[7] In critical care settings bradycardia do not always respond to a pause in laryngoscopy and re-oxygenation because they are 'unstable', they often require epinephrine and are associated with severe hemodynamic disturbance and progression to the slow, terminal rhythm that is most frequently observed in dying children.[8]

Aim of the study

To prove the effect of atropine on prevention of bradycardia in sick neonates during laryngoscopy and intubation in rapid sequence induction of anesthesia.

PATIENTS AND METHODS

After the ethical approval and written informed parental consent, 30 neonates aged 1-10 days, term, weighing 2.5-3.5 kg and from both sexes, were enrolled randomly into this double blinded clinical trial. All of cases were scheduled for urgent or semi-urgent surgical correction of congenital anomaly (omphalocele, trachea-oesophageal fistula, mal-rotation of the gastro-intestinal system or other congenital anomalies) under general anesthesia.

Neonates were randomly allocated into two equal groups, Group (A) or the study group, n=15, given atropine 0.02 mg/kg IV 5 minutes before induction of anesthesia and Group (B) or control group, n=15, atropine was not given and instead an equivalent volume of normal saline was given 5 minutes before induction of anesthesia.

Any preterm baby, absence of intravenous access, suspected difficult intubation, cardiovascular anomalies, those on a medication that influence heart rate (e.g. digoxin), hypothermic neonate and those with family history of a neuro-muscular disorder or pseudo-cholinesterase deficiency were excluded.

All neonates were fasting 4 hours before operation and intravenous fluid established to cover the fasting period and continued during and post operatively as required.

Continuous monitoring of neonate with electrocardiography (ECG) monitor, pulse oximeter (SpO_2), continuous body temperature measurement were done before and during anesthesia and end-tidal CO_2 during anesthesia until successful extubation. Stabilizing the neonate body temperature was granted by using warmed mattress. Two senior anesthesiologists were present to increase patient's safety. Preoxygenation with 100% oxygen (5 minutes before induction) using anaesthesia face mask with the Jackson-Rees breathing circuit. The pulse rate was recorded before the administration of the study solution. The study solution (Solution 1 containing 1ml of fluid with atropine 0.02 mg/kg, and solution 2 containing 1 ml of normal saline) given IV, 5 minutes before induction of anesthesia. Fentanyl 1 µg/kg IV 3 minutes before induction, thiopental sodium 3-5 mg/kg IV (sleeping dose) and suxamethonium chloride 2 mg/kg IV. Intubation attempted once the baby become apneic with no movement (rapid sequence induction). All of the intubations were done by the same anesthesiologist. An intubation was considered successful when there was confirmation of good breathing sounds, visible vapor present in the ETT (endotracheal tube), rising and stable arterial oxygen saturation and end tidal CO_2 detection. After intubation, the pulse rate recorded immediately in both groups. After the first clinical sign of recovery from suxamethonium chloride, pancuronium bromide 0.1 mg/kg IV was given to all patients. Maintenance of anesthesia was by 1.5% halothane and top-up doses of pancuronium given as needed. Ventilation was controlled by IPPV (intermittent positive pressure ventilation) with 100% oxygen. At the end of surgery reversal of residual muscle relaxation with reversal agent by 0.02 mg/kg neostigmine and 0.01 mg/kg atropine done. The baby discharged to post-surgical unite, with adequate monitoring and support then to the surgical ward.

After recording heart rate just after intubation, all the babies in the control group given atropine 0.02mg/kg as this will not affect the result of the study.

The data of the study, pulse rate before atropine, pulse rate just before laryngoscopy and pulse rate immediately

after intubation was recorded and analyzed by using Student's 't' test. The result considered significant when p less than 0.05.

RESULTS

The distribution of patients in both control and atropine groups was cleared by table 1 showing the distribution of age, sex, body weight and pulse rate before atropine. There was no statistical difference between both groups as $p > 0.05$.

The statistical analysis for pulse rate changes after atropine and just before intubation in both groups showing no statistical difference as p 0.886 ($p > 0.05$).

Table 3 showing the effect of intubation on both atropine group and the control group. The changes are quite obvious, as the control group showing a well noticed reduction in heart rate after intubation. The statistical analysis between both groups showing a remarkable statistical significance with $p < 0.0001$.

The graph bars chart below showing the relation of pulse rate just before laryngoscopy and just after intubation in both atropine and control group.

Table 1. Patients distribution in age, sex, body weight and pulse rate before giving atropine.

		Study group					
		Atropine group			Control group		
		Mean	Standard Deviation	Count	Mean	Standard Deviation	Count
Heart rate before atropine		135	9		140	9	
Age in days		5	4		6	4	
Sex	Male			6			10
	Female			9			5
Body weight		2.91	0.12		2.94	0.24	

Table 2. Showing the pulse rate before atropine and just before laryngoscopy in both groups.

	Study group			
	Atropine group		Control group	
	Mean	Standard Deviation	Mean	Standard Deviation
Heart rate before atropine	135	9	140	9
Heart rate just before laryngoscopy	165	9	139	9
Heart rate just after intubation	128	11	82	14

Table 3. The pulse rate mean and Standard deviation just before laryngoscopy and just after intubation in both groups.

	Study group			
	Atropine group		Control group	
	Mean	Standard Deviation	Mean	Standard Deviation
Heart rate just before laryngoscopy	135	9	140	9
Heart rate just after intubation	128	11	82	14

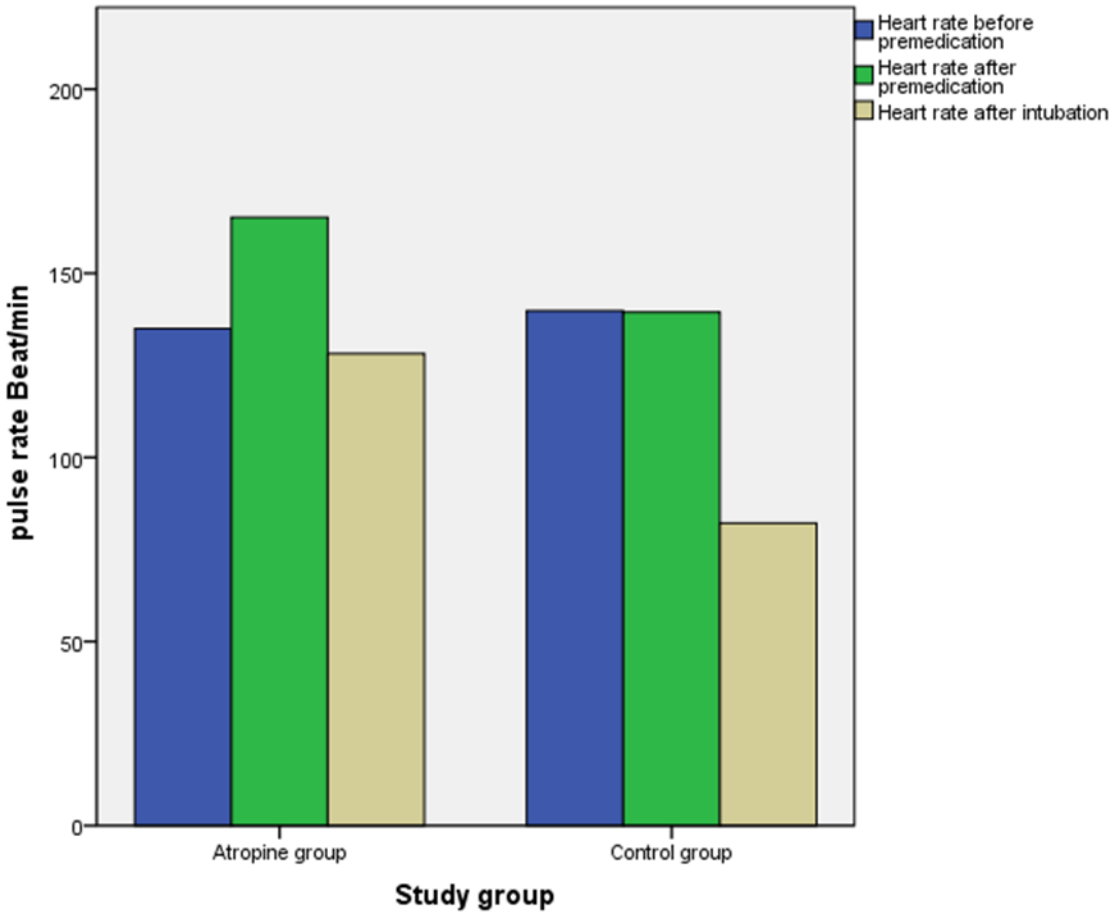

Figure 1. Showing the relation of pulse rate just before laryngoscopy and just after intubation between both atropine and control group.

DISCUSSION

The use of premedications in this study does not require indisputable proof that they improve the long-term outcomes of the infants; in the contrary to study of Kelleher J.et al. and Li J. et al. as they concluded that "there is no absolute proof that awake intubation adversely affects long-term outcomes in neonates undergoing endotracheal intubation",[4, 5] but that is not used as an excuse for performing this painful and unpleasant act without premedication.

Administration of atropine in neonates prior to general anesthesia, had shown no significant clinical changes in this study, but the post-intubation effect is quite obvious. It had prevented the unwanted bradycardia that would happen after endotracheal intubation of the neonates. The bradycardia in neonates is less than 100 heart beats per minute according to the free medical dictionary and Costa et al.[9, 10] By preventing the occurrence and limiting its effect, the fluctuation in blood pressure and tissue perfusion will be eliminated.[11] The cholinergic anti-inflammatory response, whereby infection triggers vagal efferent signals that dampen production of proinflammatory cytokines, would be predicted to result in increased vagal signaling to the heart and increased heart rate variability. In fact, decreased heart rate variability is widely described in humans with sepsis.[12] In the late period of the 90s, the use of atropine almost abundant after the introduction of drugs which are less cardiotoxic like muscle relaxants other than succinylcholine and inhalational agents like sevoflorane.[13-16] Cook had shown in 1976 that atropine is used in a dose of 14.3 µg /kg body weight is fair enough as a vagolytic in children below the age of 2 years, and much less than this dose to reduce salivation.[17]

Conclusion

We can conclude that the use of atropine as a premedication in rapid sequence induction in neonate

will prevent the bradycardia that is associated with laryngoscopy and intubation in sick newborn baby.

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