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Midazolam and morphine for elective intubation in NICU

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ABSTRACT

Objective

To assess the use of midazolam and morphine as premedication for elective intubation in neonates, and to compare the intubation conditions with these combination versus awake intubation.

Methods

A non blind randomized prospective study was conducted at Prince Hashim Hospital between November 2009 and December 2010. Forty premature neonates in intensive care unit requiring nonemergency intubation were assigned to receive 0.1 mg /kg IV morphine followed by 0.1 mg/kg IV midazolam two minutes before intubation (study group) or awake intubation (control group). Number of attempts, duration of procedure, heart rate and blood pressure were monitored.

Results

Out of 40 intubations, 20 were enrolled in each group; there were no significant demographic differences between the groups. Successful intubation on first attempt was achieved in 16 premature (80 %) in study group versus 8 (40%) of controls. After 10 minutes post intubation, median increase of mean blood pressure in study group were - 5.9, versus 0.15 in control group. Mean time for intubation in study group was significantly less; 38.05 versus 123.05 seconds in control group. Incidence of bradycardia was 50% in control group and 60% in study group. 70% of study group had hypoxemia after one minute versus 55% of control group; 45% of study group had severe hypoxia versus 30% of control group.

Conclusion

Morphine and midazolam decreased time and number of attempt needed for intubation, however, neonates should have cardiorespiratory, oxygen saturation, and blood pressure monitoring during intubation. (Rawal Med J 2012;37:42-45).

Keywords

Premedication, elective endotracheal intubation, midazolam.

INTRODUCTION

Premature infants likely have an increased sensitivity to pain,¹ which can lead to chronic pain or neurobehavioral and developmental sequel.² Tracheal intubation of both the term and preterm newborn is a frequently performed stressful procedure in the neonatal intensive care unit (NICU), and has the potential for airway injury. The experience of

being intubated is unpleasant and painful and seriously disturbs physiologic homeostasis.³ Endotracheal intubation is associated with acute increases in blood pressure and intracranial pressure, bradycardia and hypoxemia⁴ and potential risk of intraventricular hemorrhage in preterm infants.⁵ Bradycardia is presumed to be vagal in origin, because the very rapid onset is suggestive of a reflex etiology.⁴

Several studies that evaluated the success rate of neonatal endotracheal intubations have reported that successful intubations frequently require more than 1 attempt and are rarely accomplished within the currently recommended time frame.^{6,7} Several trials have demonstrated that the use of premedication for intubation of the newborn significantly improved intubating conditions, decreased time and number of attempts needed to complete the intubation procedure, and minimized the potential for intubation-related airway trauma.⁸⁻¹⁰ We aimed to evaluate the efficacy of morphine and midazolam, in achieving better intubation conditions and success while maintaining vital signs stability.

PATIENTS AND METHODS

All infants of all gestational age admitted to NICU King Hussein Medical Center and Prince Hashim Hospital were eligible for inclusion in this study. Informed consents were obtained from parents before the need for intubation. Infants with airway abnormalities, absence of an intravenous access, known or family history of a neuromuscular disorder, renal impairment, liver dysfunction and cyanotic congenital heart disease were excluded from the study. When intubation was required, infant was given 100 mcg/kg morphine intravenous slowly over one minute followed by 100 mcg/kg midazolam slow intravenous bolus to avoid severe hypotension and seizures. These relatively low doses

were chosen to avoid the side effect of both drugs. One to three minutes after infants received medication positive pressure ventilation was done by self resuscitation bag or neopuff and oxygen as needed. Suctioning of the airway was done as necessary.

All intubations were conducted by the same neonatologist fellows. Information about intubation situation, complications, intubation time and results of each attempt were recorded on a worksheet following each intubation. FiO_2 was set to 40% for the first 10 minute after procedure. Hypoxemia was defined as O_2 sat < 85%, bradycardia as HR < 100 b.p.m, hypotension as mean blood pressure (MBP) > 2SD below the age. All intubation attempts were made within 5-8 minutes of administration of the medication. An intubation attempt was defined as insertion and removal of the laryngoscope blade.

Intubation time was measured from the introduction of endotracheal tube until removal of the blade after successful intubation. In case that there was more than one attempt, the time recorded continued between attempts until successful intubation confirmed by auscultation. Successful intubation was confirmed if there was appreciable and bilaterally equal air entry on auscultation, rising of oxygen saturations and heart rate, visible vapor present in the ETT and confirmed by chest radiograph.

Elective intubation were done due to blocked tube, self extubation, increasing respiratory depression and failed planned extubation. Data obtained for each infant included birth weight, gestational age, age at time of intubation, weight at time of intubation, gender and reason for intubation, and any complication were also recorded. All the intubations were done by the oral route. Termination of the intubation attempt was made if spo_2 fell below 65% or the attempt exceeded 38 seconds.

RESULTS

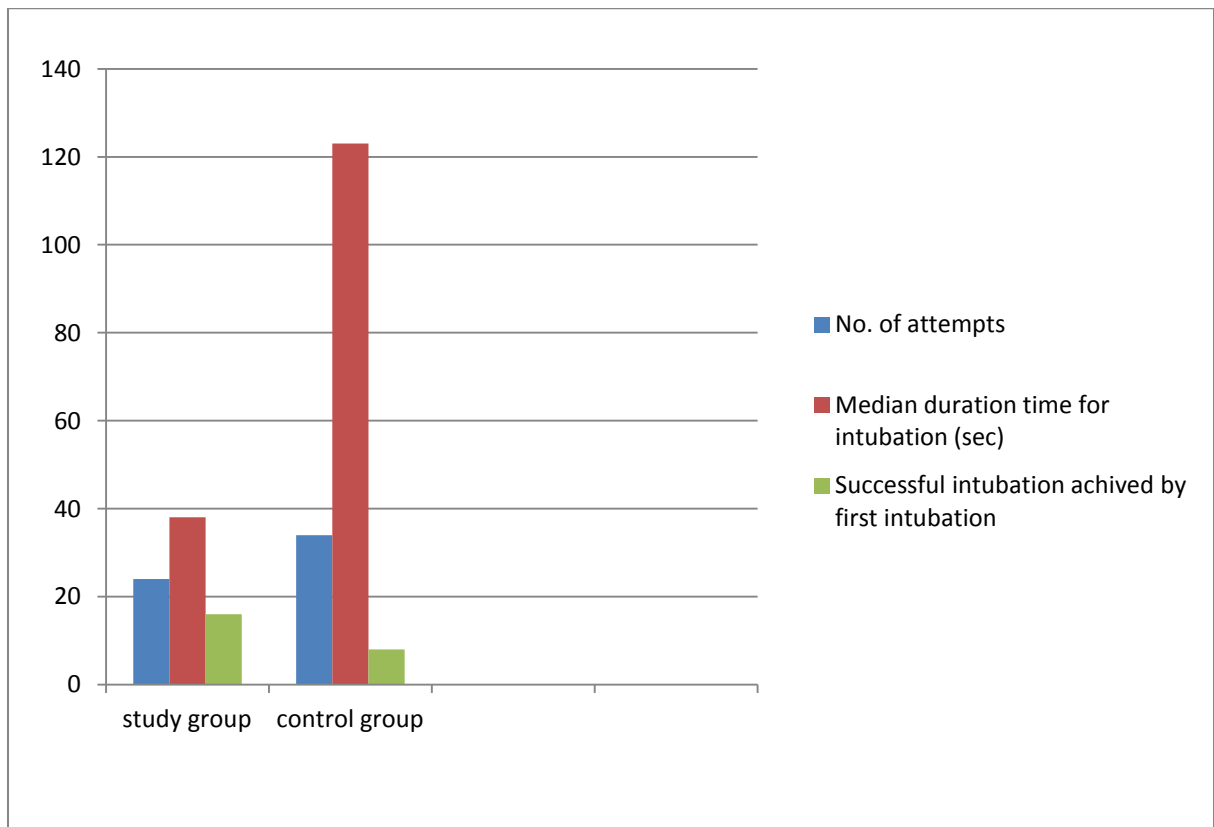
Both groups were comparable in gestational age; weight at time of intubation, vital sign, age at intubation and gender (Table 1).

Table 1. Demographic characteristics of two groups.

Characteristics		Midazolam and morphine group (n=20)	Control group (n=20)
Gender	Female	9	13
	Male	11	7
Gestational age, wk		32,2±2,68	31,6±2,97
Age at time of intubation, days		4,5±3,86	4,9±4,87
Birth weight, grams		1715,5±583	1639,5±579
Birth weight at time of intubation, grams		1658,5±570	1626,5±546
Mode of delivery	Vaginal delivery	11	10
	Cesarean	9	10
Reason for intubation	• Respiratory depression	3	2
	• Blocked tube	7	7
	• Self extubation	8	7
	• Failed extubation	2	4

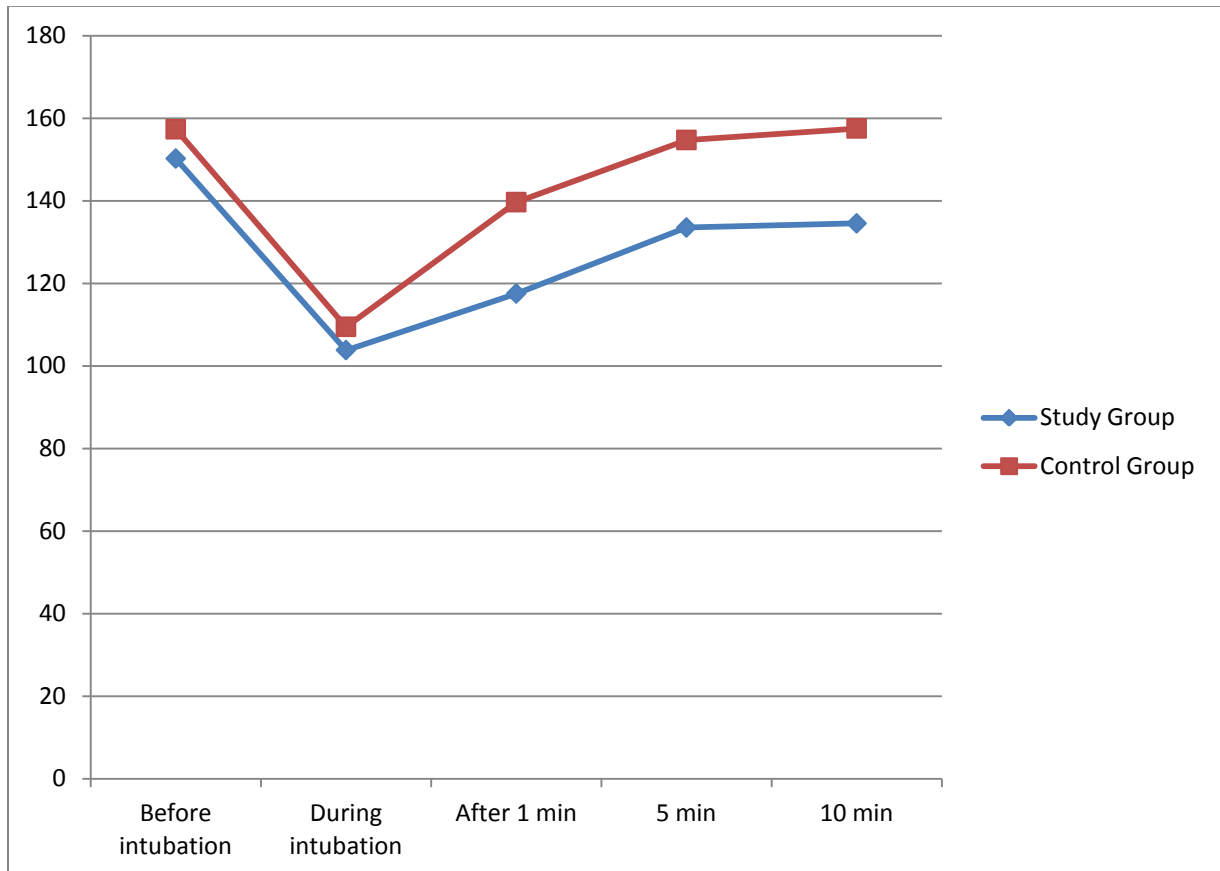
Successful intubation on first attempt was achieved in 16 infants (80 %) in study group versus 8 (40%) of control. A second attempt was needed in four infants in study group and in ten in controls; two premature in control group needed three attempts to achieve successful intubation.

Fig 1. Number of attempts, duration time and rate of successful intubation.



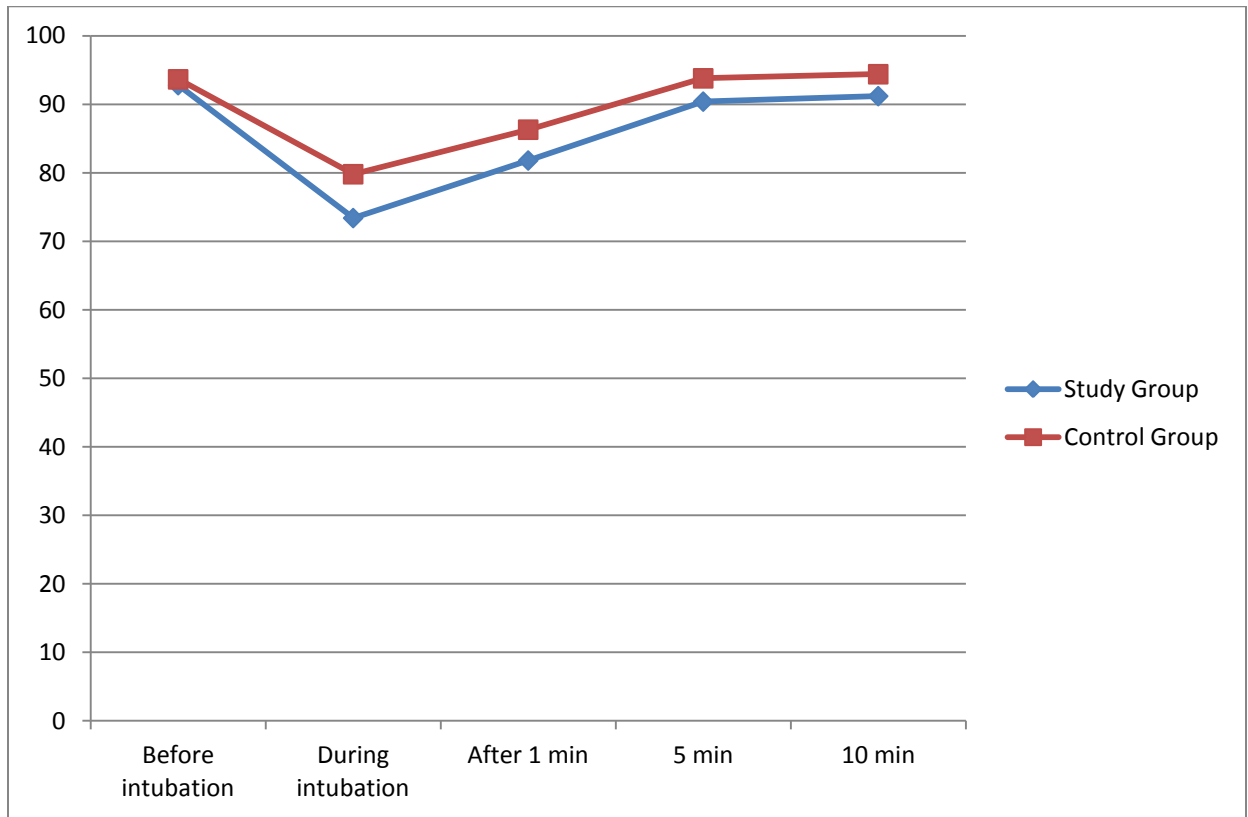
Mean time for intubation in study group was significantly less; 38.05 versus 123.05 seconds. Number of attempts in the study group was 24 versus 34 in the control group (Fig 1).

Fig 2. Change of heart rate in different stage of intubation.



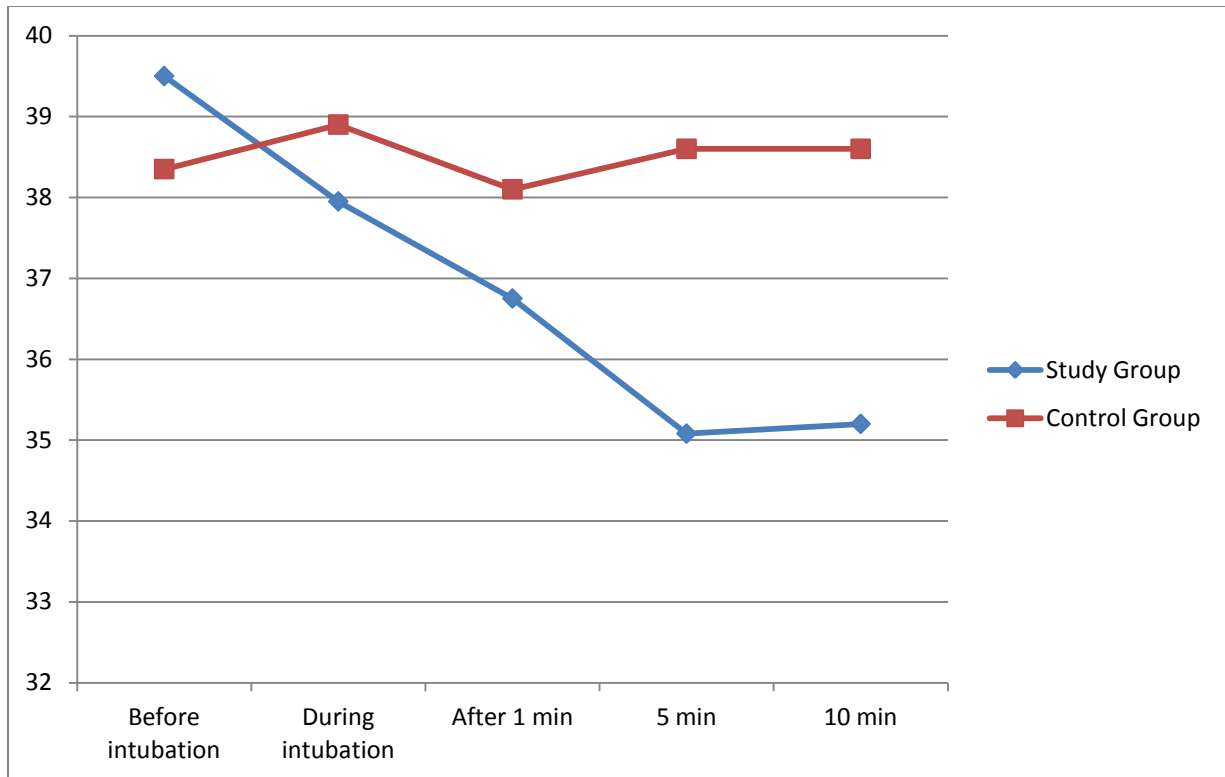
Regarding the hemodynamic variables, bradycardia in control group was 50% versus 60% in study group.

Fig 3. Change of O₂ saturation during different stage of procedure.



After 10 minutes post intubation, the median increase of mean BP in study group was -5.9 versus 0.15 in control group. Drop of blood pressure was mild and no one needed treatment.

Fig 4. Change of mean blood pressure in different stage of intubation.



All infants developed hypoxemia (O_2 sat. $<85\%$) one minute after the procedure; 70% in study group versus 55% in control group (Fig 2,3,4).

DISCUSSION

Premature infants and newborn infants may have increased pain sensitivity as compared with older infants and age groups.¹¹ Premedication is not a common practice for the intubation of infants and most intubations in NICU are performed with the infants awake, without analgesia or muscle relaxation, possibly due to fear of producing cardiovascular or ventilator depression.¹² Anand suggested that tracheal intubation without the use of

analgesia or sedation should be restricted to life-threatening situation when intravenous access is not available.¹³

Midazolam is a short acting benzodiazepine that acts on specific receptors in the central nervous system which are present in the fetus from seven weeks gestation and these potentiate the neuronal inhibitory pathways mediated by gammaaminobutyric acid (GABA).¹⁴ Midazolam is preferred in infants over other benzodiazepines because of its water solubility and rapid clearance.¹⁵ The mechanism of midazolam-induced hypotension was thought to be vasodilation related to levels of extra vascular prostanoids and calcium.¹⁶ Morphine is the most frequently used drug for analgesia in ventilated neonates but has a slow onset of analgesia.¹⁷

Our study showed that the combination of midazolam and morphine facilitated intubation but the duration of hypoxemia and bradycardia was longer in study group and decrease in blood pressure is more. Kelly and Barrington using atropine and a muscle relaxant, demonstrated a reduction in vagal bradycardia and a dampening in the rise in intracranial pressure.¹⁸ In a randomized, double-blind trial (stopped after only 16 intubations because of adverse events), preterm infants who received midazolam and atropine for intubation had more desaturations and 29% required cardiopulmonary resuscitation compared with those who received either atropine alone or no premedication.¹⁹ In our study, we used a low and a slow administration of midazolam in order to avoid these complications.

A study in 34 premature infants, morphine failed to demonstrate the effectiveness of in reducing the physiological instability or time needed to perform elective intubations.²⁰ This effect was thought to be due to delayed onset of action of morphine.²¹ There is no

consensus about the drug, combination of drugs or doses for premedication mainly regarding tracheal intubation in NICU.^{11,21} Midazolam and morphine have been showed to be a good combination, although there is a concern about the transient hypotension and bradycardia. Further study may be needed to prove that or to find a better combination as premedication for intubation.

CONCLUSION

Morphine and midazolam, decreased time and number of attempts needed for intubation. However, desaturation, bradycardia and hypotension were observed and these premature babies should have cardiorespiratory, oxygen saturation, and blood pressure monitoring during intubation.

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