Original Article

Postoperative apnea of ex-premature infants after inguinal herniorrhaphy

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Objectives: To determine the impact of anesthetic drugs, being used recently, on the occurrence of postanesthetic apnea (PAA) after inguinal hernia repair in premature infants.

Methods: A retrospective chart review of 61ex-premature infants undergoing inguinal herniarepair from March2010 to December 2013 was undertaken. Collected data included gestational age at birth, postconceptual age (PCA), weight at birth, weigh at surgery, past and current medical history, type of inhalation anesthetics, type of muscle relaxants, anesthetic record, and presence of apnea.

Results: The incidence of postanesthetic apnea was 4.9% (95% CI 1.0-13.7).Type of anesthetic durgs (sevofluranevs. desflurane and atracuriumvs. rocuronium) showed no statistical difference. A significant difference was observed inbronchopulmonary dysplasia (p=0.03), weight at surgery (p=0.03) and PCA (p=0.02) between the PAA group and non-PAA group.

Conclusion: Compared to the drugs used in the past, currently used general anesthetics seem to be more safe. Selection between sevoflurane and desflurane, and between atracurium and rocuroniumcan be made with confidence. (Rawal Med J 2014;39: 193-196).

Key Words: Anesthetics, apnea, herniorrhaphy, premature infant.

INTRODUCTION

Postanesthetic apnea (PAA) is one of the most serious post-operative complications in neonates and infants that can lead to severe complications such as hypoxic brain damage or death. The higher incidence of apnea in preterm infants was first described by Steward,[1] and it appears particularly increased in preterm infants less than 60 weeks PCA (postconceptual age: the sum of gestational age and postnatal age). The reported incidence varies widely.[2,3]As the mechanisms that may cause PAA, immaturity of the brain stem,[4] fatigue of respiratory muscles due to lack of type I muscle fibers[5]and defect of the arousal response to hypercapnea and hypoxia[6] have been suspected. Development of neonatology has increased the survival of preterm infants with multiple co-morbidities. We conducted this study under the hypothesis that the new anesthetic agents can significantly increase or decrease the incidence of PAA. We investigated incidence of PAA per each pharmaceutics in premature infants less than PCA 60 weeks, who underwent surgery for inguinal hernia under general anesthesia.

METHODOLOGY

From March 2010 to December 2013, preterm infants with PCA less than 60 weeks who underwent inguinal hernia surgery under general anesthesia were selected and their medical records were reviewed. Cases of sustained mechanical ventilation given until the day of surgery or failure to extubate within 24 hours after surgery were excluded from the study. Baseline characteristics like weight at birth, weight at surgery, gestational age, postconceptual age, the presence of ventilator support at birth, the presence of oxygen therapy at birth, anemia (hematocrit less than 30%), respiratory distress syndrome, bronchopulmonary dysplasia, history of apnea, and the presence of patent ductus arteriosus were recorded. Anesthetic factors included the American Society of Anesthesiology (ASA) physical status classification, the type of muscle relaxants used, the type of inhalation anesthetics given, and the operative time. After the end of the surgery, the occurrence of apnea was checked for over the next

24 hours from medical records. Our hospital defines apnea as respiratory arrest lasting longer than 20 seconds or respiratory arrest under 20 seconds with O_2 desaturation (SPO_2<85%) or bradycardia (HR <100/min).

Data were divided into the apneic group and the non-apneic group. They were compared by Fisher's exact test for the categorical variables and Wilcoxon's rank sum test for the continuous variables. The incidence of apnea was obtained and the Clopper-Pearson Method was employed to calculate the 95% exact confidence interval. P<0.05 was considered statistically significant.

RESULTS

Out of 61 infants, three (4.9%) had PAA (CI 1.0-13.7). Between the apneic group and the non-apneic group, the mean weight at birth and weight at surgery was 940.0±295.1 g vs. 1547.3±776.8 g (p=0.17) and 2503.3±656.8 g vs. 4124.1±1562.5 g (p=0.03), respectively, (Table 1, Figure 1).

Table 1. Baseline characteristics and comparison between the groups.

	Apnea	Non-apnea	P value
No. of patients	**3 (4.9)**	**58 (95.1)**	
Weight at birth(grams)	940.0 ±295.1	1547.3 ±776.8	0.171
Weight at surgery(grams)	2503.3 ±656.8	4124.1 ±1562.5	0.031
GA(weeks)	26.5±1.8	31.2±4.2	0.072
PCA(weeks)	39.1±3.9	44.9±4.1	0.020
VASD	3 (100.0)	28 (48.3)	0.238
OSAD	3 (100.0)	38 (65.5)	0.544
History of apnea	3 (100.0)	34 (58.6)	0.279
History of anemia	2(66.7)	35(60.3)	1.000
Anemia	1 (33.3)	17 (29.3)	1.000
RDS	3 (100.0)	27 (46.6)	0.113
BPD	3 (100.0)	17 (29.3)	0.032
PDA	2 (66.7)	21 (36.2)	0.551

GA: gestational age, **PCA**: postconceptual age, **VSAD**: ventilatory support after delivery, **OSAD**: oxygen support after delivery, **History of anemia:** hematocrit < 30 for all studies, **Anemia:** hematocrit < 30 for last study, **RDS**: respiratory distress syndrome, **BPD**: bronchopulmonary dysplasia, **PDA**: patent ductusarteriosus.

Gestational age showed no difference between the two groups (26.5±1.79 weeks vs. 31.2±4.2 weeks, p=0.07) and there was a difference in PCA (39.1±3.85 weeks vs. 44.9±4.1 weeks, p=0.02) (Table 1, Figure 2). Past history of bronchopulmonary dysplasia showed a difference between two groups (p=0.03), and there were no difference in oxygen support after delivery, ventilator support after delivery, anemia at surgery, history of anemia, history of apnea, respiratory distress syndrome, and patent ductusarteriosus (Table 1). Apnea occurred in PCA 35, 39, and 43 weeks respectively, and recovery in all the episodes was achieved by proper stimulation and oxygen supply without any complications.

Figure 1. Comparison of weight at surgery between the groups.

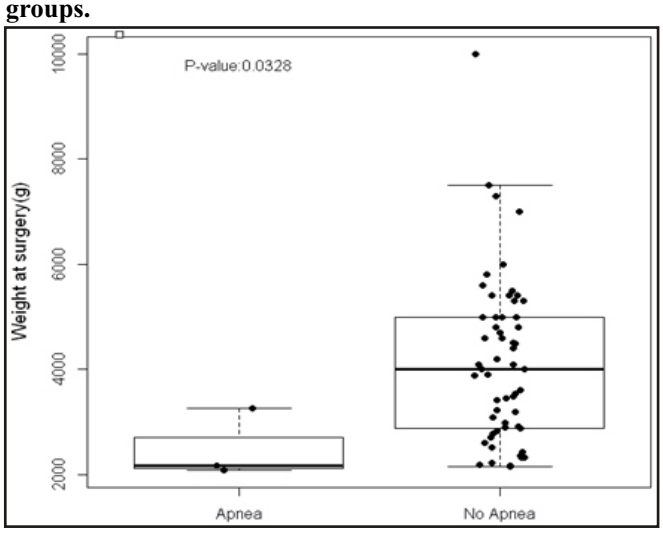

Figure2.Comparisonof PCAbetweenthegroups.

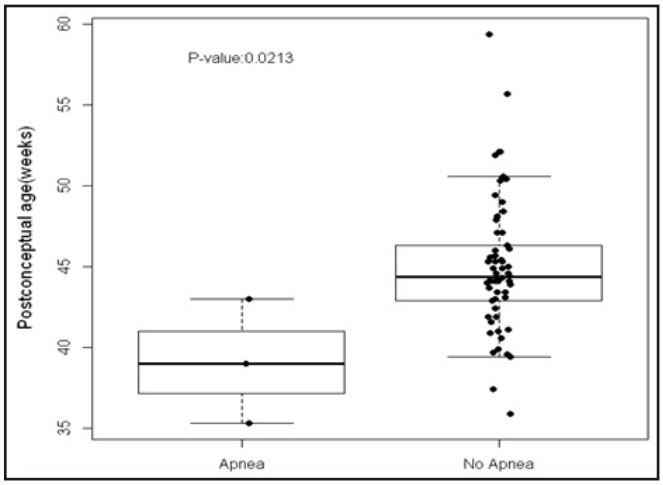

Table 2. The correlations between postanesthetic apnea and anesthetic factors.

		Postanesthetic apnea		
Variable	**Overall (n=61)**	**Yes (n=3)**	**No (n=58)**	**P value**
ASA class				
>=3	8 (13.1)	0 (0.0)	8 (13.8)	1.000
<3	53 (86.9)	3 (100.0)	50 (86.2)	
Muscle relaxant				
Atracurium	2 (3.3)	0 (0.0)	2 (3.5)	1.000
Rocuronium	58 (96.7)	3 (100.0)	55 (96.5)	
Inhalational anesthetic				
Desflurane	7 (11.5)	0 (0.0)	7 (12.1)	1.000
Sevoflurane	54 (88.5)	3 (100.0)	51 (87.9)	
Surgery duration(min)				
	71.8±24.1	63.3±20.2	72.2±24.3	0.493

In the comparison of sevoflurane and desflurane, incidence of apnea showed no statistical difference (p=1.00). Comparison of atracurium and rocuronium also showed similar results (p=1.00). In the comparison of ASA physical status and operation time, no significant differences were found (Table 2).

DISCUSSION

Apnea of prematurity was reported to be caused by an immature respiratory system[7]and a relevance between apnea and immaturity of the brain stem functions was postulated.[4] Fatigue of the respiratory muscles may be the cause of apnea in preterm infants.[5] Hunt et al. reported that infants with an apneic history had a defect in the arousal response to hypoxia and hypercarbia.[6] These studies suggest that apnea occurs in the situation of immature organ ogenesis, and we can expect that with a lower PCA, a higher likelihood of apnea in premature infants occurs.

Although many studies looking for the mechanism and pathophysiological factors of PAA, attention should be given to the part of anesthetic drugs. Steward reported the incidence of PAA as 39%, using halothane and N_2O and muscle relaxants were not used and concluded that the cause of PAA was suppressive effect of halothane to chemoreceptor regulating respiration and respiratory muscle fatigue due to rapid respiration induced by halothane.[1] For over 30 years, inhalation anesthetics have been replaced by agents such as enflurane, isoflurane, sevoflurane, and desflurane that minimize the risk of side effects, allow fast induction of anesthesia and recovery. In addition, long acting muscle relaxants such as gallamine and pancuronium have been replaced with short acting drugs such as atarcurium and rocuronium, which allow improved surgical view and controlled respiration during surgery. However, Murphy et al. reported that sevoflurane siginificantly increased the incidence of apena.[3] Also, In muscle relaxants inhibited respiratory response to hypoxia by acting on nicotine receptors on carotid body from animal experiments[8] and an association of apnea with muscle relaxants and opioids was noted, advising against using these drugs.[9]

In the meta-analysis, incidence of apnea was reported to be 5 to 49%.[2]In our study, apnea occurred in 4.9% infants and it is close to Murphy's reported incidence of 4.7%.[3] In comparison of inhalant agents, there was no significant difference between sevoflurane and desflurane, which corresponds to report by Sale et al.[10] Muscle relaxants atracurium and rocuronium showed no significant difference between them.

As the factors that can cause PAA, PCA, weight at surgery, past history of apnea, oxygen supply at birth, ventilatory support at birth, respiratory distress syndrome, bronchopulmonary dysplasia, patent ductusarteriosus and history of anemia wereconsidered.[2,3,1113] Among them, there was a significant difference in past history of bronchopulmonary dysplasia, body weight at surgery as well as PCA between PAA group and non-PAA group (Figure 1, 2). A higher risk in ex-preterm infants less than 44 weeks was reported [11,12] and it was recommended that ambulatory surgery for infants PCA less than 46 weeks should be carefully considered.[14] In our study, the PCA of infants with apnea was 35, 39, and 43weeks respectively, and all were less than 44 weeks.

With the exception of PCA, many studies have reported different risk factors for PAA. Our study showed that bronchopulmonary dysplasia and weight at surgery were significant. However, it is noticeable that history of bronchopulmonary

dysplasia and low body weight at surgery were observed from all three PAA group patients. In case of low PCA accompanied by history of BPD and low body weight at surgery, the risk of PAA is thought to be even higher, so it may be desirable to proceed operation after PCA increase and weight gain as possible.

CONCLUSION

Compared to the drugs used in the past, currently used drugs seems to be more safe and choices of inhalant anesthetics (sevoflurane Vs. desflurane) and muscle relaxants (atracurium Vs. rocuronium) can be done with confidence. We found that postconceptual age was an independent risk factor associated with postanesthetic apnea and history of brochopulmonary dysplasia and weight at surgery showed statistical difference.

Postanesthetic apnea were observed in infants whose PCA was less than 44 weeks. Given these results, in premature infants younger than PCA 44 weeks, especially with the history of bronchopulmonary dysplasia and low weight at the time of surgery, more careful postoperative management is needed.

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