의학박사 학위논문

Effect of spontaneous breathing on atelectasis during induction of general anesthesia in infants

: a prospective randomized clinical trial

영아에서 마취 유도 시 자발호흡 유지 여부가 무기폐 발생에 미치는 영향

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서울대학교 대학원

의학과 마취통증의학전공

지 상 환

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지도교수 김 희 수

이 논문을 의학박사 학위논문으로 제출함

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지상환의 의학박사 학위논문을 인준함

2021년 7월

위 원 장 ______________________

부위원장 ______________________

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Abstract

Effect of spontaneous breathing on atelectasis during induction of general anesthesia in infants

: a prospective randomized clinical trial

Sang-Hwan Ji

College of Medicine

Major in Anesthesiology and Pain Medicine

The Graduate School

Seoul National University

Background: Atelectasis commonly occurs during induction of general anesthesia in children, particularly infants. Maintaining self-respiration rather than using positive-pressure ventilation is known to reduce the risk of atelectasis. I hypothesized that maintaining spontaneous ventilation can reduce atelectasis formation during anesthetic induction in infants. The aim of this study was to compare spontaneous ventilation and manual positive-pressure ventilation in terms of atelectasis formation in infants.

Methods: Infants undergoing general anesthesia were enrolled and randomized into either "spontaneous" group or "controlled" group. Oxygenation was provided after loss of consciousness, with spontaneous ventilation was maintained in the "spontaneous" group while conventional bag-mask ventilation was provided in the "controlled" group, with fraction of inspired oxygen of 100%. After 5 minutes of oxygenation, patient's chest was divided into 12 observational area with combination of right/left, upper/lower, anterior/lateral/posterior regions and lung ultrasound was performed to compare atelectasis formation between the groups. For each region, both juxtapleural consolidation and presence of B-line were evaluated and separately graded with scores 0, 1, 2 or 3, larger number representing worse condition. Definition of atelectasis was set as presence of consolidation of score 2 or 3 in any regions of the chest. Exclusion criteria were history of hypoxemia during previous general anesthesia, development of a respiratory tract infection within 1 month, current intubation or tracheostomy cannulation, need for rapid sequence intubation, preterm birth and age within 60 weeks of the postconceptional age, and the presence of contraindications for rocuronium or sodium thiopental.

Results: Atelectasis after oxygenation was seen in seven (26.9%) out of 26 patients in the “spontaneous” group and 22 (73.3%) out of 30 patients in the “controlled” group (P = 0.001). The relative risk of atelectasis in the “spontaneous” group was 0.391 (95% CI 0.211 to 0.723). Regarding ultrasound pictures of consolidation, the total sum score and sum of scores in the dependent regions were significantly lower in the “spontaneous” group than in the “controlled” group (P = 0.007, P = 0.001, respectively). Within patients, the posterior region showed significantly higher consolidation score and B-line score compared to the anterior and lateral regions. There was a strong positive correlation between consolidation score and B-line score for both groups. In the “controlled” group, there was a moderate negative correlation between age and total B-line score.

Conclusions: Maintaining spontaneous ventilation during induction of general anesthesia has preventive effect against atelectasis in infants, particularly in the dependent portion of the lung.

Key words: anesthetic induction, atelectasis, lung ultrasound, positive-pressure ventilation, spontaneous respiration

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1. Introduction

1.1. Study Background

Atelectasis formation is common complication during induction of general anesthesia in children, with a reported incidence ranging from 68% to 100% [1-4]. Atelectasis may have negative effects on patients' outcome with worse oxygenation, less compliance, greater pulmonary vascular resistance, and risk of lung injury [5]. Pediatric patients, particularly infants, are more prone to atelectasis formation during anesthesia since they have a greater closing volume and lower compliance [6,7].

Atelectasis formation during anesthesia is influenced by several factors, such as the fraction of inspired oxygen (F_IO_2), obesity, chronic obstructive pulmonary disease, closing volume, positive end-expiratory pressure, and muscle relaxation [6,8,9].

There can be various pathogenesis of atelectasis that can occur during general anesthesia [10]. Compression atelectasis is a result of decreased transmural pressure so that the alveolus collapse. When the diaphragm is paralyzed and displaced cephalad during anesthesia, its separation effect of intrathoracic pressure and abdominal pressure diminishes. Consequently, the pleural pressure increases and compresses adjacent lung tissue, resulting in decrease of functional residual capacity (FRC). Also, intercostal muscle loses its function when exposed to volatile anesthetic agents especially in children, resulting in decreased FRC [11]. This compression atelectasis is predominant in dependent portion of the lung [12,13].

Resorption atelectasis occurs when an area of lung with low ventilation to perfusion ratio experiences increase in F_IO_2, resulting in increased oxygen flux from the alveolus to the capillary. If the gas flow exceeds inflow, the alveolus collapses [14,15].

Impairment in pulmonary surfactant may occur by increased tidal volume [16] or sequential air inflations to total lung capacity [17] and its function may be deteriorated by volatile anesthetic agents [18].

However, the influence of maintaining spontaneous ventilation on atelectasis formation during anesthetic induction in children is controversial and there have been no prospective study reported [1,19], although the incidence of atelectasis has been reported to be lower in children under light sedation with spontaneous ventilation compared to those undergoing positive-pressure ventilation [2,3].

Traditionally, chest computed tomography (CT) has been used for the evaluation of atelectasis [1,3,4,20]. However, CT is not suitable for real-time assessment of the lungs during anesthesia in most clinical settings. In the past few years, lung ultrasound has gained popularity for its convenience and acceptable reliability in the diagnosis of atelectasis [12,21,22].

1.2. Purpose of Research

In this study, the hypothesis is that maintaining spontaneous ventilation rather than providing manual bag-mask ventilation would reduce the risk of atelectasis formation in infants during anesthetic induction. To test the hypothesis, a prospective randomized controlled trial using lung ultrasound was performed.

2. Methods

2.1. Study design and population

This study was designed as a randomized, controlled, single-blinded clinical trial. The study protocol was approved by the Institutional Review Board of the Seoul National University Hospital (1810-076-979, Chairperson Prof K. H. Kim, approval date: 08/11/2018) and was registered at http://clinicaltrials.gov (NCT03739697, publish date: 15/11/2018). The study was conducted in a single tertiary hospital, located in Seoul, Republic of Korea. Patients were recruited from November 2018 to December 2019.

After obtaining informed consent from one of the parents, infants who were scheduled to undergo surgery under general anesthesia were included in the study. Exclusion criteria were history of hypoxemia during previous general anesthesia, development of an upper or lower respiratory tract infection within 1 month, presence of atelectasis in routine preoperative chest radiograph, current intubation or tracheostomy cannulation, need for rapid sequence intubation, preterm birth and age within 60 weeks of the postconceptional age, the presence of contraindications for rocuronium or sodium thiopental, any history of neuromuscular diseases, and the refusal for enrolment by one or more parents or legal guardians.

2.2. Randomization and blinding

Study patients were allocated to “spontaneous” and “controlled” groups at a ratio of 1:1. A randomization table was obtained from the website https://sealedenvelope.com/. A nurse who was not participating in the study held the randomization table. After confirmation of enrolment, the nurse referred to the table and announced the group allocation of the subject. Anesthesia was induced according to the study protocol for the allocated group, including lung ultrasound examination and recording by a single anesthesiologist, the author of this thesis. Subsequently, another anesthesiologist (Y. E. Jang, 5 years of experience in lung ultrasound examination), who had not participated in the anesthetic induction and was blinded to group allocation, interpreted the recorded lung ultrasound pictures and determined the scores according to the study protocol. To assess repeatability of the interpretation, another anesthesiologist (I. S. Song, 2 years of experience in lung ultrasound examination), who were also blind to group allocation, was designated as second interpreter and reviewed the images and determined the presence of atelectasis. The anesthesiologist who performed the examination did not influence the scoring.

2.3. Study protocol

On patients' arrival at the operating room, their electrocardiogram, non-invasive blood pressure, and arterial oxygen saturation by pulse oximetry (SpO_2) were monitored. Anesthesia was induced with 0.02 $mg \cdot kg^{-1}$ of atropine premedication and 6 $mg \cdot kg^{-1}$ of sodium thiopental, and 100% oxygen was supplied via a fitting mask. For both groups, a circle system was used as breathing system, with pediatric breathing circuit (Ace Medical, Gyeonggi-do, Korea) connected to anesthesia machine (Primus®, Dräger Korea, Seoul, Korea). Intrinsic positive end-expiratory pressure (PEEP) of the circuit was not taken into account, since I used same circuit for both groups. After loss of consciousness, 3–4 vol% was administered. Oxygenation was provided for 5 min with the following method: For patients in the “spontaneous” group, a mask was fit to the face with the jaw-thrust technique, maintaining the patient's spontaneous ventilation; and for patients in the “controlled” group, 0.6 $mg·kg^{-1}$ of rocuronium was injected, and manual bag-mask ventilation targeted at a tidal volume of 6–8 $ml·kg^{-1}$ was then provided. The rate of ventilation was adjusted in order to keep the level of end-tidal carbon dioxide between 35 mmHg and 45 mmHg. Tidal volume was automatically displayed at the monitor of the anesthesia machine. In the “controlled” group, I maintained peak airway pressure not exceeding 15 cmH_2O to avoid hyperinflation of the lung and unintentional alveolar recruitment. I adopted the value of 15 cmH_2O from previous studies on gentle facemask ventilation during anesthetic induction [23,24]. No oropharyngeal/nasopharyngeal airway was used for both groups. F_IO_2 was maintained at 100% in both groups. Oxygenation was maintained by anesthesiologists with an experience of more than 500 bag-mask ventilations. After oxygenation, ultrasound examination focused on the lung was performed. Details of ultrasound examinations are provided in the next section. Subsequently, an endotracheal tube or a supraglottic airway device was placed for airway maintenance during the surgery, followed by the alveolar recruitment maneuver if any sign of atelectasis was present. In the “spontaneous” group, a neuromuscular blocking agent was administered, if necessary.

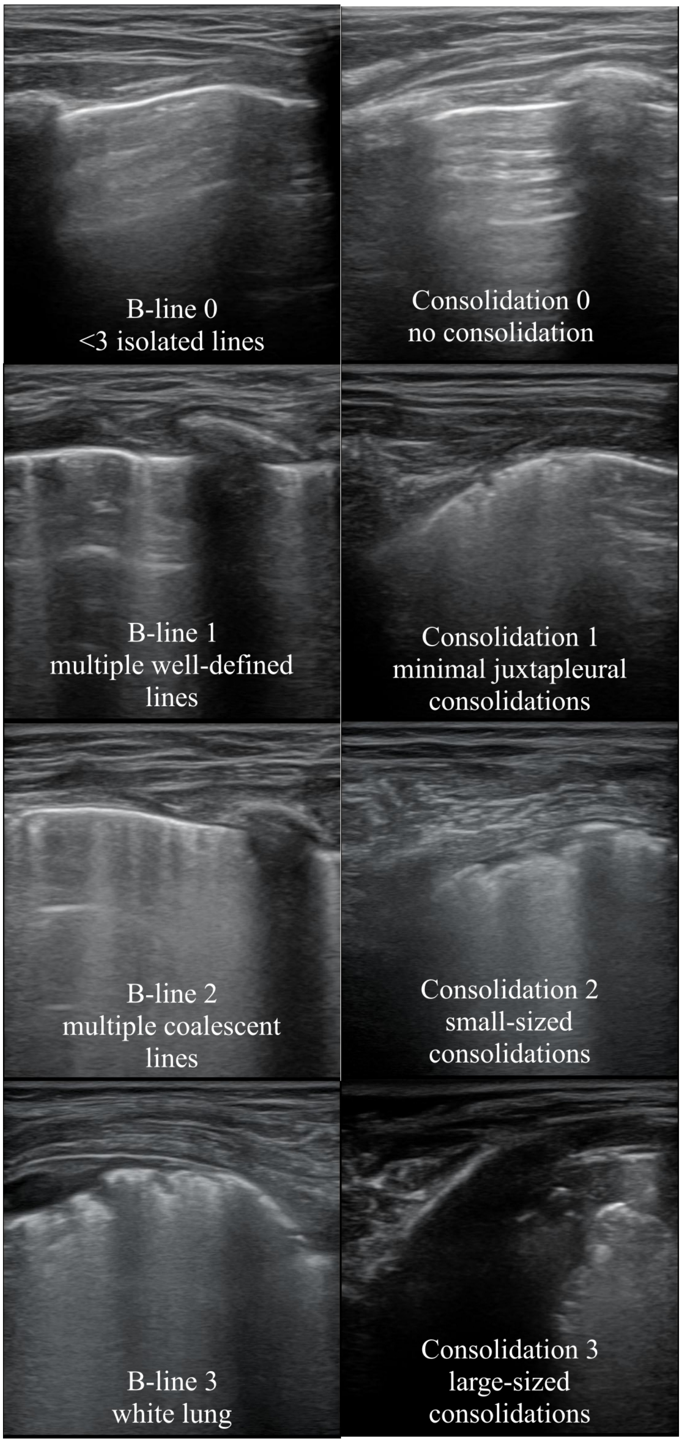
2.4. Lung ultrasound examination

Chest ultrasound was performed with E-CUBE i7 (Alpinion Medical Systems Co., Ltd., Gyeonggi-do, Korea) using a 3–12-MHz linear probe. According to the classification reported by Acosta and colleagues [12], the chest was divided into 12 regions in combinations of left/right, upper/lower, and anterior/lateral/posterior regions. Upper and lower region was bordered by a horizontal line connecting points 1cm above both nipples. Anterior and lateral region was bordered by a vertical line from anterior axilla, lateral and posterior region was separated by a vertical line from posterior axilla. Examinations were performed in the order of anterior–lateral–posterior, right–left, and upper–lower. With a probe placed parallel to the ribs, the consolidation, B-line, A-line, air-bronchogram, pleural effusion, and pneumothorax of the lung were assessed for each region.

Images from all 12 regions were stored and interpreted subsequently. In each region, scores ranging from 0 to 3 were assigned for each consolidation and B-line according to the method described by Song and colleagues [25], with a greater number representing a worse condition. Figure 1 shows the details and examples. Definition of atelectasis was set as presence of consolidation of score 2 or 3 in any of the regions [22].

Figure 1. Examples of scored lung ultrasound images for consolidation or B-line.

Each small image is captioned with subject, score, and definition.



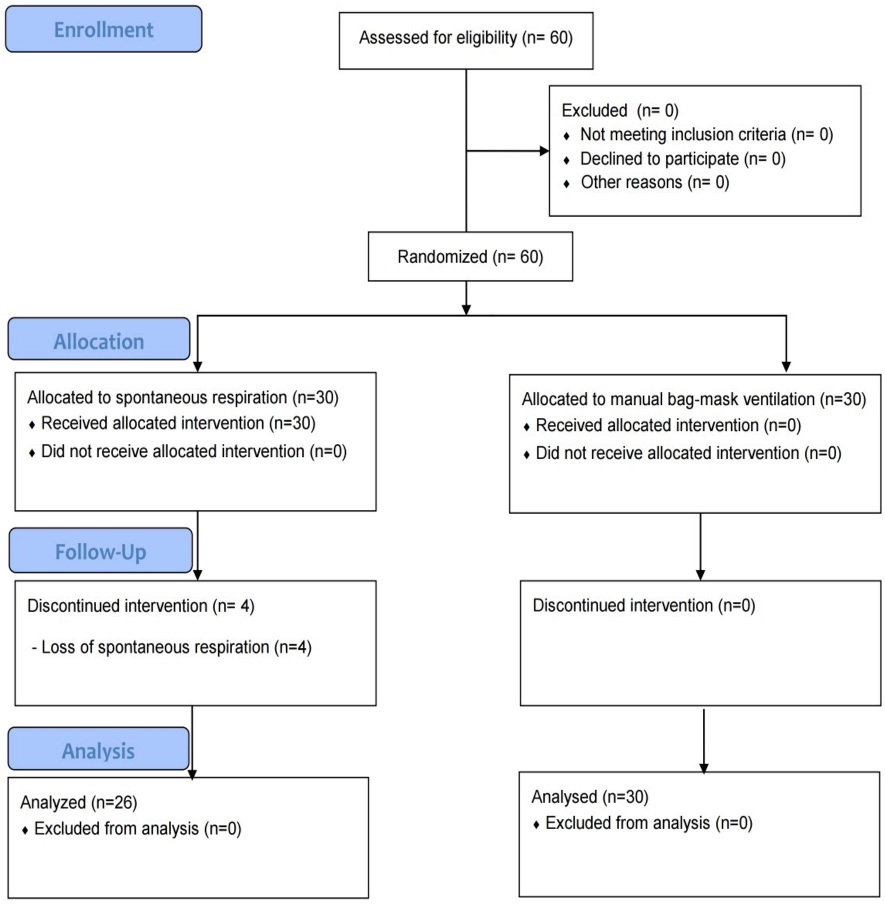
2.5. Sample size calculation

As I had not performed any pilot study, I adopted the data of a previous study [2], assuming the proportion of patients developing atelectasis as 42% in the “spontaneous” group and 80% in the “controlled” group. With an alpha error of 0.05 and power of 80%, the required sample size was 25 patients for each group, i.e. 50 patients in total. Expecting a dropout rate of 20%, I planned to enroll 60 patients. Calculations were performed using MedCalc® (MedCalc Software Ltd., Ostend, Belgium).

2.6. Statistical analysis

The primary outcome was set as the proportion of patients in each group who developed significant atelectasis, which was compared using the chi-squared test. The secondary outcome was set as the sum of the consolidation scores or B-line scores in the anterior, lateral, posterior, or all regions, which was compared using Student's *t*-test. Consolidation scores and B-line score were drawn as a scatter plot and Pearson's correlation coefficient was obtained to investigate the correlation among patients' age, sum of consolidation scores, and sum of B-line scores. The SpO_2, mean blood pressure, and heart rate were recorded at the start of anesthetic induction, at the time of supraglottic airway device insertion, 5 min after anesthetic induction, and at the end of surgery. The Kolmogorov–Smirnov test was performed for normality distribution. Student’s *t*-test, Mann-Whitney *U* test, and Chi-squared test were used as appropriate to compare demographic data and vital signs between the two groups. The incidence of desaturation events ($SpO_2 \leq 94\%$) [26] throughout the anesthetic period was recorded. Agreement about presence of atelectasis between two ultrasound interpreters was analyzed by Cohen's Kappa [27]. Statistical analyses were performed using SPSS®, version 22 (IBM®, Chicago, IL, USA).

Figure 2. CONSORT diagram of patient recruitment



3. Results

A total of 60 patients were enrolled, including 30 patients in each group. Four (13.3%) patients were excluded from the “spontaneous” group because of the loss of spontaneous ventilation. Figure 2 shows the Consolidated Standards of Reporting Trials flow diagram for the study protocol. Table 1 shows the baseline characteristics of enrolled patients, and table 2 shows ventilation profiles and vital signs measured at baseline and at the end of the oxygenation.

Atelectasis was seen after 5 min of oxygenation in seven (26.9%) out of 26 patients in the “spontaneous” group and 22 (73.3%) out of 30 patients in the “controlled” group ($P = 0.001$). The relative risk of atelectasis in the “spontaneous” group was 0.391 (95% confidence interval, 0.211–0.723).

For agreement on presence of atelectasis between two interpreters, the opinion was coherent for 53 (94.6%) patients, which was almost perfect agreement with Cohen’s Kappa of 0.857 ($P < 0.001$).

Table 1. Baseline characteristics of patients.

	Spontaneous group (n = 26)	Controlled group (n = 30)	p-value
Sex (Male:Female)	19:7	22:8	0.983
Age (month)	8.5 [5-10.3]	7.5 [5-9.3]	0.452
Height (cm)	72.2 [65.9-75.1]	70.1 [65.9-75.0]	0.578
Weight (kg)	9.0 [7.5-9.9]	8.6 [7.6-9.5]	0.499
ASA-PS*			0.206
1	13 (50%)	20 (66.7%)	
2	13 (50%)	10 (33.3%)	
Anesthesia time (min)	52.5 [35.0-75.0]	62.5 [45.0-165.0]	0.196
Operation time (min)	32.5 [15.0-50.0]	45.0 [25.0-125.0]	0.091

The spontaneous group were maintained spontaneous ventilation and the controlled group underwent manual bag-mask ventilation for 5 minutes during oxygenation period. Values are median [IQR] or number (percent).

*: American Society of Anesthesiologists Physical Status

Table 2. Ventilation profiles during the oxygenation and vital signs of patients

	Spontaneous group (n = 26)	Controlled group (n = 30)	p-value
Peak inspiratory pressure (cmH_2O)	-	13.5 [9 - 15]	
Tidal volume per body weight ($ml \cdot kg^{-1}$)	4.5 [3.9 - 7.6]	6.7 [4.2 - 8.8]	0.065
Respiratory rate ($\cdot min^{-1}$)	31.2 ± 5.9	28.8 ± 7.0	0.177
Baseline F_EO_2* (%)	88.6 ± 5.9	86.8 ± 6.0	0.246
F_EO_2 after 5 min of oxygenation (%)	89.6 ± 4.7	89.1 ± 4.4	0.672
Baseline mean blood pressure (mmHg)	68.0 [61.0 - 72.0]	60.5 [57.0 - 64.0]	0.006
Mean blood pressure after 5 min of oxygenation (mmHg)	54.0 [42.0 - 63.3]	57.0 [50.8 - 64.5]	0.240
Baseline heart rate ($beats \cdot min^{-1}$)	153.0 [136.0 - 164.0]	160.0 [148.0 - 168.0]	0.128
Heart rate after 5 min of oxygenation ($beats \cdot min^{-1}$)	161.0 [154.0 - 168.0]	160.0 [156.0 -164.0]	0.850
Baseline SpO_2** (%)	100 [100 - 100]	100 [100 - 100]	
SpO_2 after 5 min of oxygenation (%)	100 [100 - 100]	100 [100 - 100]	
Desaturation event ($SpO_2 \leq 94\%$) during surgery	1 (3.8%)	1 (3.3%)	1.000

The spontaneous group were maintained spontaneous ventilation and the controlled group underwent manual bag-mask ventilation for 5 minutes during oxygenation period. Values are median [IQR], mean ± SD or number (percent).

*: fraction of oxygen in expired air, **: arterial oxygen saturation by pulse oximetry

For consolidation and B-line, the sum of scores in the anterior, lateral, and posterior regions as well as their total sum was calculated. As for consolidation scores, the sum of scores in the posterior regions and that of scores in all regions were significantly higher in the "controlled" group than in the "spontaneous" group while the sum of scores in the anterior regions or that of scores in the lateral regions showed no statistically significant difference between the groups. As for B-line scores, there were no significant differences between the groups in the sum of scores in any region or in the total sum. Detailed values and comparisons are presented in Table 3.

Consolidation and B-line scores in the anterior, lateral, and posterior regions within patients were analyzed. As for consolidation scores, the posterior region showed a significantly higher score compared to the anterior and lateral regions. As for B-line scores, the posterior region showed the highest score, followed by the lateral and anterior regions, with statistical significance (Table 4).

Table 3. Sum of consolidation scores and B-line scores from geometrical anterior, lateral and posterior regions of patients' chest.

Score (region)	Max score	Total (n = 56)	Spontaneous group (n = 26)	Controlled group (n = 30)	p-value (spontaneous vs controlled)
Consolidation (anterior)	12	0.32 ± 0.88	0.42 ± 1.14	0.23 ± 0.57	0.424
Consolidation (lateral)	12	0.34 ± 0.96	0.15 ± 0.46	0.50 ± 1.22	0.160
Consolidation (posterior)	12	3.86 ± 3.03	2.50 ± 2.57	5.03 ± 2.94	0.001
Consolidation (total)	36	4.52 ± 3.82	3.08 ± 3.02	5.77 ± 4.05	0.007
B-line (anterior)	12	1.14 ± 1.55	1.04 ± 1.28	1.23 ± 1.77	0.644
B-line (lateral)	12	1.77 ± 1.61	1.50 ± 1.53	2.00 ± 1.66	0.249
B-line (posterior)	12	4.77 ± 2.55	4.31 ± 2.41	5.17 ± 2.64	0.212
B-line (total)	36	7.68 ± 4.44	6.85 ± 3.83	8.40 ± 4.85	0.194

Spontaneous group were maintained spontaneous ventilation and the controlled group received manual bag-mask ventilation. Values are mean ± SD.

Table 4. Comparison of sum of consolidation scores or B-line scores from geometric anterior, lateral and posterior regions of chest within subjects.

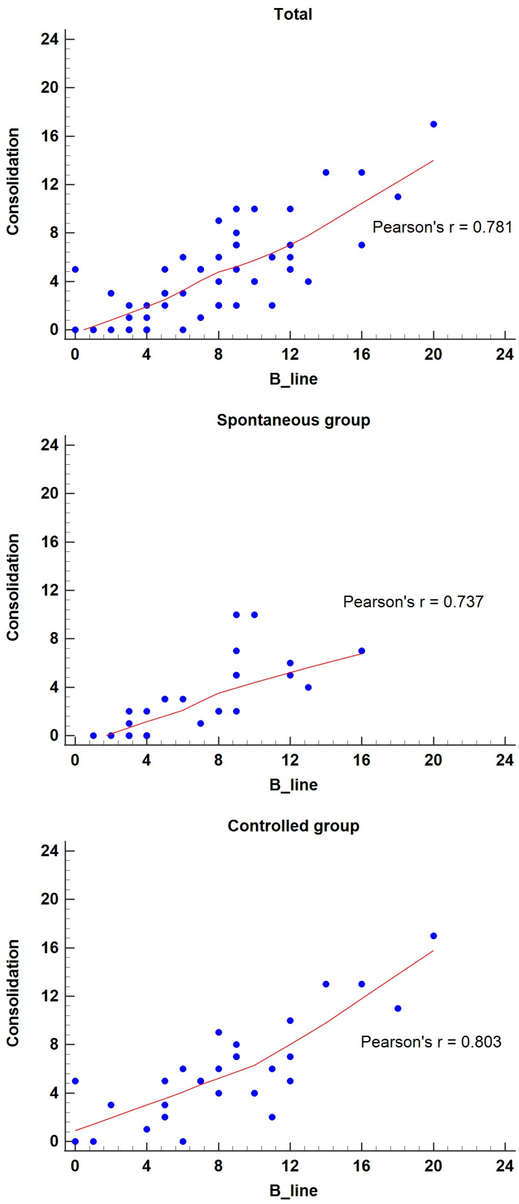
	Total (n = 56)	Spontaneous group (n = 26)	Controlled group (n = 30)
Comparison		Difference (95% C.I.) (p-value)	
Consolidation (anterior vs lateral)	-0.02 (-0.30 – 0.26) (0.898)	0.27 (-0.22 – 0.76) (0.271)	-0.27 (-0.56 – 0.03) (0.073)
Consolidation (lateral vs posterior)	-3.52 (-4.25 – -2.78) (<0.001)	-2.35 (-3.32 – -1.38) (<0.001)	-4.53 (-5.52 – -3.54) (<0.001)
Consolidation (anterior vs posterior)	-3.54 (-4.36 – -2.72) (<0.001)	-2.08 (-3.21 – -0.94) (0.001)	-4.80 (-5.82 – -3.78) (<0.001)
B-line (anterior vs lateral)	-0.63 (-1.02 – -0.23) (0.003)	-0.46 (-1.05 – 0.13) (0.123)	-0.77 (-1.33 – -0.21) (0.009)
B-line (lateral vs posterior)	-3.00 (-3.67 – -2.33) (<0.001)	-2.81 (-3.84 – -1.77) (<0.001)	-3.17 (-4.10 – -2.23) (<0.001)
B-line (anterior vs posterior)	-3.63 (-4.33 – -2.95) (<0.001)	-3.27 (-4.26 – -2.28) (<0.001)	-3.93 (-4.89 – -2.98) (<0.001)

Spontaneous group were maintained spontaneous ventilation and the controlled group received manual bag-mask ventilation. Mean and standard deviations of sum of scores from each region are expressed in Table 3. Differences were calculated as the latter deducted from the former.

Figure 3 shows scatter plots of the sum of consolidation scores and the sum of B-line scores. There was a strong positive correlation between those two scores for total patients (Pearson's r = 0.781, P < 0.001) and for patients in each group (r = 0.781, P < 0.001 for the "spontaneous" group and r = 0.803, P < 0.001 for the "controlled" group, respectively).

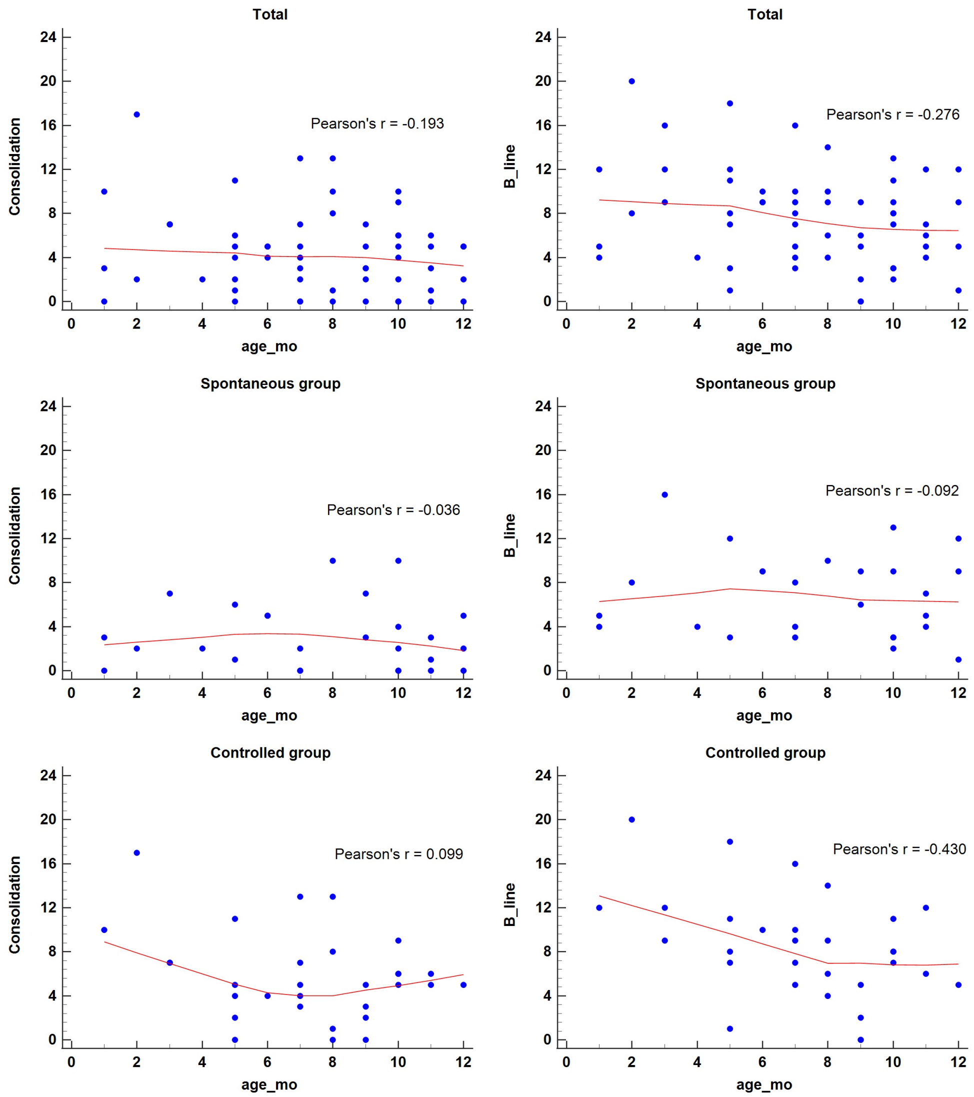
In figure 4, correlation between patients' age and the consolidation or B-line scores are shown, including subgroup analysis. There was a moderate negative correlation between age and total B-line score for patients in the "controlled" group (Pearson's r = -0.430, P = 0.018), while it was not significant in the "spontaneous" group (r = -0.092, P = 0.655). In total, the correlation was weak but significant (r = -0.276, P = 0.040).

Figure 3. Scatter plots of total consolidation score and B-line score.



There was a strong positive correlation between both scores (Pearson's $r = 0.781$, $P < 0.001$) for the whole patients. In subgroup analysis, the strong positive correlation was maintained ($r = 0.781$, $P < 0.001$ for the spontaneous group and $r = 0.803$, $P < 0.001$ for the controlled group, respectively). The locally weighted smoothing lines are shown in red.

Figure 4. Scatter plots of age in month and total consolidation score or B-line score.



There was a moderate negative correlation between age (month) and total B-line score for patients in the controlled group (Pearson's r = -0.430, P = 0.018), while it was not significant in the spontaneous group (r = -0.092, P = 0.655). In total, the correlation was weak but significant (r = -0.276, P = 0.040). Other correlations were not significant. The locally weighted smoothing lines are shown in red.

In the oxygenation period, the tidal volume per kg body weight was larger in the “controlled” group than in the “spontaneous” group, but without statistical significance (*P* = 0.065). Table 1 demonstrates the detailed values.

4. Discussion

4.1. Discussion about findings

Results of the present study supported the hypothesis of this study that maintaining spontaneous ventilation decreases the rate of atelectasis formation during induction of anesthesia in infants.

This hypothesis was developed based on previous studies comparing sedation without intubation and general anesthesia with an airway maintenance device [1], and focused on comparing spontaneous ventilation and manual positive-pressure ventilation during anesthetic induction. Moreover, as mentioned in the Introduction section, infants are more prone to hypoxemia and atelectasis. I regarded the prevention of atelectasis formation during anesthetic induction to be of greater importance in infants than older patients. Therefore, the present study was conducted for infants.

Higher incidence of significant atelectasis and higher consolidation score were observed in the "controlled" group compared to "spontaneous" group during induction of anesthesia, and this difference was confined to dependent regions of the lung (Table 4). As mentioned in the introduction, atelectasis formation during induction of anesthesia is influenced by F_IO_2 (resorption atelectasis), obesity, underlying condition of the lung, position of the patient (compression atelectasis), muscle relaxation, and profiles of ventilation [6,8-10]. By randomization and controlling of other factors, I could exclude the effect of factors other than muscle relaxation and profiles of ventilation in this study.

There was no significant difference in B-line scores between groups. Although the presence of B-lines is a common lung ultrasound finding in anesthesia-induced atelectasis, it can be found in various conditions, such as interstitial lung syndrome, pulmonary edema, acute respiratory distress syndrome, and pulmonary contusion [28,29]. B-lines originate from reverberations when the ultrasound beam is reflected at thickened interlobular septa. The cause of thickening is mostly by pulmonary edema [30], but poor aeration can also be the cause [31], which explains observation of B-lines in anesthesia-induced atelectasis [12]. Acosta and colleagues [12] also explained few but not many B-lines as representative of anesthesia-induced atelectasis.

However, there are reports that presence of B-line is non-specific in children [32], and that B-lines can be observed in healthy children without lung parenchymal change on CT image [33]. Therefore, it can be inferred that even though B-lines can be observed in patients with atelectasis, the difference can possibly be small. Also, the fact that the ultrasound exam was done only 5 minutes after intervention can also explain the insignificance of difference. This was the reason that the consolidation score was set as the primary endpoint for evaluation of atelectasis.

The peak airway pressure was limited within 15 cmH_2O in the “controlled” group to avoid overdistension of the lung, which could lead to unintentional alveolar recruitment. Additionally, this strategy might induce atelectasis formation in some patients, particularly in patients with insufficient inspiration. Although the limit of precision for tidal volume provided by the anesthesia machine is not clear, the tidal volume adjusted to the body weight were higher in the "controlled" group, even though the p-value was above 0.05. In clinical practice, manual facemask ventilation can have a tidal volume greater than 8 $ml \cdot kg^{-1}$, and peak airway pressure can be greater than 15 cmH_2O, which can lead to a reduced incidence of atelectasis. This study is of value in that it compared the negative pressure in spontaneous ventilation with the positive pressure in manual ventilation for atelectasis formation in a controlled environment of airway pressure and tidal volume.

In both groups, SpO_2 was maintained at 100% during oxygenation period in all of the patients and the incidence of desaturation during the surgery was very low. Since the enrollment was confined to patients without underlying conditions that are vulnerable to hypoxemia, atelectasis, or other respiratory complications, most of the patients were well oxygenated with either method. In clinical situations, I expect high-risk patients with underlying conditions that are vulnerable to atelectasis would benefit with maintenance of spontaneous ventilation during induction of anesthesia.

4.2. Mechanism-based interpretation

Under effect of muscle relaxants, the relaxed diaphragm cannot maintain pressure separation between the abdominal cavity and the thoracic cavity. The dependent portion of the lung is most vulnerable to this phenomenon [10,34]. Moreover, the electrical activity of the diaphragm was found to be lower during positive-pressure ventilation [35]. Findings of this study are concordant to this since the “controlled” group had received manual ventilation with neuromuscular blockade.

In spontaneously breathing infants, physiologic laryngeal braking occurs during expiration, which could help maintaining the functional residual capacity by an auto-PEEP effect. This might also explain the difference in atelectasis formation between the two groups [36]. Compression atelectasis results from reduced transmural pressure for distention of the alveolus to the extent that the alveolus could collapse [10]. According to a previous study, maintaining spontaneous ventilation applies even transpulmonary pressure to every region of the lung [37], thus leading to the possibility that compression atelectasis would not occur during spontaneous ventilation. Nevertheless, even in the “spontaneous” group, the posterior region had a significantly higher consolidation score compared to the anterior and lateral regions (Table 4). Therefore, it can be concluded that spontaneous ventilation may not totally prevent but can reduce atelectasis formation during anesthetic induction.

4.3. Limitations

This study has some limitations. First, I did not perform a lung ultrasound examination before induction of anesthesia: I thus cannot exclude that some atelectasis was already present in both groups neither to what extent the ventilation technique made it worse or not. Although I could not find evidence for formation of atelectasis in infants without predisposing condition for atelectasis at upper or lower respiratory tract, this would be a limitation. I tried to minimize this by doing randomization and excluding patients who showed atelectasis in the preoperative chest radiograph. Second, a recent study showed that the peak inspiratory pressure was lower when pressure-controlled ventilation was performed compared to when manual mask ventilation was performed during anesthetic induction [38,39]. Therefore, adding a group with pressure-controlled ventilation would have yielded a robust conclusion. Further studies on pressure-controlled ventilation and atelectasis during anesthetic induction are warranted. Third, even though I limited the airway pressure not to exceed 15 cmH_2O and the tidal volume to be 6–8 $ml \cdot kg^{-1}$ in the "controlled" group, the possibility of gastric insufflation exists, as perfect manual control of airway pressure is not possible and there are many disturbances. However, assessment of gastric insufflation at the end of oxygenation with ultrasound or other modalities was not done. Gastric insufflation increases intra-abdominal pressure [24] and can thus decrease thoracic compliance and affect atelectasis formation. It would have been better to examine the patient's stomach via ultrasound along with lung ultrasound to see whether the gastric insufflation contributed to atelectasis formation in the "controlled" group. Fourth, I used 100% oxygen as fresh gas during oxygenation despite of recent recommendations that adequate F_IO_2 should be 80% to reduce development of absorption atelectasis [40]. F_IO_2 of 100% is known to provide longer safe apnea time compared to F_IO_2 of 80% in adults [41]. I chose F_IO_2 of 100% instead of 80%, in order to minimize the risk of hypoxemia during induction of anesthesia, since this study is for infants younger than one year old, most of whom are under 10kg of weight and are always at potentially high risk of hypoxemia during airway establishment [42]. Also, guideline from the Difficult Airway Society recommends use of 100% oxygen to the high risk patients [43]. Moreover, mechanism of atelectasis I was mainly interested in this study is compression atelectasis, which is influenced by the direction of gravity applied to the patient's chest. I knew relatively high F_IO_2 during anesthetic induction could have influenced the formation of atelectasis, but I can say maintaining spontaneous ventilation decreases the rate of atelectasis formation even under F_IO_2 of 100%. Finally, it would have been better if arterial blood gas was analyzed to obtain precise arterial partial pressures of oxygen and carbon dioxide. However, making an arterial puncture is a risk-taking procedure, invasive collection of arterial blood was not considered because of ethical reason.

5. Conclusions

In conclusion, in infants younger than 1 year, maintaining spontaneous ventilation during the oxygenation period of anesthetic induction can reduce the risk of atelectasis formation more compared to manual bag-mask ventilation, particularly in the dependent region of the lung. I expect infants and children who have underlying conditions vulnerable to atelectasis and hypoxemia could benefit from this protective effect of spontaneous ventilation during induction of anesthesia. Further studies with modification of study design such as different F_IO_2, age group, other modes of ventilation, and patients' underlying condition would help understanding the relationship between spontaneous ventilation and formation of atelectasis during induction of anesthesia.

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7. Abstract in Korean

영아에서 마취 유도 시 자발호흡 유지 여부가 무기폐 발생에 미치는 영향 : 전향적 무작위 배정 임상연구

연구 배경: 소아의 마취 유도 시 무기폐는 흔하게 발생하며, 영아에서는 그 빈도가 더욱 높다. 양압환기 시보다 자발호흡이 유지되는 상황에서 무기폐의 발생 위험이 낮은 것은 어느 정도 알려져 있으나, 현재까지는 영아에서 마취 유도 시 자발호흡을 유지시키면서 무기폐 발생을 관찰한 전향적 연구는 보고된 바가 없다.

연구 목표: 본 연구에서는 1 세 미만의 영아에서 마취 유도 중 자발호흡을 유지하는 경우 그렇지 않은 경우보다 무기폐의 발생률을 줄일 수 있다는 것을 가설로 하고, 그 가설을 검증하기 위한 전향적 연구를 계획하였다.

연구 방법: 전신마취 하 수술을 받기로 예정된 만 1 세 미만의 영아 60 명을 대상으로 연구를 진행하였다. 환자들을 자발호흡을 유지하는 "spontaneous" 군과, 용수 양압 환기를 유지하는 "controlled" 군으로 무작위로 배정하였다. 통상적인 방법으로 마취 유도 후, "spontaneous" 군은 안면 마스크로 산소를 공급하면서 자발호흡을 유지하였고, "controlled" 군은 안면 마스크를 통해 백-

마스크 환기를 시행하였다. 5 분간 산소 공급 후 환자의 폐를 12 개의 구역으로 나누어 초음파로 관찰하고 무기폐 발생 여부를 확인하고 비교하였다.

연구 결과: 산소 공급 후 무기폐의 발생은 “spontaneous” 군에서는 26 명 중 7 명 (26.9%), “controlled” 군에서는 30 명 중 22 명 (73.3%)에서 관찰되었다 ($P = 0.001$). “Spontaneous” 군의 무기폐 발생에 대한 상대 위험도는 0.391 (95% 신뢰구간 0.211 – 0.723) 이었다. 경화(consolidation) 소견을 관찰하였을 때, “controlled” 군에 비해 “spontaneous” 군에서 폐의 전체 구역 및 중력의 방향과 가까운 뒤쪽 구역에서의 경화 소견 점수가 낮았다 ($P = 0.007$, $P = 0.001$).

고찰: 1세 미만의 영아에서 마취 유도 시 자발호흡을 유지하는 것이 무기폐 발생률을 낮추는 결과가 관찰되었고, 그 차이는 폐의 중력의 방향과 가까운 뒤쪽 구역에서 더 저명하였다. 신경근 차단제의 사용이 필요하지 않은 수술을 위한 영아의 전신마취 시, 마취 유도 후 산소 공급 과정에서 무기폐의 발생률을 낮추기 위해 자발호흡을 유지하는 것을 고려해볼 수 있다.

주요어: 마취 유도, 무기폐, 폐 초음파, 양압환기, 자발호흡

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