Factors Associated with Post-Intubation Hypotension in an Emergency Department: A Retrospective Observational Study

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Objective: *Hypotension is an important complication following emergency intubation. However, no study in Thailand about factors associated with post-intubation hypotension (PIH) has been published. The present study aimed to identify the factors inducing PIH.*

Material and Method: *We retrospectively analyzed data from a prospectively collected database of patients intubated in the emergency department (ED). The inclusion criteria were patients older than 18 years who were intubated in the ED. Patients were divided into a PIH group [systolic blood pressure (SBP) 90 mmHg or lower or decrease in SBP of greater than 20% from baseline within 10 minutes] and a non-PIH group to analyze risk factors.*

Results: *Of the 1,781 intubated patients, 1,435 met the study criteria and were analyzed. PIH occurred in 315 patients (22%). Propofol [adjusted odds ratio (OR) 2.16, 95% confidence interval (CI) 1.43 to 3.25], rocuronium (adjusted OR 1.39, 95% CI 1.01 to 1.90), chronic obstructive pulmonary disease (COPD) (adjusted OR 1.54, 95% CI 1.03 to 2.29), and previous stroke (adjusted OR 1.46, 95% CI 1.04 to 2.05) were associated with increased PIH.*

Conclusion: *Propofol was the most significant factor that caused PIH. Rocuronium, COPD, and previous stroke were statistically significant associated with increased risk of PIH.*

Keywords: *Post-intubation hypotension, Risk factor, Emergency department, Intubation*

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Emergency airway management is an important procedure for supporting critically ill patients. However, intubation can lead to many complications[1,2], including hypotension, hypoxemia, and arrhythmia. Post-intubation hypotension (PIH) is considered to be a major complication[3,4], and previous studies have found an association between PIH and mortality[4,5]. However, the incidence of PIH varied from 23 to 44% among different hospitals[4,6,7].

Rapid sequence intubation (RSI) using a sedative and a muscle relaxant to facilitate intubation is widely employed in emergency departments (EDs). Although this technique is associated with an increased intubation success and fewer complications after intubation[8,9], some medications, such as propofol and midazolam, might result in a fall in blood pressure.

Several previous studies have reported factors associated with PIH, including age, sepsis, and chronic obstructive pulmonary disease (COPD)[7,10-12]. Although all these studies examined the effects of RSI drugs, they found no association between drugs used and PIH. However, these previous studies[7,11,12] recruited trauma patients, and to the best of our knowledge, no study has yet examined the factors associated with PIH in a non-trauma ED in Thailand. We hypothesized that PIH would be associated with the drugs used to facilitate RSI. The primary objective of the present study aimed to identify the factors associated with PIH in patients who received intubation in ED, based on medical records and collected database, including use of drugs to assist intubation and pre-existing comorbidities. The secondary objective aimed to ascertain if subsequent in-hospital mortality differed between intubated patients with and without PIH.

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Material and Method

This retrospective study was conducted in the non-trauma ED at Siriraj Hospital, a tertiary care university hospital with approximately 12,000 non-trauma ED visits per month.

Patients

The Siriraj Emergency Medicine Intubation Database (SEMID) is a large, prospectively collected database of patients intubated in the non-trauma ED at

Siriraj Hospital since January 2010. All patients older than 18 years who were intubated in the ED from the start of the SEMID database between January 2010 and December 2013 were included in the study. Exclusion criteria were cardiac arrest before intubation and lack of data on pre- and post-intubation blood pressures. The present study was approved by the Siriraj Institutional Review Board (COA No. Si.410/2014).

Data collection

SEMID forms were completed by the intubators after intubation. The data included date of intubation, sex, pre- and 10-minute post-intubation vital statuses, oxygen saturation, indication for intubation, number of intubation attempts, intubation technique, medication used to facilitate intubation, and adverse events. The SEMID forms were completed by the intubators who may also have been treating other patients, leading to the possibility of missing information and recall bias. Missing data were retrieved from medical records, and recall bias was prevented by randomly re-checking the SEMID data with available data from the medical records. Information on pre-existing comorbidities and in-hospital mortality were retrieved from medical records.

There is currently no standard definition of PIH, and definitions in previous studies have varied[7,13-15]. Therefore, we defined PIH as systolic blood pressure (SBP) as 90 mmHg or less after intubation or decrease in SBP of greater than 20% from baseline after intubation[14,15].

Objective

The primary objective was to identify the factors associated with PIH. The secondary objective was to determine the association between PIH and in-hospital mortality.

Statistical analysis

Data analysis was performed using PASW 18.0 statistics for Windows (SPSS Inc., Chicago, IL, USA). Demographic data were presented as frequency and percentage or median and interquartile range. Baseline characteristics (age, sex, pre-existing comorbidities), indication for intubation, number of intubation attempts, drugs used to facilitate intubation, and in-hospital mortality were compared between the PIH and non-PIH groups using Chi-square test or Mann-Whitney test, as appropriate. Factors associated with PIH were identified by binary logistic regression analysis. Multivariate analysis was performed using multiple logistic regression with the forward stepwise method for all factors with a value of $p<0.1$ in univariate analysis. The results were displayed as adjusted odds ratios (OR) with 95% confidence intervals (95% CI). A p-value <0.05 was considered statistically significant.

Results

One thousand seven hundred eighty one patients were intubated in the ED between January 1, 2010 and December 31, 2013. After exclusion of 346 patients (19.4%), data for 1,435 patients were analyzed. Among these patients, 315 (22%) had PIH and 1,120 (78%) had no hypotension after intubation (Fig. 1).

Patient characteristics

The median age of the analyzed patients was 69 (56 to 78) years, and 777 (54.1%) patients were male. The baseline characteristics were shown in Table 1. There was no significant difference in age or sex between the PIH and non-PIH groups. The PIH group had more patients with previous strokes compared with the non-PIH group ($p = 0.03$). Patients with PIH tended to have more COPD, but the difference was not significant ($p = 0.06$). There were no missing data, except for comorbidities and number of intubation attempts, as shown in Table 1 and 2.

Intubation

Difficult intubation (three or more intubation attempts) occurred in 13.2% of patients, and RSI was the most commonly used technique (44.9%). There was no significant difference between the PIH and non-PIH groups in terms of number of intubation attempts or intubation technique (Table 2).

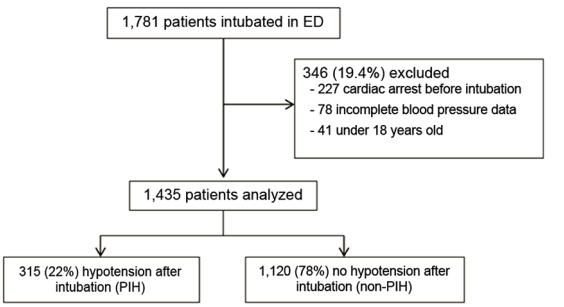

Fig. 1 Patients intubated in the ED.

Table 1. Baseline characteristics

Characteristic	Total (n = 1,435)	Non-PIH group (n = 1,120)	PIH group (n = 315)	*p*-value
Sex (male), n (%)	777 (54.1)	610 (54.5)	167 (53.0)	0.65
Age (years), median (range)	69 (56 to 78)	68 (55 to 77)	70 (58 to 78)	0.08†
Age ≥60 years old, n (%)	982 (68.4)	757 (67.6)	225 (71.4)	0.19
Comorbidity, n (%)*	(n = 1,410)	(n = 1,099)	(n = 311)	
Diabetes mellitus	480 (34.0)	370 (33.7)	110 (35.4)	0.58
Hypertension	762 (54.0)	594 (54.0)	168 (54.0)	0.99
Chronic kidney disease	254 (18.0)	207 (18.8)	47 (15.1)	0.13
Previous stroke	209 (14.8)	151 (13.8)	58 (18.6)	0.03
Heart disease	401 (28.4)	323 (29.4)	78 (25.1)	0.14
Asthma	28 (2.0)	21 (1.9)	7 (2.3)	0.70
Chronic obstructive pulmonary disease	137 (9.7)	98 (8.9)	39 (12.5)	0.06
Cancer	158 (11.2)	119 (10.8)	39 (12.5)	0.40

PIH = post-intubation hypotension
* Missing data 25 patients, † Using Mann-Whitney test, all others using Chi-square test

Table 2. Intubation details†

Characteristic	Total (n = 1,435)	Non-PIH group (n = 1,120)	PIH group (n = 315)	*p*-value
Indication, n (%)				
Upper airway obstruction	27 (1.9)	18 (1.6)	9 (2.9)	0.15
Cardiovascular cause	156 (10.9)	128 (11.4)	28 (8.9)	0.20
Respiratory cause	806 (56.2)	617 (55.1)	189 (60.0)	0.12
Alteration of consciousness	423 (29.5)	340 (30.4)	83 (26.3)	0.17
Metabolic acidosis	23 (1.6)	17 (1.5)	6 (1.9)	0.63
Techniques of intubation, n (%)				
Oral without medication	350 (24.4)	285 (25.4)	65 (20.6)	0.08
Oral with sedation only	431 (30.0)	337 (30.1)	94 (29.8)	0.93
Oral with RSI	645 (44.9)	492 (43.9)	153 (48.6)	0.14
Succinylcholine only	4 (0.3)	3 (0.3)	1 (0.3)	0.88
Nasotracheal intubation	5 (0.3)	3 (0.3)	2 (0.6)	0.33
Number of attempts, n (%)*	(n = 1,266)	(n = 997)	(n = 269)	
First-attempt success	816 (64.5)	641 (64.3)	175 (65.1)	0.82
≥3 attempts	167 (13.2)	130 (13.0)	37 (13.8)	0.76

RSI = rapid sequence intubation
* Missing data 169 patients, † Using Chi-square test

Drug administration

The most commonly used sedative drugs were etomidate (33.6%) and ketamine (26.3%), and the most commonly used neuromuscular blocking agent was succinylcholine (26.3%). Patients with PIH received more propofol and rocuronium than those without PIH (Table 3).

Analysis of risk factors

Multivariate analysis using age 60 years or older, previous stroke, COPD, propofol, and rocuronium for factor adjustment showed that propofol (adjusted OR 2.16, 95% CI 1.43 to 3.25), rocuronium (adjusted OR 1.39, 95% CI 1.01 to 1.90), COPD (adjusted OR 1.54, 95% CI 1.03 to 2.29), and previous stroke (adjusted OR 1.46, 95% CI 1.04 to 2.05) were associated with increased incidence of PIH (Table 4).

Other complications

Cardiac arrest occurred after intubation in 1% of all patients. Other serious complications were regurgitation (0.2%), arrhythmia (0.1%), desaturation (0.9%), and esophageal intubation (0.9%).

In-hospital mortality

Mortality data were missing for 83 patients because of referrals to other hospitals. The in-hospital mortality was 44% (595 from 1,352 patients). There was no significant difference in terms of in-hospital

Table 3. Medication for intubation†

Medication	Total (n = 1,435)	Non-PIH group (n = 1,120)	PIH group (n = 315)	*p*-value
Pretreatment, n (%)				
Fentanyl	46 (3.2)	38 (3.4)	8 (2.5)	0.45
Atropine	1 (0.1)	1 (0.1)	0 (0)	0.78
Sedative drugs, n (%)				
Etomidate	482 (33.6)	387 (34.6)	95 (30.2)	0.15
Ketamine	377 (26.3)	289 (25.8)	88 (27.9)	0.45
Propofol	114 (7.9)	73 (6.5)	41 (13.0)	<0.001
Midazolam	48 (3.3)	39 (3.5)	9 (2.9)	0.59
Diazepam	22 (1.5)	17 (1.5)	5 (1.6)	0.93
NMB, n (%)				
Succinylcholine	378 (26.3)	300 (26.8)	78 (24.8)	0.47
Rocuronium	258 (18.0)	188 (16.8)	70 (22.2)	0.03
Cis-atracurium	1 (0.1)	0 (0)	1 (0.3)	0.22

NMB = neuromuscular blocking agent
† Using Chi-square test

Table 4. Factors associated with post-intubation hypotension*

Factor	Crude OR (95% CI)	Adjusted OR (95% CI)	*p*-value
Propofol	2.15 (1.43 to 3.22)	2.16 (1.43 to 3.25)	<0.001
Rocuronium	1.42 (1.04 to 1.93)	1.39 (1.01 to 1.90)	0.04
COPD	1.47 (0.99 to 2.17)	1.54 (1.03 to 2.29)	0.03
Previous stroke	1.44 (1.03 to 2.01)	1.46 (1.04 to 2.05)	0.03

COPD = chronic obstructive pulmonary disease
* Using multiple logistic regression with the forward stepwise method

mortality between the PIH and non-PIH groups (43.7% vs. 44.1%, $p = 0.91$).

Discussion

The present study, based on the largest ED intubation database in Thailand, showed that propofol, rocuronium, COPD, and previous stroke were all associated with an increased risk of PIH. However, PIH had no effect on in-hospital mortality.

Our study found that propofol was the most significant factor associated with hypotension after intubation which was consistent with numerous previous studies that have reported the incidence of PIH varied from 6.7 to 35.5% after propofol administration in both operating room and ED settings[13,16-22]. As the disadvantage of causing hemodynamic instability, some emergency physicians might concern about using propofol in emergency patients. However, propofol has several benefits that support its place in RSI medication in ED. It has rapid onset and good intubation conditions. Propofol can reduce intracranial pressure, thus it is suitable for patients with increased intracranial pressure such as intracerebral hemorrhage[16]. Moreover, propofol rarely resulted in mortality[16-22] and some studies reported that hypotension occurred after propofol used was transient and rarely required further medication[18,22]. Previous studies suggested that fluid loading before intubation and reduction of doses of propofol in elderly could reduce PIH[16,23]; therefore, these interventions may be considered before giving propofol to prevent hemodynamic instability in emergency patients.

We also found that rocuronium was independently associated with a higher incidence of hypotension, in contrast with some previous studies that reported non-significant hemodynamic changes after rocuronium use[24-26]. However, data from the US Food and Drug Administration reported transient hypotension after rocuronium administration in 2% of patients[27], and Stevens et al also reported transient hypotension within three to five minutes after induction with rocuronium[28]. In addition, other studies have reported anaphylaxis related to the use of rocuronium, resulting in hypotension after intubation[29,30]. We hypothesized that rocuronium may have been associated with PIH in our ED for two reasons. Firstly, critically ill patients are likely to suffer from sympathetic hyperactivity as a result of stress[31], intubation, and

administration of RSI drugs, especially rocuronium, which paralyzes the muscles for an extended period, would reduce the sympathetic tone with a potential effect on hemodynamic instability. Secondly, we might have under estimated the incidence of rocuronium-induced anaphylaxis. Although our study reported the higher incidence of PIH after administration of rocuronium, it was inconclusive and further study was required to approve this finding because hypotension from rocuronium might have been transient and might have not resulted in long-term sequelae. Moreover, there was little data about hemodynamic instability from rocuronium and recent evidences supported the use of rocuronium in ED[16,32]; therefore, rocuronium is still an essential neuromuscular blocking agent that should be used for RSI in ED.

We identified COPD as an important factor associated with PIH, consistent with previous studies[3,10,16]. Patients with acute COPD exacerbation might develop auto-positive end expiratory pressure (PEEP) as a result of increasing airway pressure. Intubation may then cause increased intrathoracic pressure as a result of positive pressure ventilation, which combined with the effect of auto-PEEP, may further lead to hypotension[33,34].

Previous stroke was also identified as a risk factor for PIH in the current study. To the best of our knowledge, this is the first study to demonstrate this association. However, the reasons why previous stroke might cause PIH are unclear. We hypothesized that patients with previous stroke who were in dependent status may experience autonomic dysfunction[35], which might lead to subsequent hypotension after intubation. However, our study did not collect data about dependent status of patients; therefore, further study is required to support this finding.

The results of the present study showed no association between PIH and in-hospital mortality, consistent with Green et al's study[7], but in contrast to that of Heffner et al[4]. Our study differed from Heffner et al[4] in terms of the definition of PIH and the timing of blood pressure measurement; we measured blood pressure 10 minutes after intubation compared with 30 minutes in Heffner et al's study[4], which might account for the different results. Furthermore, 8.5% of patients in our study were lost to follow-up, which might have affected the mortality rate. We hypothesized that the PIH in our study might have been transient, given the shorter period after intubation, and may therefore not have affected mortality. In addition, although Green et al[7] found no association between hypotension and mortality, sustained hypotension increased the incidence of mortality compared with transient hypotension, which supports our hypothesis. However, further studies are needed to clarify the association between sustained hypotension and mortality.

The present study had several limitations. First, the study design was retrospective and some data might have been missing, including information on comorbidities, number of intubation attempts, and in-hospital mortality, which may have affected the results. Moreover, some important information may not be included in the SEMID forms, such as blood pressure-lowering medication, amount of intravenous fluid given before intubation and the response after fluid loading, or the use of vasopressors to correct hypotension. Second, the SEMID database was completed by the physician who inserted the endotracheal tube, therefore might have been subject to self-report and recall biases. Third, because of the busy conditions in the ED, the time to measure blood pressure might not have been exactly 10 minutes. Finally, our results might not be generalizable to non-tertiary hospitals that treat trauma patients.

Conclusion

Propofol, rocuronium, COPD, and previous stroke may be associated with increased risks of IH. Intervention may therefore be required to prevent hypotension after intubation inpatients with these preexisting factors. However, PIH had no apparent effect on in-hospital mortality.

What is already known on this topic?

PIH is considered to be a major complication of emergency intubation[3,4]. Several previous studies have reported factors associated with PIH, including age, sepsis, and COPD[10-12]. Although all these studies examined the effects of RSI drugs, they found no association between the drugs used and PIH. However, these previous studies recruited trauma patients, and to the best of our knowledge, no study has yet examined the factors associated with PIH in a non-trauma ED in Thailand.

What this study adds?

This study found that propofol and rocuronium used as the RSI drugs were associated with increased incidence of PIH. Moreover, this study provided the largest data of emergency intubation with and without RSI in Thailand.

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Potential conflicts of interest

None.

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การศึกษาแบบย้อนหลังเกี่ยวกับปัจจัยที่ทำให้เกิดภาวะความดันโลหิตต่ำหลังจากใส่ท่อช่วยหายใจในห้องฉุกเฉิน

ธันยพร นครชัย, พิมพา ลิ้มพันธ์อุดม, อภิชญา มั่นสมบูรณ์, อุษาพรรณ สุรเบญจวงศ์, ณัฐกานต์ ประพฤติกิจ, วันสิริ ชัยสิรินทร์, ทิพา ชาคร

วัตถุประสงค์: *ความดันโลหิตต่ำเป็นภาวะแทรกซ้อนสำคัญที่เกิดขึ้นหลังการใส่ท่อช่วยหายใจในภาวะฉุกเฉิน อย่างไรก็ตามในประเทศไทยยังไม่เคยมีการศึกษาเกี่ยวกับเรื่องนี้มาก่อน การศึกษานี้จึงจัดทำขึ้นเพื่อศึกษาปัจจัยที่ทำให้เกิดภาวะความดันโลหิตต่ำหลังใส่ท่อช่วยหายใจ*

วัสดุและวิธีการ: *เป็นการศึกษาแบบย้อนหลังโดยวิเคราะห์ข้อมูลจากฐานข้อมูลของผู้ป่วยที่ได้รับการใส่ท่อช่วยหายใจในห้องฉุกเฉิน เกณฑ์การคัดผู้ป่วยเข้าร่วมการศึกษา คือ ผู้ป่วยอายุมากกว่า 18 ปี ที่ได้รับการใส่ท่อช่วยหายใจในห้องฉุกเฉิน ผู้ป่วยถูกแบ่งออกเป็น 2 กลุ่ม คือ กลุ่มที่มีความดันโลหิตต่ำหลังใส่ท่อช่วยหายใจ (ความดันโลหิต systolic <90 mmHg หรือ ความดันโลหิต systolic ลดลงมากกว่าร้อยละ 20 จากความดันโลหิตตั้งต้น ภายใน 10 นาที) และกลุ่มที่ไม่มีความดันโลหิตต่ำ แล้วนำข้อมูลมาเปรียบเทียบเพื่อหาปัจจัยเสี่ยงที่ทำให้เกิดความดันโลหิตต่ำหลังการใส่ท่อช่วยหายใจ*

ผลการศึกษา: *ผู้ป่วยได้รับการใส่ท่อช่วยหายใจในห้องฉุกเฉิน 1,781 ราย เข้าเกณฑ์การคัดเลือกผู้ป่วย และนำมาวิเคราะห์ 1,435 ราย เกิดความดันโลหิตต่ำหลังใส่ท่อช่วยหายใจ 315 ราย (ร้อยละ 22) ปัจจัยเสี่ยงที่มีผลต่อภาวะความดันโลหิตต่ำหลังใส่ท่อช่วยหายใจ คือ propofol (adjusted OR 2.16, 95% CI 1.43-3.25) rocuronium (adjusted OR 1.39, 95% CI 1.01-1.90) โรคปอดอุดกั้นเรื้อรัง (adjusted OR 1.54, 95% CI 1.03-2.29) และโรคหลอดเลือดสมอง (adjusted OR 1.46, 95% CI 1.04-2.05)*

สรุป: *Propofol เป็นปัจจัยที่สำคัญที่สุดที่ทำให้เกิดภาวะความดันโลหิตต่ำหลังใส่ท่อช่วยหายใจ rocuronium โรคปอดอุดกั้นเรื้อรัง และโรคหลอดเลือดสมองมีความสัมพันธ์กับเกิดภาวะความดันโลหิตต่ำหลังใส่ท่อช่วยหายใจอย่างมีนัยสำคัญทางสถิติ*