

การศึกษาเปรียบเทียบลักษณะของสายเสียงในขณะใส่ท่อช่วยหายใจระหว่าง ใช้ยาหย่อนกล้ามเนื้อ Cisatracurium กับยาดมสลบ Sevoflurane ในผู้ป่วยนรีเวช

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*กลุ่มงานวิสัญญีวิทยาโรงพยาบาลมหาราชนครราชสีมา นครราชสีมา ประเทศไทย

**กลุ่มงานอายุรกรรมโรงพยาบาลมหาราชนครราชสีมา นครราชสีมา ประเทศไทย

Comparison Study for Vocal Cords Conditions for Intubation between Cisatracurium and Sevoflurane in Patient Undergoing Gynecological Surgery

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บทนำ: การระงับความรู้สึกและใส่ท่อช่วยหายใจ นิยมใช้การนำสลบด้วยยาระงับความรู้สึกทางหลอดเลือดดำร่วมกับยาหย่อนกล้ามเนื้อ แต่วิธีนี้มีข้อควรระวังในผู้ป่วยที่ใส่ท่อช่วยหายใจยากหรือไม่สามารถเปิดหลอดเลือดดำได้ ซึ่ง sevoflurane สามารถใช้นำสลบและยังมีฤทธิ์หย่อนกล้ามเนื้อเมื่อเพิ่มระดับความลึกของการดมยาสลบ และเมื่อลดความเข้มข้นของ sevoflurane กล้ามเนื้อก็จะค่อยกลับมาสามารถในการหดตัวได้เช่นเดิม

วัตถุประสงค์: เพื่อเปรียบเทียบลักษณะของสายเสียงในขณะใส่ท่อช่วยหายใจหลังได้รับ Sevoflurane เทียบกับ Cisatracurium

วิธีการศึกษา: ศึกษาแบบสุ่มไปข้างหน้าอำพรางสองฝ่าย กับผู้ป่วย 124 คน แบ่งออกเป็น 2 กลุ่ม คือ กลุ่ม M (Cisatracurium) และกลุ่ม V (Sevoflurane) ให้ premedication ด้วย Fentanyl และ Midazolam และ Preoxygenated เป็นเวลา 3 นาที และนำสลบด้วย 8% Sevoflurane, N₂O 4 ลิตร/นาที O₂ 2 ลิตร/นาที โดยให้ผู้ป่วยหายใจเองจน loss of eye lash reflex ในกลุ่ม M จะปิด sevoflurane แล้วให้ cisatracurium 0.15 mg/kg และควบคุมการหายใจต่อ 3 นาทีจึงใส่ท่อช่วยหายใจสำหรับกลุ่ม V ควบคุมการหายใจด้วย 8% Sevoflurane,

Background: Intravenous induction (IV) followed by tracheal intubation using Neuromuscular blocking agent (NMB) during general anesthesia is a common practice in modern anesthesia. Avoidance of NMB is concerned in anticipated difficult airway or difficult IV access. Sevoflurane is an agent of choice for inhalation induction. Its gradual deepening of anesthesia and return of muscle tone when lightening.

Objective: To exam the conditions of vocal cords for endotracheal intubation by sevoflurane without the NMB agent compared to those by cisatracurium.

Methods: This prospective double blind control study. Randomly allocated 124 patients and divided into 2 groups; Group M (cisatracurium) and Group V (sevoflurane). In both groups premedication with Fentanyl and Midazolam then preoxygenated by 3 minutes. Anesthesia was induced with 8% sevoflurane N₂O 4 LPM, O₂ 2 LPM. Spontaneous breathing until loss of eye rash reflex. Group M; the sevoflurane was closed then a bolus dose of cisatracurium 0.15 mg/kg IV and control ventilation 3 minute. Group V; controlled ventilation was continuously extended from the induction phase for 3 minutes and then each patient

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N₂O, O₂ ต่ออีก 3 นาที จึงใส่ท่อช่วยหายใจ

ผลการศึกษา: เปรียบเทียบลักษณะสายเสียงในกลุ่ม V และกลุ่ม M; สายเสียงเปิดและนิ่ง 90.32% VS 83.87% (95%CI, P<0.03). ความดันโลหิตต่ำ ก่อนใส่ท่อช่วยหายใจ 66.13% ในกลุ่ม V และ 50% ในกลุ่ม M (95%CI, P=0.07)

สรุป: Sevoflurane สามารถนำมาใช้นำสลบและใส่ท่อช่วยหายใจได้ไม่ด้อยกว่า การใส่ท่อช่วยหายใจด้วย Cisatracurium

คำสำคัญ: Cisatracurium, sevoflurane, ลักษณะของสายเสียง

from each group was endotracheal intubated similarly by a nurse anesthetist.

Result: In the non-inferior analysis, Comparing vocal cord conditions Group V with Group M, opened and standing was 90.32% VS 83.87% (95%CI, P<0.03) . Incidence of hypotension before intubation (Proportion test) was 66.13% in group V and 50% in group M (95%CI, P=0.07)

Conclusion: Sevoflurane offers a smooth technique for induction and intubation non-inferiorly to intubation with neuromuscular blocking agent.

Keywords: Cisatracurium, sevoflurane, vocal cords condition

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Background

Intravenous induction (IV) followed by tracheal intubation using neuromuscular blocking agent (NMB) during general anesthesia (GA) is a common practice in modern anesthesia. The NMB can be classified as depolarizer and non-depolarizer agents. Succinylcholine (SCh), a depolarizer agent with ultra-short duration, is frequently used to optimize rapid sequence induction (RSI) and intubating condition. However, most anesthesiologists are very concerned about its side effects. As a result, non-depolarizer agents have long been applied for endotracheal intubation as an alternative technique except for RSI because of their onset, but non-depolarizing NMB may not suitable for difficult airway patients, difficult IV access.

Inhalation induction of anesthesia is a well-recognized technique in the management of the difficult airway. Its inherent safety depends on gradual and smooth deepening of anesthesia. If loss of muscle tone which leads to loss of airway patency then anesthesia inevitably lightens with return of muscle tone. In previous study, either high concentration or low concentration inhalation is accepted as induction techniques with low complications¹. We believe that sevoflurane is becoming regarded as the agent of choice for inhalation induction of anesthesia. Several studies have demonstrated that rapid and smooth induction of anesthesia in both children and adults. Owing to its low blood-gas partition coefficient and lack of pungency^{2,3}. Furthermore, sevoflurane in induction phase accompanied by NMB

agent is also suitable for endotracheal intubation. In case of contraindication of NMB agent, intubation under sevoflurane alone could be unavoidable.

The hypothesis of this study was the condition of vocal cord for endotracheal intubation by sevoflurane without the NMB agent was not inferior to those by NMB agent (cisatracurium).

Methods

This prospective double blind control study was conducted after the approval from the Ethics Committee of Maharat Nakhonratchasima Hospital and written informed consent form each patient. We randomly allocated 124 patients of ASA physical status I-II, aged 15-65 years old, scheduled for elective gynecologic surgery under GA in MRH during March-September 2016. Patients with pregnancy, full stomach, allergy for anesthesiologic drugs or predicted difficulty in ventilation and/or tracheal intubation were excluded from the study. Patients were equally divided into 2 groups of 62 patients by the computer randomization. The one was group M (intubation using NMB agent; sevoflurane induction and cisatracurium intubation.) and the other was group V (intubation using only volatile agent; sevoflurane induction and intubation). Premeditations given 3 minutes before the induction phase of general anesthesia⁴ in both groups consisted of Fentanyl 1 mcg/kg and Midazolam 1 mg IV if BW ≤ 50 kg, or 2 mg IV if BW > 50 kg. On arrival at the operating room, routine monitorings were applied for every patient by

recording mean arterial blood pressure (MAP), heart rate (HR), and oxygen saturations. Induction was preceded by a 3-minute period of preoxygenation using 100 % oxygen fresh gas flow (FGF) 6 L/min. Anesthesia was induced with 8 % volatile sevoflurane, adjusted 4 L/minute N₂O and 2 L/minute O₂⁵. Then, patients took spontaneous breathing⁶ until loss of eye lash reflex similarly in both groups. For Group M (n=62), the volatile agent was closed then a bolus dose of cisatracurium 0.15 mg/kg IV was early administered and the ventilation would have been controlled for 3 minutes after receiving cisatracurium. For group V (n=62), controlled ventilation was continuously extended from the induction phase for 3 minutes and then each patient from each group was endotracheal intubated similarly by the well trained nurse anesthetist who had at least 5-year experience in anesthesia and did not know which group the patients belonged to. The primary outcome was vocal cord condition (open and standing or open and movement) while the secondary outcomes⁷ were coughing, involuntary movement, laryngospasm, airway trauma and esophageal intubation, in PACU will record about nausea, vomiting, throat pain and awareness which would be recorded in both groups by nurse anesthetist and compared between each group.

With regarding the hemodynamic parameters (MAP, HR, O₂ saturation), they were recorded for 4 times, firstly when the patient entered the operating room (MAP1), secondly after the patient lost eye lash reflex (MAP2), thirdly before intubation (MAP3), and the last time (MAP4) just after the intubation (MAP, HR, O₂ saturation, and ETCO₂). In the recovery room, the patients would be observed and recorded about nausea, vomiting, awareness and throat pain. If

hypotension (MAP 20 % lower than the base line) or bradycardia (HR below 50 bpm) occurred, anesthesiologist would decide whether to treat the patient with Ephedrine 6-12 mg IV or Atropine 0.6 mg IV, respectively.

As a double blind research, the induction of anesthesia and the hemodynamic record were performed by the authors while the endotracheal intubation was performed, and the vocal cord condition and other complications were recorded by the nurse anesthetist who insert the ETT.

Statistical analysis

The sample size was calculated based on the data from the pilot study (20 cases/group) and the non-inferiority analysis (power = 80 % and $\alpha = -0.1$)⁸ was used to compare the vocal cord condition for tracheal intubation as a primary outcome between Group M (P₁=33.3%) and Group V (P₂=22.7%). If P-value was < 0.05, it would be considered statistically significance. This resulted in total of 124 subjects needed.

In addition, continuous data such as MAP3, which the reason that we used it because MAP3 was the consequence after difference intervention in both groups were compared using the proportion test, P-value < 0.05 was considered statistically significant. Nominal scales such as the coughing, movement, laryngospasm, airway trauma, esophageal intubation, nausea, vomiting, throat pain, and awareness were analyzed using the frequency and percentage.

Results

The patients' characteristic between the two groups have no difference (Table 1).

Table 1 Demographic data

	Group M (n=62)	Group V (n=62)
Age (mean, S.D.)	44.3 (9.62)	43.3 (9.92)
BMI (mean, percentile 25, 75)	24.9 (22.20 , 27.30)	23.0 (21.10 , 25.40)
ASA physical status		
1 (n, %)	25 (40.30)	29 (46.80)
2 (n, %)	37 (59.70)	33 (53.20)

Note: BMI=Body mass index

The vocal cords conditions for tracheal intubation in both groups either opened and standing or opened and moving were similar with P -value 0.03 (Table 2).

The lower bound the 95% CI of vocal cord condition difference ($-\Delta$) in this study is within the lower limits of non-inferiority (Δ), the result demonstrates the non-inferiority between group M and group V, which the proposed method result was no exceed standard acceptable value (Figure 1).

Moreover, The MAP3 subsequence points; before intubation. Patients who had MAP3 value less than 80%

from baseline were found in 31 of Group M (50 %) and 41 of Group V (66.10 %) and was no different significantly between both groups (Table 3). Furthermore, MAP4 in group M, there was no patient decreasing MAP 20 % from baseline and association with laryngoscopy and tracheal intubation. There were no treatment effects or interaction with regarding complication results.

There were no laryngospasm, airway trauma, esophageal intubation and awareness in both groups. Coughing, body movement, nausea, vomiting and sore throat were equally in both groups (Table 4).

Table 2 Conditions of vocal cords for tracheal intubation

	Group M (n= 62)		Group V (n=62)		P value
	Opened andstanding	Opened and Moving	Opened and standing	Opened and Moving	
Vocal cord	52	10	56	6	0.03*
N (%)	(83.87%)	(16.13%)	(90.32%)	(9.68%)	

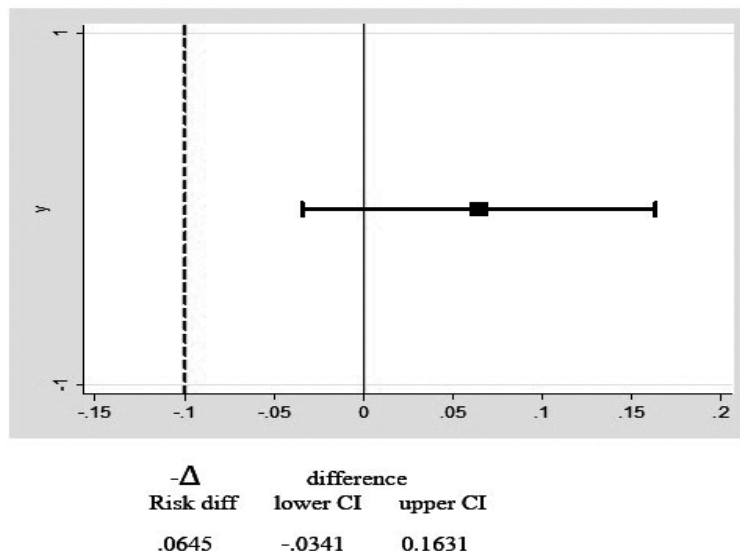


Figure 1 Vocal cord condition results

Table 3 A comparing of MAP3 value less than 80% from baseline

	Group M, n=62	Group V, n=62	Pr(Z = z)
	MAP<80% from baseline	MAP<80% from baseline	
MAP3 (n, %)	31(50%)	41(66.13%)	0.07

Note: MAP 3 is mean arterial blood pressure before tracheal intubation

Table 4 A comparing of complication results

	Group M (n=62)	Group V (n=62)
Coughing	26 (41.49%)	27 (43.55%)
Body movement	44 (70.97%)	37 (59.68%)
laryngospasm	0	0
Airway trauma	0	0
Esophageal intubation	0	0
Nausea	3 (4.87%)	4 (6.45%)
Vomiting	1 (1.61%)	0
Sore throat	10 (16.13%)	10 (16.13%)
awareness	0	0

Discussion

In this research, we compared two anesthetic techniques with similarly started with volatile induction in both groups to reduce the confounders. Sevoflurane was effectively shown no inferior to the neuromuscular blocking agent, cisatracurium, for endotracheal intubation in the gynecologic surgery. We verified our hypothesis that sevoflurane could relax muscles such as vocal cord, and skeletal muscles until it was good condition for intubation that was effectively comparable to neuromuscular blocking agent.

The present research showed that the good tracheal intubation condition could be achieved by sevoflurane without neuromuscular blocking agent which was not different from those provided by the neuromuscular blocking agent. During induction in Group V, sevoflurane was found to have deleterious hemodynamic side effect (< 80 % of baseline at MAP3). In previous study¹ in 2000, Yurino and Kimura found blood pressure was decreased via the direct effects of sevoflurane on vascular smooth muscle and cardiac function and these were opposed by the baroreceptors that had been unloaded. When difference between groups at baseline was adjusted, the variances in pre-induction, pre-intubation and post-intubation MAP were not significantly different. The incidence of hypotension in Group M might be from premedication, sevoflurane induction before administration of NMB and long fasting associated with hypovolemia. The study in 1997⁴ suggested that baroreflex was blunted during receiving fentanyl pretreatment. Our results suggest

that sevoflurane is equal to neuromuscular blocking agent for tracheal intubation.

Other complications during induction in the two groups, there was no untoward airway response during volatile induction of anesthesia with a spontaneous breathing and no adverse airway responses including the laryngospasm, airway trauma and esophageal intubation in response to intubation. The incidences of coughing and body movement were similar in both groups. In response to post intubation, there was no awareness while the incidences of nausea, vomiting and throat pain were equal in both groups. We also reported other observations that were not central to the research goal.

A potential limitation of volatile induction technique for tracheal intubation was the hypotension⁷ probably associated with the delivery of a high concentration of sevoflurane. However, in all cases, the peripheral perfusion was still adequate based on observation of the good skin color and the unimpaired oxygenation using the pulse oximeter. Moreover, MAP was restored to level above the conscious baseline immediately after tracheal intubation. The clinician needs to be aware that this wide hemodynamic swing associated with sevoflurane when it is used for tracheal intubation, might be poorly tolerated by the older and less healthy population.

Conclusion

Sevoflurane offers a smooth technique for induction and intubation non-inferiorly to intubation with neuromuscular blocking agent.

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