Gender determines the effect of atracurium priming technique in a randomized study

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ABSTRACT

Objective: To evaluate the effect of priming atracurium over onset time and intubating time of general anesthesia between different genders.

Methodology: Sixty-six male and sixty-four female patients, ASA I-II, aged 18-65 years, were randomly divided into four groups: group M₁: male patients with saline priming; group M₂: male patients with priming atracurium dose of 0.05 mg/kg; group F₁: female patients with saline priming; group F₂: female patients with priming atracurium dose of 0.05 mg/kg. General anesthesia was induced with midazolam (0.1 mg·kg⁻¹) propofol (0.75 mg·kg⁻¹), intubation dose of atracurium (0.5 mg·kg⁻¹), fentanyl (3 µg·kg⁻¹). The incidences of dizziness, diplopia, heavy eyelids and dyspnea were observed. Neuromuscular tension was quantified by using TOF-Guard neuromuscular monitor, and intubating time was defined as the duration from the infusion of intubation dose of atracurium to the time when T₄/T₁=0.

Results: The intubating time of group F₂ was shorter than that of group F₁. There was no significant difference between group M₁ and group M₂. The incidences of dizziness, diplopia and heavy eyelids in group F₂ were higher than those in group M₂.

Conclusion: Atracurium priming technique could shorten the intubation time of female patients, but not for male patients, and the gender plays a key role in affecting the clinical outcome of atracurium priming.

KEY WORDS: Atracurium, Priming technique, Gender, Intubation time.

INTRODUCTION

Atracurium is one of the non-depolarization neuromuscular blocking agents, and can be used safely for patients with malfunction in liver and kidney owing to its unique degradation of ester hydrolysis and the Hoffman reaction.¹ Its onset time is slower than succinylcholine,² which limits the usage in rapid-sequence inducing of general anesthesia. Atracurium priming is one of the methods to shorten the onset time. Some studies have suggested that it was helpful to speed up the onset time. Atracurium priming with dose of 0.1mg/kg or 0.09mg/kg could shorten the onset time of atracurium.³,⁴ However some other researchers did not support this conclusion.⁵ Although the result is controversial, up to now, no studies have evaluated whether the gender is a key factor to affect the outcome of atracurium priming. So we aimed to investigate the different effect of priming atracurium between male and female patients.

METHODOLOGY

This study was approved by hospital ethics committee (Jiangsu Cancer Hospital, 2011RA0028). One hundred thirty patients(sixty-six males and sixty-four females), aged from 18 to 65 years, ASA physical status I or II, 19< BMI (body mass in-
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Six males and four females were finally ruled out for unanticipated difficulty in tracheal intubation. There were no significant differences between group M1 and group M2 on age, weight, height and BMI (Table-I). There were no significant differences between group F1 and group F2 on age, weight, height and BMI (Table-II). Six males and four females were finally ruled out for unanticipated difficulty in tracheal intubation. There were no significant differences between group M1 and group M2 on age, weight, height and BMI (Table-I). There were no significant differences between group F1 and group F2 on age, weight, height and BMI (Table-II). The tracheal intubation time of four groups were compared (Fig.1). Intubating time in group F2 was the least, (114.4±31.8 seconds, the 95% confidence interval for mean:102.6-126.3 s); intubating time of group F1 was 154.8±39.2 s (95% CI: 140.2-169.4 s); intubating time of group M2 was 148.3±49.2 s (95% CI: 129.9-166.7 s); intubating time of group M1 was 171.7±38.8 s (95% CI: 157.2-186.2 s). The side effects of group F2 and group M2 were observed, and the incidences in group F2 were 46.7%, 56.7%, 63.3%, 10.0%; the incidences in group M2 were 20.0%, 26.7%, 33.3%, 3.3% for dizziness, diplopia, heavy eyelids and dyspnea, respectively (Fig.2).

### DISCUSSION

Among the neuromuscular blocking agents, suxamethonium may be the fastest drug over onset time, as one kind of depolarization muscular...
relaxants, but the side effects of succinylcholine, such as hyperkalemia, intracranial hypertension, myalgias and others has limited its clinical use. So atracurium, one special non-depolarization neuromuscular blocking agent that is metabolized and eliminated independently on hepatic and renal function, is regarded as an optimal candidate for inducing in general anesthesia. It is cheaper than cisatracurium and vecuronium. However, the onset time of atracurium is slower than suxamethonium and some other non-depolarization muscular relaxants. So how to accelerate the onset time and to shorten the intubating time was the main problem in its clinical use in general anesthesia. Enlarging the dose of intubation or to increasing the infusion speed may increase the incidences of hypotension and tachycardia related to histamine release. The other way is to apply priming technique. Priming atracurium with 0.05mg/kg could shorten the intubating time of atracurium itself, although atracurium with priming technique was still slower than suxamethonium over onset time, it was still an optimal choice of rapid-sequence inducing under the condition of succinylcholine contraindication. Interestingly, ephedrine following rocuronium priming could improve the intubating condition, but ephedrine could not enhance the intubating condition following priming with atracurium.

Reserchers found atracurium priming with 1/10 of intubating dose at 2-4 minutes ahead of intubating dose administration can accelerate onset time about 30-60s, and then tracheal intubation could be performed about 90s after the intubating dose was injected. However our results showed that atracurium priming can only speed up the onset time and shorten the intubating time for women, but not for men. Pharmacodynamics showed that gender was one of the affecting factors, and the onset time of atracurium in females was quicker than that in males. Age and gender could affect the pharmacodynamics of atracurium and the dose-response of atracurium was related to age and sex closely. The clearance of atracurium in males was greater than that in females, and the elimination in males was shorter than in females, but sex and age could not affect the volume of distribution of atracurium. Therefore women were more sensitive to neuromuscular blocking induced by atracurium than men. Our results showed the intubating time of female patients was shorter than that of male patients with atracurium priming. This illustrated that women were more sensitive to priming dose of atracurium than men. Studies have showed that the males needed more doses of atracurium to take effect than the females, and the duration of atracurium in males was shorter than that in females. We did not find significant differences between the males and the females without atracurium priming over intubating time, which might be explained that the intubating dose of atracurium was enough to take effect regardless of sensitivity discrimination. Moreover, for females, even after the intubating dose (0.5mg*kg⁻¹) was infused, it still needed about 114s to reach the condition of tracheal intubation. These disagreements may ascribe to the different ethnicity to some extent, and the drug itself may also be one of the affecting factors.

We also observed the dizziness, diplopia and heavy eyelids, found incidences in females were higher than that in males. The incidences of dizziness, diplopia and heavy eyelids of group F2 is higher than that of group M2 (*, p<0.05).
higher than those in males. Other studies revealed that priming of atracurium led to heavy eyelids and double vision,\textsuperscript{11} and priming atracurium dose with 0.02mg/kg did not lead to orbicularis fade.\textsuperscript{19} Interestingly, one research thought females were more inclined to experience adverse effects to suxamethonium, and men were more likely to suffer an adverse effects to atracurium.\textsuperscript{20} However our research did not support this, the incidences of adverse effect to priming atracurium in females was higher than that in males. Atracurium priming could take effect on swallowing,\textsuperscript{21} and priming dose with 0.1 ED95 of atracurium was safe and did not enhance the risk of pre-curarization.\textsuperscript{22} Priming technique should be performed carefully, although most of these adverse effects were mild and no special treatments were needed. In this study we found that gender could affect the outcome of atracurium priming technique, and only female patients could benefit from atracurium priming. But what is the fundamental reason for this result? Maybe the differences of activity of plasma esterase between sexes\textsuperscript{23} is a possible reason. It is also possible that the threshold to muscular relaxant of different genders is different, or the amount or construction of N2-acetylcholine receptor cation channel is various between man and woman. It deserves further investigation to illustrate the mechanism.

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REFERENCES

1. Hughes R, Chapple DJ. The pharmacology of atracurium: a new competitive neuromuscular blocking agent. Br J Anaesth. 1981;53(1):31-44.
2. Scott RP, Goat VA. Atracurium: its speed of onset. A comparison with suxamethonium. Br J Anaesth. 1982;54(9):909-911.
3. Nielsen HK, May O, Ravlo O, Bach V. Priming principle with atracurium. Acta Anaesthesiol Belg. 1990;41:313-317.
4. Glass PS, Wilson W, Mace JA, Wagoner R. Is the priming principle both effective and safe? Anesth Analg. 1989;68:127-134.
5. Geldner G, Fleischmann U, Weinberger J, Braun GG. Drug onset time of atracurium after pancuronium priming in elderly patients. Anaesthesist Reanim. 1997;22(2):46-49.
6. Miller RD. Miller’s Anesthesia. 7th. ELSEVIER. Churchill Livingstone. 2009:1713.
7. Xue FS, Zhang YM, Liao X, Liu JH, An G. Influences of age and gender on dose response and time course of effect of atracurium in anesthetized adult patients. J Clin Anesth. 1999;11(5):397-405.
8. Xue FS, Liao X, He N, Zhang YM, An G. Influences of age and gender on dose-response and recovery time-course of atracurium. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2001;23:54-57.
9. Parker CJ, Hunter JM, Snowdon SL: Effect of age, sex and anaesthetic technique on the pharmacokinetics of atracurium. Br J Anaesth. 1992:69:439-443.
10. Locks Gde F, Almeida MC. Priming dose of atracurium: measuring orbicularis oculi muscle fade and tracheal intubation conditions at the first minute with suxamethonium, rocuronium and different priming techniques of vecuronium. Br J Anaesth. 1999;73:720-727.
11. Light KP, Lovell AT, Butt H, Fauvel NJ, Holdcroft A. Adverse effects of neuromuscular blocking agents based on yellow card reporting in the U.K.: are there differences between males and females? Pharmacoepidemiol Drug Saf. 2006;15:151-160.
12. Yusuf AH, Okeke CI, Merah NA, Olatosi JS, Kushimo OT. Comparison of suxamethonium and priming with atracurium for rapid sequence orotracheal intubation in a Nigerian adult population. Niger Postgrad Med J. 2006;13(4):313-318.
13. Leykin Y, Pellis T, Luca M, Gullo A: Effects of ephedrine on intubating conditions following priming with rocuronium. Acta Anaesthesiol Scand. 2005;49:792-797.