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Antagonism of atracurium-induced block in obese patients

Purpose: To investigate the relationship between total body weight (TBW) or body mass index (BMI) and atracurium reversal time.

Methods: The study population comprised 25 patients with TBW <80 kg and 25 patients with TBW ≥80 kg anaesthetised with midazolam, thiopentone, fentanyl, nitrous oxide and halothane. Neuromuscular block was induced with 0.5 mg·kg^{-1} atracurium and maintained with doses of 0.15 mg·kg^{-1}. Neuromuscular transmission was recorded using train-of-four (TOF) nerve stimulation and mechanomyography. Neostigmine, 0.07 mg·kg^{-1}, was administered when the first twitch in TOF had recovered to 10% of control. Reversal time was defined as: time from administration of neostigmine until TOF ratio recovered to 0.70.

Results: There was no difference in reversal time between patients with TBW <80 kg (7.2 ± 2.6 min, mean ± SD), and patients with TBW ≥80 kg (6.9 ± 3.6 min). When patients were grouped according to BMI there was no difference in reversal time between groups with low BMI (6.9 ± 2.6 min) or high BMI (7.1 ± 3.6 min). There was, furthermore, no difference in reversal time between the 15 patients in the study population with the smallest TBW or BMI and the 15 patients with the greatest TBW or BMI. There was no correlation between TBW or BMI and reversal time.

Conclusion: When atracurium-induced neuromuscular block is antagonised with 0.07 mg·kg^{-1} neostigmine, TBW or BMI have no influence on reversal time.

Objectif : Examiner la relation entre le poids corporel total ou l'index de masse corporelle (IMC) et le temps nécessaire pour inverser l'effet de l'atracurium.

Méthodes : La population étudiée se composait de 25 patients avec poids <80 kg et 25 patients avec poids >80 kg, tous anesthésiés avec midazolam, thiopental, fentanyl, N_2O et halothane. Le bloc neuro-musculaire était obtenu avec de l'atracurium à raison de 0,5 mg·kg^{-1} et maintenu avec des doses de 0,15 mg·kg^{-1}. La transmission neuro-musculaire était évaluée au moyen de la stimulation nerveuse de type train de quatre (TOF) et de la mécano-myographie. La néostigmine était administrée à raison de 0,07 mg·kg^{-1} lorsque la première réponse au train de quatre avait récupéré à 10% de la valeur contrôle. Le temps nécessaire à inverser l'effet de l'atracurium était calculé à partir du début de l'administration de la néostigmine jusqu'à ce que la valeur du TOF soit de 0,7.

Résultats : Il n'y a pas eu de différence dans le temps nécessaire pour inverser l'effet de l'atracurium entre les patients du groupe de <80 kg 7,2 ± 2,6 min., moyenne ± ET) et ceux du groupe >80 kg (6,9 ± 3,6 min.). Lorsque les patients sont regroupés selon leur IMC, il n'y a pas de différence entre ceux avec IMC bas (6,9 ± 2,6 min.) et ceux avec IMC élevé (7,1 ± 3,6 min.). En outre, il n'y avait pas de différence dans le temps d'inversion du bloc entre les 15 plus petits patients selon le poids ou l'index et les 15 plus gros. Il n'y avait pas de corrélation entre le temps d'inversion du bloc et le poids ou l'index de masse corporelle.

Conclusion : Lorsque le bloc neuro-musculaire induit par l'atracurium est antagonisé par la néostigmine 0,07 mg·kg^{-1}, le poids ou l'IMC n'ont pas d'influence sur le temps nécessaire à l'inversion de l'effet de l'atracurium.

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IN the obese patient atracurium has a prolonged duration of action when dosed on a $mg \cdot kg^{-1}$ total body weight (TBW) formula.[1] It is believed that this prolonged duration of action is due to a relative overdose of the blocking agent.[1] It has also been demonstrated that atracurium has a slightly cumulative effect.[2] The anticholinesterase neostigmine[3,4] has a low fat solubility, and when dosed on a $mg \cdot kg^{-1}$ TBW formula, a large dose relative to lean body mass is given to the obese patient. Our goal in the present study is to determine if atracurium reversal time is influenced by TBW or body mass index (BMI) when atracurium and neostigmine are dosed on a $mg \cdot kg^{-1}$ TBW formula.

Methods

The protocol was approved by the local Ethics Committee, and written informed consent was obtained from each patient. The study population comprised 50 ASA physical status 1 or 2 women, 25 with a TBW <80 kg (group I) and 25 with a TBW ≥80 kg (Group II).

Total body weight was measured, and body mass index (BMI) was calculated as TBW in kg divided by the squared height in metres.[5] The patients were also grouped according to BMI in a high BMI and a low BMI group. In order to get more distinct groups in respect to TBW and BMI, groups consisting of the 15 patients with the lowest TBW/BMI and the 15 patients with the highest TBW/BMI were formed.

Patients were premedicated with 50 mg dixyrazine (a phenothiazine derivative) *po.* Anaesthesia was induced with 0.04 $mg \cdot kg^{-1}$ midazolam and 3 $\mu g \cdot kg^{-1}$ fentanyl followed by 5 $mg \cdot kg^{-1}$ thiopentone and maintained with halothane 0.5% end-tidal concentration (Normac®, Datex, Helsinki, Finland), 65 to 70% nitrous oxide in oxygen, and supplementary doses of 100 μg fentanyl, 50 mg thiopentone, or 1 mg midazolam as required. Both halothane and nitrous oxide concentrations were kept constant throughout the study. Temperatures were monitored centrally and peripherally. (TR9®, Ellab, Copenhagen, Denmark).

The ulnar nerve was stimulated supramaximally at the wrist (Myotest DBS®, Biometer, Odense, Denmark). When the neuromuscular response to train-of-four (TOF) stimulation had stabilised, T1, the magnitude of the first twitch in TOF was recorded as the control twitch (T1 control). The evoked contractions in the adductor pollicis muscle were recorded using a force-displacement transducer with a pre-load of 200–300 g (Myograph 2000®, Biometer, Odense, Denmark).

Neuromuscular block was induced with a bolus dose of 0.5 $mg \cdot kg^{-1}$ atracurium and maintained with supplementary doses of 0.15 $mg \cdot kg^{-1}$. After the end of surgery and when T1 had recovered to 10%, the neuromuscular block was antagonised by 0.07 $mg \cdot kg^{-1}$ neostigmine preceded by 0.028 $mg \cdot kg^{-1}$ atropine. The neostigmine dose was based on clinical recommendations.[6] Reversal time was defined as: time from administration of neostigmine until the TOF ratio had recovered to 0.70.

Statistics

Students t test for unpaired data, F-test (variance ratio test) and linear regression analyses were used, $P < 0.05$ was considered as statistically significant.

Results

Age and TBW of the patients in group I was 40 ± 6 yr mean ± SD and 62 ± 9 kg respectively, and in group II, 45 ± 8 yr and 90 ± 10 kg, respectively. Body mass index was 22.5 ± 2.5 $kg \cdot m^{-2}$ in the 25 patients with the lowest BMI (low BMI group) and 32.3 ± 4.7 $kg \cdot m^{-2}$ in the 25 patients with the highest BMI (high BMI group).

There was no difference in reversal time between group I and II, 7.2 ± 2.6 and 6.9 ± 3.6 min respectively. When the patients were grouped according to BMI there was no difference in reversal time between the low and the high BMI group, 6.9 ± 2.6 and 7.1 ± 3.6 min respectively.

When the 15 patients with the lowest TBW/BMI were compared with the 15 patients with the greatest TBW/BMI, there was still no difference in reversal time, $P > 0.05$, (Tables I and II).

There was no difference in reversal time variance between any of the groups. Linear regression showed no correlation between reversal time and TBW or between reversal time and BMI.

The temperature at the thenar eminence was >32.0°C and the central temperature was >36.0°C at all times.

TABLE I Reversal time in the 15 patients with the lowest total body weight (TBW) and in the 15 patients with the highest TBW

	low TBW			*high TBW*		
	Mean	SD	(range)	mean	SD	(range)
TBW kg	56.3	4.0	(46–61)	95.6	9.5	(88–119)
Reversal time (min)	8.3	2.6	(3.8–13.5)	6.9	3.8	(1.8–13.5)

TABLE II Reversal time in the 15 patients with the lowest body mass index (BMI) and in the 15 patients with the highest BMI

	low BMI			*high BMI*		
	Mean	SD	(range)	mean	SD	(range)
BMI $kg \cdot m^{-2}$	20.8	1.4	(18.6–22.8)	34.4	4.8	(30.9–45.7)
Reversal time (min)	7.9	2.7	(3.5–13.5)	7.1	4.1	(1.8–15.2)

Discussion

The study demonstrates that neostigmine induced reversal time from atracurium block is unaffected by obesity.

It is known that neostigmine has a maximum "ceiling" effect.[7] The exact maximum dose in humans is not known, but it is probably between 0.035 and 0.07 $mg \cdot kg^{-1}$.[8,9] All the patients in the present study received neostigmine 0.07 $mg \cdot kg^{-1}$ TBW. Thus, every patient received a neostigmine dose that should result in the maximum effect. This may be one of the explanations why reversal time was independent of TBW and BMI.

A second factor that may influence reversal is the large atracurium dose relative to lean body mass given to the obese patient. As the 25–75% recovery time increases with increasing doses of atracurium[2] reversal time may increase too. However, the neostigmine dose given to the obese patient is also large relative to lean body mass and may balance the effect of the large atracurium dose, resulting in a reversal time unaffected by body build.

There is also the possibility that the difference between the groups is too small to be detected. With a power of 75% and a significance level of 5% the study is capable of detecting a minimal difference of approximately 2.3 min. However a difference in reversal time of <2.5–3 min seems clinical unimportant.

Body Mass index is the weight in kg divided by the squared height in metres.[5] The BMI is thus better correlated with the percentage of fat in the human body than is total body weight. The patient population was, therefore, also grouped and compared according to BMI. However, similar results and conclusions were obtained whether TBW or BMI were used in the tests.

In conclusion, when an atracurium-induced neuromuscular block (T1 10% of T1 control) is antagonised by neostigmine 0.07 $mg \cdot kg^{-1}$, reversal time is independent of body build (TBW and BMI).

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