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Recovery of Neuromuscular Block After Tourniquet Inflation: Comparison of Atracurium and Vecuronium

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Abstract : To determine the influence of circulatory factors on recovery from neuromuscular block, we measured train of four (TOF) response in the arm with tourniquet inflated during TOF = 0.1 and compared this with data from a control arm in 40 patients under fentanyl-propofol-nitrous oxide-isoflurane anaesthesia. Patients were allocated randomly to receive either atracurium 0.5 mg/kg (n=20) or vecuronium 0.1 mg/kg (n=20). The TOF response of ulnar nerve in both arms was recorded in every 12 sec. When neuromuscular block was 90% (TOF = 0.1), the tourniquet was inflated to a pressure of 300 mmHg, and when a neuromuscular block recovery of 75% was reached, the block recovery time in both perfused and tourniquet arms was determined. The recorvery from neuromuscular block was markedly delayed in the tourniquet arms in both groups ($p<0.01$). As the recorvery time was longer in the vecuronium group than in atracurium group, we suggest the use of vecuronium in the microsurgery of the isolated extremities.

Key Words: Neuromuscular block, atracurium, vecuronium, measurement of response.

Introduction

The onset of neuromuscular block is determined by the rate at which blocker molecules reach the neuromuscular junction and this, in turn, is thought to depend to a large extent on circulatory factors, which influence the interval between injection of the drug in a peripheral vein and its arrival at the neuromuscular junction (1, 2). Cardiac output has been recognised as a factor modifying the onset time of depolarizing and nondepolarizing agents (3, 4). In humans, the role of muscle blood flow is likely to explain the faster onset with respiratory muscles than with peripheral muscles.

If muscle blood flow were the only determinant of onset time, interruption of circulation to the muscle would be expected to affect intensity of paralysis, and the block should remain constant in a muscle without blood supply. The application of a tourniquet to interrupt blood flow has been used during recovery after systemic injection of atracurium. In spite of the lack of circulation in the arm, recovery was found to continue more slowly in the isolated than in the perfused arm. This finding was explained by Hoffman degradation and ester hydrolysis in the non perfused arm (5, 6).

The purpose of this study was to measure the onset of nevromuscular block in an arm with a tourniquet inflated during onset, compared with a normally perfused arm. To determine if the results depended on the mechanism of the action of the blocker used, we studied two groups of patients, one receiving vecuronium and the other atracurium (7, 8).

Patients and Methods

After obtaining approval from the Hospital Research Etchics Committee, we studied 40 ASA I-II adult patients undergoing orthopedic and gynaecological surgery who were between 20-55 years of age. Patients had no renal, hepatic or neuromuscular disease and were not receiving any drug. Patients were allocated randomly to one of two drugs: group I to systemic atracurium 0.5 mg/kg, and group 2 to systemic vecuronium 0.1 mg/kg.

Patients received atropine 0.01 mg/kg IM and pethidine 1 mg/kg IM as premedication, 1 hour before surgery. On arrival in the operating room, a 20 gauge IV cannula was inserted into a dorsal hand vein. ECG, pulse oximetry, capnometry and arterial pressure were monitored noninvasively. A tourniquet cuff was placed around the right arm. Surface electrodes were applied near the ulnar nerve at both wrists. The electromyographic response was recorded with a Fischer-Paykel NS 242 innervator.

Anaesthesia was induced with propofol 2.5 mg/kg IV and fentanyl 0.5 μg/kg IV maintained with 1% isoflurane and 50% nitrous oxide in oxygen. After a stable TOF response was obtained, group 1 received atracurium 0.5 mg/kg, group 2 received vecuronium 0.1mg/kg over 20 seconds. After induction of anaesthesia, TOF stimulation of 50 mA was applied to both ulnar nerves at the wrists every 12 seconds. When twich depression was 90 %(TOF = 0.1), the tourniquet on the right arm was inflated to a pressure of 300 mmHg within 5 seconds in both groups. At the same time, the patient was intubated when maximum neuromuscular block was attained. The lungs were ventilated to maintain end-tidal carbondioxide partial pressure within the range 35-40 mmHg. The TOF response was recorded up to a twitch recovery of 75% in both forearms and the tourniquet was deflated. Meanwhile venous blood samples were obtained from the right forearm vein.

The following measurements were made:

1) duration between the administration of the neuromuscular block and a twitch depression of 90%

2) duration between the 90% twithch depression and 75% recovery from neuromuscular block of the perfused arm,

3) duration between a 90% twitch depression and 75% recovery from neuromuscular block of the arm with tourniquet,

4) venous blood pH before tourniquet inflation and before deflation.

Statistical data was presented. Data, between the arms of the same patients were compared by Student's t test and $p<0.01$ was considered as statistically significant.

Results

There were no differences in age, sex, ASA status, weight or height between group 1 and group 2 (Table 1).

Peripheral skin temperatures in both arms remained stable and normal throughout the study and peripheral venous pH was within physiological limits. The pH of venous blood samples obtained from the arm with tourniquet was 7.39+-0.07 in group 1 and 7.36+0.10 in group 2 ($p<0.01$). These values for the perfused arm were 7.41+-0.08 in group 1 and 7.40 + -0.08 in group 2($p>0.01$).

Table 1. Patient data [number or mean (SD or range)]

	atracurium (n=20)	vecuronium (n=20)
age (yr)	51.1	49.8
sex (m/f)	6/14	4/16
weight (kg)	62.3 +-5.3	60.1+-4.2

Onset time of the neuromuscular agents was 4.64+-0.70 min in group 1 (atracurium) and 4.82+-0.75 min. in group 2 (vecuronium). There was no statistical significance between the 2 groups in time of onset ($p>0.01$) (Table 2).

Table 2. Onset characteristics of atracurium and vecuronium groups.

	atracurium M(SD)	vecuronium M(SD)
Tourniquet inflation time (TOF=0.1)	4.64 (0.70)	4.82(0.75)
Time for 75% recovery		
Perfused arm	20.55(2.40)	25.93(2.41)
Tourniquet arm	33.48(3.32)	37.32(3.24)
pH (venous blood)		
before tourniquet inflation	7.41(0.08)	7.40(0.08)
before tourniquet deflation	7.39 (0.07)	7.36 (0.10)

In perfused arms, the recovery time of group 2 (25.93+-2.41 min) was greater than that of group 1 (20.55 + -2.40 min). There was a statistically significant difference between the groups ($p<0.01$) in the recovery time of neuromuscular agents. This significance was also obtained between groups when tourniquet arms were compared. The recovery time of group 1 was 33.48+-3.32 min where as 37.32+-3.24 min in group 2 (Table 2). Recovery of the neuromuscular block in isolated arms (tourniquet arm) was markedly delayed in comparison with the control arm (perfused arm) in both groups ($p<0.01$) (Figure 1).

Discussion

We found that interruption of arterial blood flow by tourniquet delays the recovery of the neuromuscular block. In this respect, atracurium and vecuronium behaved similarly.

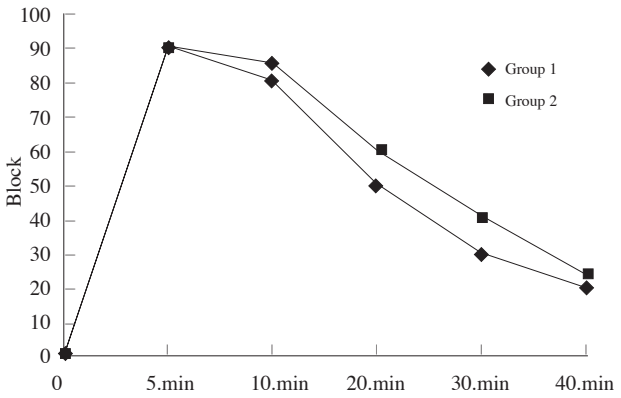

Figure 1. Changes in the neuromuscular block in the tourniquet arm.

The tourniquet has been used in the study of recovery inferences on the mode of action of neuromuscular blockers (9, 10). In our study, administration of the neuromuscular blocker was systemic, not in the isolated arm, and the tourniquet was inflated durign onset, not during recovery. In other studies the drug was injected in the isolated forearm or the tourniquet was inflated to assess recovery after systemic injection of the neuromuscular blocker (11, 12, 13). The doses of the neuromuscular blockers were chosen to achieve adequate neuromuscular block for intubation and were approximately equipotent. Onset time was 4.64+-0.70 min in the atracurium group and 4.82+-0.75 min in the vecuronium group, comparable with the findings of the other studies (12, 13).

The tourniquet was inflated when 90% block was achieved. We chose not to inflate the tourniquet at a fixed time after injection, because the amount of drug arriving at the neuromuscular junction is likely to be different for both agents, which have different kinetics.

İschaemia of the arm, although very short, might be suspected to induce local pH modifications or hypoxia, which would modify the action of neuromuscular blockers. After inflation of the tourniquet, peripheral venous pH remained with in the physiologic range (7.34-7.44), and there was no statistical difference between the two arms in either group.

In perfused arms, recovery of the neuromuscular block in the atracurium group (20.55+2.40 min.) occurred earlier than in the vecuronium group (25.93+2.41 min.) as expected because the elimination half-life of vecuronium is greater then that of atracurium. Results for the tourniquet arms were also similar in the atracurium group (33.48+3.32 min.) and in the vecuronium group (37.32+3.24 min.).

The onset of the action of blockers occurs in two steps: the time for molecules pass from the injection site to the muscle, and the time for molecules to redistribute from non-junctional areas to the neuromuscular junction. The elimination of the atracurium is dependent on spontaneus degradation to laudanosine in physiological conditions (Hoffman degradation) (5, 6). We suggest that the relative importance of these steps differs between different blockers. Atracurium block in the isolated (tourniquet) forearm recovers rapidly, although not faster than with systemic injection; this is consistant with a drug that is retained in the biophase despite rapid plasma metobolism. Vecuronium block in the isolated forearm is slow to recover, compared with atracurium; this suggest that a high affinity for the biophase may contribute to its long duration of action.

The practical result of this study is that neuromuscular function returns in the isolated arm, which may then move in response to surgical stimulation, unless other aspects of the anaesthesia are adequate. This is potentially serious for the succes of surgery, for example during microsurgery on the hand. Moreover, the administration of more neuromuscular blockers is ineffectual unless the tourniquet is deflated to allow access to the neuromuscular junction.

We suggest the use of vecuronium in the microsurgery of the isolated extremities.

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