EFFECT OF CARBON DIOXIDE ON GALLAMINE AND SUXAMETHONIUM BLOCK IN MAN

Preliminary Communication

BY

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SUMMARY

In nine anaesthetized human subjects, the effect of carbon dioxide changes on the neuromuscular block of gallamine and suxamethonium has been investigated by twitch myography. Increased carbon dioxide antagonized gallamine block and slightly potentiated suxamethonium block.

The effect of carbon dioxide on the neuromuscular blocking effect of tubocurarine in the anaesthetized human subject has been investigated in a previous study (Baraka, 1964). It was shown that respiratory acidaemia is associated with high plasma levels of the drug and prolonged neuromuscular block, whereas respiratory alkalaemia is associated with low levels of tubocurarine and rapid recovery from its block. These effects were attributed to the fact that the tubocurarine molecule contains, beside its quaternary ammonium groups, two phenolic hydroxyl groups which have pKa values of 8.1 and 9.1, and so vary their degree of ionization within the range of pH changes associated with variation in ventilation.

The aim of the present investigation was to observe in the human the effect of respiratory alkalaemia and acidaemia on the neuromuscular block of other relaxants, viz. gallamine triethiodide and suxamethonium. These compounds possess only quaternary ammonium groups with a pKa value above 13 (Albert, 1952) and are therefore completely ionized within the range of pH changes.

Payne (1958) has shown in the cat that both these relaxants are antagonized by the administration of carbon dioxide.

METHOD

The method of investigation employed in this study has been previously described (Baraka, 1964). The observations were carried out in nine healthy adult patients undergoing routine lower abdominal or limb surgery.

Anaesthesia.

Sleep was induced with thiopentone 250 mg intravenously. This was followed by the administration of a 50 per cent mixture of cyclopropane with oxygen and by topical laryngeal anaesthesia with 4 per cent lignocaine to facilitate intubation and controlled respiration. Anaesthesia was then maintained using a mixture of nitrous oxide (3 l./min) and oxygen (1 l./min).

Blood carbon dioxide levels.

The range of carbon dioxide tensions aimed for was within that observed commonly with different techniques of clinical anaesthesia.

A low arterial carbon dioxide tension was achieved by including the Boyle Mark III soda-lime canister in the circuit. A high arterial carbon dioxide tension was achieved by excluding the soda-lime canister and adding carbon dioxide to the fresh gas flow. Blood taken for the Pco2 and pH estimations was "arterialized venous" (Brooks and Wynn, 1959). The values were then estimated with the capillary electrode following the method described by Robinson and Utting (1961). During hyperventilation, the average blood carbon dioxide tension was 22 mm Hg (18–25 mm Hg), and the average pH was 7.50 (7.44–7.56). During hypercarbia, the average blood carbon dioxide tension was 78 mm Hg (45–90 mm Hg), and the average pH was 7.16 (7.13–7.20).
Observations on the neuromuscular transmission.

The ulnar nerve was supramaximally stimulated by tetanic bursts at intervals of 10 seconds. The resultant twitch response was recorded by attaching the ring finger to a flat steel spring myograph recording with ink on a rotating drum.

General procedure.

Precautions were taken to achieve a steady state before observing effects and sampling for blood gas values. Gallamine 4 mg per stone (6.3 kg) was injected in three patients during pulmonary hyperventilation. The neuromuscular block produced was compared with that obtained when the same dose was injected in a further three patients during hypercarbia. A continuous infusion of suxamethonium (0.2 per cent) was used in a further three patients. After a satisfactory level of partial neuromuscular block was obtained under hyperventilation, the soda-lime was excluded from the circuit, and carbon dioxide added to the inhaled mixture. This experiment was carried out twice in every patient.

RESULTS

Gallamine.

The neuromuscular blocking effect, as estimated by the reduction in the recorded height of the twitch response, of gallamine (4 mg/stone) was much greater and more prolonged in the three patients with low carbon dioxide tension than in the three patients with elevated carbon dioxide tension (fig. 1).

Thirty minutes after injection, recovery was nearly complete when gallamine was injected during hypercarbia, while a marked degree of neuromuscular block was still present when it was injected during hyperventilation. The tracing in figure 2 is typical of the response obtained under both conditions.

Suxamethonium.

Partial steady neuromuscular block was achieved by suxamethonium infusion under hyperventilation. Subsequent inhalation of carbon dioxide increased the degree of suxamethonium neuromuscular block. The previous degree of block was restored when carbon dioxide was discontinued and hyperventilation resumed. The example shown in figure 3 shows response identical to that occurring in the other two patients.

![Diagrammatic representation of the neuromuscular block percentage depression of the original twitch response after gallamine 4 mg per stone (6.3 kg) in three patients during respiratory alkalaemia and in a further three patients during respiratory acidaemia.](https://academic.oup.com/bja/article-abstract/39/10/786/258848)
Hyperventilation
Carbon dioxide 10%,
Hyperventilation
Continuous infusion of succinylcholine
Infusion off
Time intervals 10 seconds

FIG. 3
Kymograph tracing showing the influence of inhalation of carbon dioxide on the neuromuscular block produced by the infusion of 0.2 per cent suxamethonium. Carbon dioxide potentiated the block.

DISCUSSION
The ability of carbon dioxide to antagonize gallamine and to potentiate suxamethonium block cannot be related to altered ionization of their cationic ammonium groups with a pKa above 13 (Albert, 1952), or of the anionic endplate receptors which, according to Cavallito (1962), are most probably phosphoric acid groups with a pKa around 2.5. Both groups are completely ionized within our range of pH changes.

A possible mechanism is the ability of pH changes to vary the activity of both pseudo-cholinesterase (Augustinsson, 1948) and true cholinesterase (Nachmanson, 1959), reaching a peak velocity at a pH of 8.5. Carbon dioxide will therefore act as a physiological anticholinesterase (Gesell, Mason and Brassfield, 1949) which can antagonize the antidepolarizing block of gallamine and potentiate suxamethonium block.

Although this effect of carbon dioxide on gallamine is similar to Payne's (1958) findings in the cat, the effect on suxamethonium is minimal and in the opposite direction to his results. This can be explained by the marked species difference in the effect of depolarizing relaxants (Zaimis, 1952).


REFERENCES