THE EFFECT OF GENERAL ANAESTHETIC AGENTS ON NERVE CONDUCTION VELOCITIES

BY

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SUMMARY

Nerve conduction velocity has been studied in the ulnar nerve of human subjects before and during anaesthesia. No significant changes in velocity were observed following the administration of thiopentone, nitrous oxide, oxygen and halothane in normal clinical quantities. A transient increase in nerve conduction velocity was noted following the administration of paralytic doses of gallamine triethiodide to subjects receiving nitrous oxide, oxygen and halothane anaesthesia in whom ventilation was controlled.

Using modern techniques and equipment the measurement of both sensory and motor nerve conduction velocities is possible and often useful (Dawson, 1956; Gilliatt et al., 1965; de Jong, Hershey and Wagman, 1966; de Jong and Nace, 1967).

During investigations into the degree of damage to the central nervous system present in children born with spina bifida it was necessary to make conduction velocity measurements during surgical operations (Brown, Porter and Whitaker, 1968). The question was soon raised as to what effect, if any, the anaesthetic agents being used might have on the conduction velocity measurements being made. There appeared to be little information in the literature on this subject, although some sources stated that large doses of certain anaesthetic agents in vitro reduced nerve conduction velocities (Wyke, 1965). de Jong, Hershey and Wagman (1966) report that halothane in inspired concentrations up to 2.5 per cent has an insignificant effect on motor nerve conduction velocity at temperatures between 35° and 36°C, in man and cat. This lack of effect has been subsequently confirmed for ether, methoxyflurane, halothane, and nitrous oxide in the cat (de Jong and Nace, 1967).

It was therefore decided to make a series of nerve conduction velocity measurements on patients during operations not involving the nerves on which measurements were to be made.

METHOD

The nerve chosen for study was the ulnar nerve. As this nerve runs superficially in certain parts of its course in the human subject, measurements could be made using surface electrodes rather than needle electrodes. The method used was similar to that first used by Dawson (1956), and consisted of giving a short electrical stimulus to the nerve at the wrist and then detecting the combined orthodromic sensory, and antidromic motor impulses at the elbow joint. The voltage detected was displayed on a storage oscilloscope from which a polaroid photograph could be taken if necessary (fig. 1). Only one measurement was made from each photograph, this being the interval of time between the electrical stimulus and the peak of the signal detected over the nerve at the level of the elbow. Measurement of the distance between the stimulating cathode and the

Fig. 1

Typical action potential recorded over ulnar nerve at wrist following stimulation of ulnar nerve at elbow. First deflection represents stimulus.
detecting electrodes enabled a conduction velocity to be determined.

To establish a baseline conduction velocity for each patient, a reading was first made on the day preceding operation and then in the anaesthetic room just before induction of general anaesthesia. Measurements were then made at 10-minute intervals after induction for as long a period as possible. It did not prove practicable to leave the electrodes in position on the patient from the day preceding operation. However, the electrodes attached in the anaesthetic room were not removed whilst the patient was taken into the operating theatre. This eliminated a possible error in measurement due to inconsistent electrode placement. Skin temperature was measured continuously at the site of application of the electrodes using a thermistor.

Measurements were made in a total series of 43 male and female patients. In all the cases premedication consisted of the intramuscular injection of morphine 10 mg and atropine 0.6 mg 1 hour pre-operatively. Induction of anaesthesia was carried out using 2.5 per cent thiopentone, with maintenance by 70 per cent nitrous oxide and 30 per cent oxygen with 0.5—1.5 per cent halothane. In addition a number of patients received paralyzing doses of gallamine triethiodide in order to achieve full muscular relaxation for intra-abdominal surgery. In a smaller series sub-paralytic doses of gallamine triethiodide (40 mg) were used in conjunction with nitrous oxide oxygen and halothane; short periods of spontaneous ventilation were permitted in these cases. The patients receiving paralyzing doses of gallamine (120 mg) were all intubated using a cuffed orotracheal tube.

For the purpose of analysis the results were divided into four groups:

A Patients in whom gallamine was not used.
B Patients in whom gallamine 40 mg was used and spontaneous respiration permitted.
C Patients in whom paralyzing doses of gallamine was used and ventilation controlled.
D 11 further cases (7 females and 4 males) receiving thiopentone, nitrous oxide, oxygen and halothane, gallamine 120 mg and controlled ventilation were then studied in greater detail as Groups B and C appeared to show time dependence conduction velocity changes. All the cases received similar premedication. Induction and maintenance was carried out with thiopentone, nitrous oxide, oxygen and halothane together with gallamine 120 mg. Conduction velocity was measured, where possible, immediately before injection of gallamine, and at 5, 10, 15, 20 and 30 minutes following paralysis and initiation of controlled ventilation.

Any changes in conduction velocity were expressed as a percentage change from pre-induction measurements.

RESULTS

The pre-operative mean conduction velocity in 32 patients was 58.0 m/sec. In Group A (6 patients receiving thiopentone, nitrous oxide, oxygen and halothane) the mean percentage change between pre-operative readings and the observations taken at 10-minute intervals after induction was —0.40 per cent (n=13, P=0.8). This change is not significant.

In Group B (6 patients receiving thiopentone, nitrous oxide, oxygen, halothane and gallamine 40 mg, breathing being spontaneous). The mean percentage change between pre-operative readings and the observations taken at 10-minute intervals after induction was +0.78 per cent (SE of mean 0.78 per cent, n=13, P=0.3). This change is not significant.

In Group C (11 patients receiving thiopentone, nitrous oxide, oxygen, halothane and gallamine 120 mg, ventilation being controlled) the mean percentage change between pre-operative readings and the observations taken at intervals of 10 minutes after induction was +2.33 per cent (SE of mean 0.56 per cent, n=35, P<0.001). This change is significant.

In Group D (11 further cases, 7 females and 4 males, receiving thiopentone, nitrous oxide, oxygen, halothane and gallamine 120 mg, ventilation being controlled), which were studied in greater detail because Groups B and C appeared to show time dependence of conduction velocity changes, the results (fig. 2) showed an overall increase in the mean conduction velocity, following the intravenous injection of gallamine of 1.7 per cent (SE of mean 0.39 per cent, n=40, P<0.001). This change is significant.
These observations confirmed the previous suggestion arising from the results from Groups B and C that there was a relationship between the percentage change and the time after the administration of gallamine.

<table>
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<th>Σx</th>
<th>n</th>
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<th>SEM</th>
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<td>+0.15</td>
<td>0.25</td>
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When the values for Groups C and D are compared with those for Group A (gallamine 120 mg against cases who received no gallamine), the difference was significant for both C and D (Group C, \( P < 0.05 \); Group D, \( P = 0.06 \)). Due to the scatter of the cases in Group A the significance is not as great as one would expect.

There was a statistically significant increase in nerve conduction velocity following the intravenous administration of gallamine, with a return to normal velocities at approximately 25–35 minutes after injection. There was no significant change in nerve conduction velocity in patients receiving thiopentone, nitrous oxide, oxygen and halothane, and breathing spontaneously.

**DISCUSSION**

A number of possible explanations for the time dependence of the nerve conduction velocity following the administration of gallamine.

Temperature change: de Jong, Hershey and Wagman (1966) showed that nerve conduction velocity decreases linearly with temperature. In the case of the peroneal nerve of the human subject this decrease was of the order of 1.84 m/sec/°C between 36° and 23°C. The observed results in the present series could therefore be explained by an increase of body temperature of approximately 1°C. Observations of skin temperature did not show such increases. Transient increase in the temperature of blood perfusing the nerve could account for this change, but during anaesthesia with nitrous oxide, oxygen and halothane only this effect was not demonstrated, and to account for it gallamine must have properties ascribed to it which have not heretofore been attributed to it. Temperature change is
therefore an unlikely explanation of this phenomenon.

Carbon dioxide. Alkalaemia is known to increase the excitability of nervous tissue (Wyke, 1965) and may well give rise to an increase in nerve conduction velocity. Such an alkalaemia is likely to develop following controlled ventilation as a result of respiratory alkalosis. It has been shown (Robinson, 1961) that such an alkalaemia may take up to 1 hour to develop as a result of passive hyperventilation, and therefore is unlikely to be the explanation for the initial rise in conduction velocity found to occur following the administration of gallamine. Furthermore, the development of alkalaemia is likely to be sustained longer than the observed change in nerve conduction velocity which returns towards the baseline about 10 minutes after the administration of gallamine.

Similarly a change in the level of carbon dioxide tension and stores follows the same pattern as the development of alkalaemia with the attainment of a new level of carbon dioxide tension, the 95 per cent change occurring in about 20 minutes follows the change of ventilation. Carbon dioxide tension is likely to rise after the administration of gallamine 40 mg and spontaneous ventilation, though no change in nerve conduction velocity was noted in these cases. Change in carbon dioxide tension is therefore itself unlikely to account for the observed pattern of change in the nerve conduction velocity following the administration of gallamine. Rate of change of carbon dioxide and pH might, however, account for this observed phenomenon, and in some way influence ionic transfer in nerve tissue.

The effect of gallamine. The close correlation between the return to normal values of the nerve conduction velocity after the administration of gallamine, and the known duration of clinical effect, suggest that the increase in nerve conduction velocity could be directly attributed to the action of gallamine. The fact that small doses of gallamine did not produce any marked change in nerve conduction velocity suggests that amount of gallamine may be a factor in producing these changes. There is evidence to suggest a central excitatory action of gallamine on the nerve system (Halpern and Black, 1967). The observed effects could, however, in some way be a function of neuromuscular blockade and may not be specific to the use of gallamine.

Further studies using other neuromuscular blocking agents are in progress, and investigations into the possible effects of carbon dioxide are being continued. In the meantime, although the observed changes are admittedly small, work to date suggests that caution should be employed in evaluating nerve conduction velocities from one single observation and, in addition, regard should be paid to the possible effects of neuromuscular blocking agents.

ACKNOWLEDGEMENTS

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REFERENCES


BOOK REVIEW


This 179-page paperback is written by fourteen Canadian anaesthetists—most of whom are well known—under the editorship of the Editor of the Canadian Anaesthetists' Society Journal. We are not told the writers of individual chapters, which vary somewhat in their standard and which overlap occasionally. The opening challenging preface puts the subject in true perspective for students. Its fifteen chapters deal with all the aspects of anaesthesia with which a medical student and newly qualified doctor should be familiar. One might disagree with the topics on which special emphasis has been placed, but such criticism must take into consideration the requirements of the doctors in the country for which the book is intended.

Starting towards the end of the book, the chapter (12) on complications of anaesthesia deserves special mention and is worth reading by doctors of all grades. It certainly emphasizes the seriousness with which beginners should approach the administration of an anaesthetic. On a par with this is the section on "Cardiovascular homeostasis in relation to anaesthesia and resuscitation" (Chapter 9). The introduction to this is excellent; in a very brief space the physiology of the whole topic is very clearly explained, with lots of good clear definitions. It is regrettably spoiled by a sweeping statement (page 86) that "the safety of any anaesthetic depends more on the skill with which it is administered . . . than on any inherent property of the drug". While agreeing that this is partially true, one has to ask how ethyl chloride and chloroform fit into this generalization. (Perhaps these drugs should not be used by students, but they are discussed on pages 32 and 33.) Should a warning not be given as to their cardiovascular toxicity?

Virtually every sentence of the short opening seven-page chapter on "Evaluation of the patient" is a fount of information, but the four references at the end seem quite irrelevant and a fuller bibliography would help here. One would like more detailed explanation of some aspects of the topic (such as in renal disease or porphyria) rather than short dogmatic statements. Probably the right approach for educated persons is to give more relevant background information, although the other might be ideal in a manual for nurse-anaesthetists. While realizing that anaesthesia is only one of the many subjects to be covered by the medical student in a short period of time and that a long book would be of little use to them, the degree of brevity adopted in this chapter may put the student off. This didactic style is continued in the second short (too short?) chapter on premedication where there is a lack of clarity in describing the objects of premedication and the (placbo) value of a pre-operative visit by the anaesthetist.

Chapter 3, especially page 15, makes certain assumptions as regards the basic knowledge possessed by readers, e.g. what controlled respiration is and what it entails or what a cuffed endotracheal tube is. An illustration here would have been most helpful.

The longest chapter (4) on general anaesthesia is adequately illustrated with circuits, etc., except for the need for a simple line drawing of a gas machine on page 38. An opening definition of what is general anaesthesia and what is local anaesthesia would have been helpful. This also applies to the terms "neurolept anaesthesia", "depth of anaesthesia", "hypnotics", "sedatives", etc.

On a point of personal interest, the reviewer deprecates the continued use of the misleading term "ultra-short acting" in relation to intravenous barbiturates, particularly in a work written for students. It is also worth correcting the statement (page 35) that "Flaxedil was the first barbiturate anaesthetic used". It certainly was the first rapidly acting barbiturate, and this point should be clarified.

There is a clear and simple exposition of the action of muscle relaxants and the ten pages devoted to this strike a good balance in relation to what a student should know about these drugs. In contrast, the six pages devoted to regional anaesthesia, however, seem totally inadequate, even for students, particularly since only half a page is devoted to nerve blocks.

Obstructed respiration is still probably the most important aspect of the handling of the unconscious patient, as far as the beginner anaesthetist is concerned, and deserved more space than that devoted to it in Chapter 7, although this is discussed fully elsewhere (Chapter 12). Finding Table 1 in Chapter 7 caused the reviewer some trouble until it was realized that the tables and figures in each chapter were numbered separately. One wonders whether this useful chapter should not have come immediately after that on respiration.

The book ends with a challenging section on the special problems associated with paediatric anaesthesia which should stimulate some to consider that anaesthesia is a worthwhile subject for specialization.

Despite any criticisms made in this review, and the occasional printing error, this is still a most helpful book. Its greatest use in this country would appear to be for those intending to spend a year or so in Canada or to join the "brain drain". It pioneers a new idea of paperback anaesthetic books for students, which is quite commendable.

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