PREVENTION, DIAGNOSIS AND TREATMENT OF PROLONGED APNOEA

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The increasing understanding of the mechanism of action of the muscle relaxants has led to a high degree of safety in their use. Nevertheless, the occasional patient is still encountered in whom the response to the drug is greater than anticipated. There are already a number of reports in the literature outlining the almost unlimited number of causes for this prolonged response (Paton, 1958; Churchill-Davidson, 1956, 1959; Foldes, Rendell-Baker and Birch, 1956).

The aim of this review is to analyze the principles for the clinical use of the muscle relaxants with the maximum degree of safety—particularly in the light of recent investigations in neuromuscular transmission.

THE CHOICE OF MUSCLE RELAXANT

Despite numerous attempts to discover new compounds, there are essentially only three drugs in regular clinical use in this country, namely, d-tubocurarine chloride, gallamine triethiodide, and suxamethonium chloride. In earlier days decamethonium iodide enjoyed a spate of popularity, but the absence of an effective antidote, coupled with the possible occurrence of a dual block, has virtually led to its abandonment in most centres.

The choice of a particular relaxant depends largely upon the circumstances of the operation. For example, a short procedure lasting only a few minutes is satisfactorily accomplished with suxamethonium. This drug has certain possible disadvantages—the occurrence of muscle pains in the postoperative period, an excessively prolonged response in the presence of a low plasma cholinesterase concentration, and finally the production of a dual block, which occasionally may occur even after small doses of the drug have been used. Despite these facts, suxamethonium still enjoys widespread popularity which is likely, however, to be lost as soon as an effective short-acting non-depolarizing drug is discovered.

Either d-tubocurarine or gallamine is used for the longer periods of muscle relaxation required in abdominal surgery. The main disadvantage of d-tubocurarine is that it may produce hypotension when used in large doses, although the fall is rarely excessive. In combination with halothane the drop in pressure may be much greater and for this reason gallamine, which has the added advantage in this connection of a raised pulse rate (due to an atropine-like action), is usually employed.

ADMINISTRATION OF RELAXANTS

Theoretically, a test dose of any relaxant is desirable, but the difficulty of assessing the result, coupled with the discomfort to the patient, has prevented its widespread adoption. Nevertheless, the assessment of the dose of relaxant for a particular patient still remains the most important single factor.

Following a period of controlled respiration the initiation of respiratory activity depends upon three factors. These are: firstly, the amount of depression of the respiratory centre caused by the premedication, the use of intravenous analgesics, and the concentration of other anaesthetic drugs in the circulation; secondly, the carbon dioxide level of the blood (the activity of the centre ceases if the level is either too low or too high); thirdly, even when the centre is ripe for activity sometimes a suitable afferent stimulus must be provided to initiate the return of spontaneous respiration—usually this is provided by the surgical stimulus, by movement of the endotracheal tube, or by deflation of its balloon. Bearing these points in mind, muscular relaxation may be obtained either by the use of large doses of a relaxant drug with nitrous oxide and
PREVENTION, DIAGNOSIS AND TREATMENT OF PROLONGED APNOEA

oxygen analgesia or by smaller doses of relaxant supplemented by a more potent inhalational anaesthetic agent—the duration of effect of such an agent clearly depending upon its speed of elimination from the circulation.

Long-acting intravenous analgesics such as pethidine are difficult to use with controlled respiration because there is no satisfactory method of assessing the effect of a particular dose upon respiratory activity. Such drugs, or a heavy pre-medication combined with a large induction dose of barbiturate, are often responsible for a delay in the return of respiration at the end of an operation.

The minute volume used with controlled respiration is another important factor, because few anaesthetists are capable of ventilating a patient so accurately that the carbon dioxide tension of the arterial blood remains within the normal range. Underventilation may be very harmful to some patients; mild overventilation should, therefore, always be used, and then one also knows on which side of the fence one lies. At the end of operation the patient should not be left for periods of apnoea in order to allow the carbon dioxide level of the blood to rise; this practice merely causes periods of asphyxia. Rather, it is better to turn off the carbon dioxide absorber and then ventilate the lungs with a high flow of gases (such as 14 litres per min, which approximates to twice the normal resting minute volume) to which 5 per cent carbon dioxide has been added.

If the carbon dioxide tension of the arterial blood (Pco₂) is low, due to mild overventilation during the operation, it will rapidly rise towards the normal physiological level. On the other hand, if the anaesthetist has unwittingly allowed the carbon dioxide level to rise then the high flow of gases with overventilation will minimize any further rise. Assuming normal respiration is not resumed within 5 minutes then the concentration of carbon dioxide should be reduced to 2 per cent and the mild overventilation continued. Theoretically, in these circumstances the Pco₂ level of the blood should gradually approach normality whether the previous level be high or low. Such a method is designed for guidance in clinical practice where accurate instrumentation is not available. It tends to prevent violent fluctuations in the carbon dioxide level of the blood, thus producing conditions suitable for the return of normal respiration and at the same time neither anoxia nor carbon dioxide accumulation can occur.

The use of anticholinesterase drugs to reverse any residual effects of the muscle relaxants is also important. It is often suggested that such drugs should not be used in the presence of apnoea and should only be given once the first signs of respiration have occurred. This caution is unjustified. Following even a small dose of a muscle relaxant neuromuscular transmission does not appear to return to normal for at least 1 to 2 hours. Ninety per cent recovery is usually achieved rapidly but the attainment of complete normality is a long process in the anaesthetized patient. The administration, therefore, of 2.5 mg neostigmine methylsulphate (preceded by 1 mg atropine sulphate) in such cases is always followed by some improvement in neuromuscular transmission.

DIAGNOSIS OF APNOEA AND RESPIRATORY INADEQUACY

The term "prolonged apnoea" has never been satisfactorily defined but a patient should certainly be breathing satisfactorily within 10 minutes of the end of operation. Alternatively, respiratory activity may start but the minute volume be inadequate. In either case the correct diagnosis of the underlying cause is essential. Briefly there are three main causes—those due to depression of the respiratory centre, those due to mechanical defects in the respiratory system and those due to peripheral causes which can usually be directly related to the use of a muscle relaxant.

The only satisfactory method of distinguishing a peripheral cause from the other two groups is by the use of a peripheral nerve stimulator (fig. 1). It is known that the respiratory muscles of normal patients always recover their activity before the hand muscles. Therefore, if on peripheral nerve stimulation there is marked activity of the muscles in the hand it can safely be concluded that the respiratory muscles have also recovered from the effects of the muscle relaxant and consequently the cause of the apnoea must
be of central or mechanical origin. The only exception to this rule is found in certain severe cases of myasthenia gravis where the respiratory muscles rather than the upper limb muscles are principally involved in the disease. These cases can always be detected by an adequate clinical history and examination before operation. On the other hand, if the nerve stimulator produces only a very weak or absent response in the hand muscles, a prolonged action of the relaxant must be suspect. Frequent use of a nerve stimulator soon enables the anaesthetist to detect even minor degrees of paresis. Furthermore, it is also possible to diagnose the exact type of neuromuscular block present at a particular moment. This is particularly useful when dual block is suspected but is also of value in assessing the effectiveness of the reversal of a d-tubocurarine block by an anticholinesterase drug. The electrical changes that occur with both a depolarization and a nondepolarization block have already been described (Churchill-Davidson and Christie, 1959). The mechanical movements of the hand and finger muscles are just as characteristic—thus:

Depolarization block.

The responses are similar whether fast (tetanic) or slow (twitch) rates are used (fig. 2), and there is no improvement in the response after a prolonged burst of tetanus, and no post-tetanic facilitation.

Nondepolarization block.

A fade is seen in both the mechanical and the electrical response to fast and slow rates of stimulation (fig. 3). Furthermore, following a prolonged burst of tetanus there is a temporary but marked improvement in neuromuscular transmission, indicating post-tetanic facilitation. This type of response is diagnostic of a nondepolarization block and it can be confidently anticipated that a suitable dose of an anticholinesterase drug will remove the “fade” in the responses and lead
to an improvement in neuromuscular transmission. If this response is found after the use of a depolarizing drug then a dual type of neuromuscular block is present.

Confronted with the problem of the patient who fails to breathe adequately at the end of an operation some suggestion of the cause may be given by the rate and nature of the respiratory movements. A slow rate suggests central respiratory depression, whereas a more rapid rate together with the use of the abdominal and accessory muscles of respiration (and tracheal tug) points to either a mechanical fault or a peripheral cause due to the muscle relaxant.

The use of the nerve stimulator will rapidly differentiate between a central and a peripheral cause. A mechanical cause of inadequate ventilation, however, is more difficult to diagnose and is sometimes overlooked. In a patient who has just undergone an abdominal operation the use of a stethoscope alone on the thorax often does little more than suggest "bronchospasm". Contrary to time-honoured belief it is possible to demonstrate postoperative pulmonary collapse radiologically within minutes of the end of an operation. Similarly, a pneumothorax due to a ruptured bulla may be the cause of the mechanical defect, or alternatively simple bronchospasm may be present. This latter diagnosis (because it is so simple) should never be made until all other causes of a mechanical defect have been excluded. If a mechanical defect of the respiratory system is suspected then it is essential that an X-ray picture is taken immediately.

**TREATMENT**

It is important to emphasize that there is no direct evidence to suggest that the muscle relaxants are ever responsible for a fatal outcome. On the contrary, provided adequate ventilation is maintained, there is abundant evidence that massive doses of these drugs can be used for a week or more without ill effect. The most essential element of treatment, therefore, is to ensure that both the oxygen and carbon dioxide tensions of the patient's blood are kept normal. In a patient with severe emphysema the pre-operative level of carbon dioxide in the blood may be high and great difficulty may be experienced in restarting respiration unless the relevant laboratory data are available.

The emphysematous patient who comes to operation with a high blood PCO₂ may prove particularly difficult to manage postoperatively. Without adequate laboratory facilities it is extremely difficult for the clinician to judge when the carbon dioxide tension of the blood has reached the pre-operative figure. In anaesthesia there is no satisfactory substitute for accurate measurement and it seems certain that in the future most hospitals will need to be equipped with suitable apparatus for this type of case.

The administration of an analgesic-antagonist (where indicated) or a central nervous system stimulant (such as nikethamide) in order to increase the sensitivity of the respiratory centre may help to restart the breathing.

If a peripheral cause is responsible for the apnoea the line of treatment depends upon the diagnosis of the type of neuromuscular block that is present. If a depolarization block is found by the stimulator, then only measures designed to improve the cardiac output, the peripheral circulation and the renal excretion will prove helpful. An abundant supply of patience is the most essential factor in the treatment. On the other hand, if a nondepolarizing type of block is present, then an adequate dose of anticholinesterase drug should be given. A maximum dose of 5 mg of neostigmine should not be exceeded except in those patients in whom the initial dose yields positive evidence of some improvement in neuromuscular transmission and yet a "fade" of the mechanical response still persists.

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