RESPIRATORY FLOW RESISTANCE AFTER CURARE AND PANCURONIUM, MEASURED BY FORCED OSCILLATIONS*

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INTRODUCTION

CURARE is known to be one of many drugs that releases histamine¹ and vascular effects such as cutaneous flushing and hypotension after curare administration are attributed in part to this effect. However, the matter of histamine induced bronchoconstriction after curare is quite controversial²⁻⁷ and the anaesthetists' use of curare is appropriately ambiguous. While most anaesthetists will avoid the use of curare in the frank asthmatic, curare is frequently used in other forms of airways obstructive disease. Furthermore, curare is often used in status asthmaticus to paralyze the patient to permit ventilation. Pancuronium bromide‡ is said not to induce histamine release⁸ but there have been no quantitative studies of its effects on the lung.

The purpose of this study was to re-examine the effect of curare on respiratory resistance and compare it to the effect of pancuronium.

METHOD

Resistance measurements were made using the method of forced oscillations. This method of measurement of respiratory flow resistance (R_{rs}) was introduced by DuBois in 1956.⁹ Originally, he applied oscillations to the airway at the resonant frequency of the respiratory system – usually 6 to 8 cps. The choice of resonant frequency and the theory of the method are well documented.^{10,11} The equation of motion of the lung¹² is

$$P = \frac{1}{C} V + R\dot{V} + I\ddot{V}$$

where P is the driving pressure, C , R and I the total respiratory compliance, flow resistance and mass inertia, and V , $\dot{V}$ and $\ddot{V}$ the resulting volume, flow and volume acceleration. The method is based on this equation and the fact that at resonance the elastic impedance and inertial impedance are of equal magnitude and opposite sign.¹³ Therefore, at resonance, the applied pressure is used to overcome only flow resistance. Flow resistance is then easily determined as $\Delta P/\Delta \dot{V}$.

Since Du Bois' original work the method has been considerably simplified and

*Presented at the Canadian Anaesthetists' Society Annual Meeting, Halifax, Nova Scotia, June 1972.

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‡Pavulon (NA-97) provided through the courtesy of Organon Inc., Montreal, P.Q. Investigational drug.

FIGURE 1. Apparatus for producing and recording the oscillations.

refined.^{10,14} We have used the modification of Goldman *et al.*¹⁰ which measures $\Delta\dot{V}$ between points of zero acceleration and ΔP between the corresponding pressure points. By choosing the points of zero acceleration neither elastic nor inertial impedance accounts for any pressure difference occurring between the two instants; the pressure difference must, therefore, relate only to the flow resistance of the system. Resonance has been artificially achieved and it becomes unnecessary to apply the oscillations exactly at the resonant frequency of the patient's respiratory system. This method of resistance measurement is particularly applicable for use with anaesthetized or seriously ill patients since it eliminates the need for oesophageal balloons and body plethysmographs.

The repeatability of the method has been shown to be good, with Hyatt¹⁴ finding an 8 per cent variation in R_{rs} on repeated measurements in the same subject. Since most of the variation is due to changes in lung volume and flow pattern during the normal breathing cycle, it will essentially disappear in paralyzed apnoeic patients, as used in this study.

Figure 1 shows our apparatus for producing and recording the oscillations. The oscillations are produced by a 12" loudspeaker* driven by a sine wave function generator and power amplifier. Impedance matching is obtained by the cone. A constant bias flow of 0.4 litres/second prevents carbon dioxide retention. The oscillations are applied to the patient's respiratory system by direct connection to the endotracheal tube. The oscillatory flow is measured by a pneumotachograph and mouth pressure relative to ambient pressure by a differential pressure transducer. Flow and pressure signals are circuited to a direct writing recorder.

*Acoustic Research Inc. (type AR-1W), Cambridge, Mass.

FIGURE 2. Reproduction of a typical trace in the apnoeic patient, illustrating the calculation of R_{rs} .

A typical trace in an apnoeic anaesthetized patient is shown in Figure 2.

Forty-two patients undergoing abdominal surgical procedures were studied after premedication with pantopon and hyoscine. Induction was with thiopentone followed by intubation under succinylcholine relaxation without topical anaesthetic spray to the trachea. Anaesthesia was then maintained by nitrous oxide in oxygen delivered by a volume ventilator. At this point the patient was disconnected from the ventilator for a 10- to 20-second period of apnoea during which oscillations at 5 cps with a peak to peak pressure of 2 cm H₂O were applied to the respiratory system. This established the control resistance measurement at the spontaneous FRC of the paralyzed subject. Following this, 25 patients were given curare (0.4–0.5 mg/kg) and 17 patients were given pancuronium (0.06–0.07 mg/kg). Resistance measurements were then repeated at 2, 5 and 10 minutes after the relaxant. Systolic blood pressures were recorded, the chest was auscultated, and the facial, neck and chest skin were observed for flushing, before and after curare or pancuronium administration. Informed written consent was obtained from all patients participating in this study.

RESULTS

Figure 3 shows the results in the curare group. The control (pre-curare) resistance value for each patient is indicated by a horizontal line and the maximum increase or decrease in resistance after administration of curare by a vertical line. These results were analysed using the paired *t* test and show that,

1. Considering all subjects, there is a significant rise in resistance after administration of curare ($P < 0.02$).
2. In those with an essentially normal control resistance (the 20 patients with

FIGURE 3. Results in the curare group. The control R_{rs} value for each patient is indicated by a horizontal line and the maximum increase or decrease after administration of curare by a vertical line.

FIGURE 4. Results in the pancuronium group. The control R_{rs} value for each patient is indicated by a horizontal line and the maximum increase or decrease after administration of pancuronium by a vertical line.

R_{rs} values less than 6 cm H₂O/l/sec., mean 4.6 cm H₂O/l/sec.) the rise, although significant ($P < 0.02$), is small and physiologically of little significance.

3. In those subjects with a high initial resistance (the 5 patients with R_{rs} values greater than 8.5 cm H₂O/l/sec.) the increase is very large and highly significant, both statistically and physiologically. None of these subjects had a history of asthma; four of the five had a history of chronic bronchitis and/or emphysema while the fifth gave a history of Mendelson's syndrome 27 years previously. The salient features of these five patients are presented in Table I.

In contrast, Figure 4 shows the results in the group of patients given pancuronium. This group, overall, showed statistically significant ($P < 0.02$) decreases in respiratory flow resistance after administration of pancuronium. None showed a significant increase. Significantly, patients with a high control R_{rs} dropped their resistance after pancuronium, in contrast to similar patients in the curare group whose resistance invariably increased. The most interesting patients in this group were patient 11, a severe refractory asthmatic presenting for lung lavage and patient 15, a moderate severe asthmatic, both of whom showed no increase in resistance and in fact developed lower flow resistance after pancuronium. There was no evidence of cutaneous vasodilatation in this group and less tendency for decreases in systolic blood pressure. These findings support the claims that pancuronium neither releases histamine nor blocks sympathetic ganglia.

DISCUSSION

The measurement of respiratory flow resistance by the method of forced oscillations proved readily adaptable to the operating room situation; measurements were complete within 20 seconds, with minimum interference with the normal conduct of anaesthesia. The mean control R_{rs} value of 4.6 cm H₂O/l/sec., documented above, compares with the normal reported by Fisher *et al.*¹¹ of 2.3 ± 0.5 cm H₂O/l/sec. for normal, sitting, conscious subjects breathing at a mean FRC of 3.3 litres. The higher value reported here is explained on the basis of the lower lung volume that accompanies the supine position and anaesthesia, tracheal intubation and the heterogeneous group of patients.

The results show unequivocally that curare causes an increase in respiratory resistance which can logically be attributed to broncho-constriction. This increase is insignificant in patients with normal airways but very marked in those with pre-existing airways obstructive disease. It is not possible to conclude definitely that curare-induced histamine release is the mechanism of the large resistance increases; however, vascular dilatation manifested by cutaneous flushing and accompanied by a fall in blood pressure, observed in over one half of the patients in the curare group, is presumptive evidence of histamine release.¹ None of the five cases (Table I) had asthma and, although complete pulmonary function studies were not done, the pre-existing airways obstruction appears, in four of the five, to be due to chronic bronchitis and/or emphysema. These cases generally have a "fixed obstruction," in that they do not respond dramatically to isoproterenol inhalations. However, it is clear from these data that they are highly susceptible to agents that will induce bronchospasm.

TABLE 1
DATA FOR THE FIVE PATIENTS IN THE CURARE GROUP WHO REACTED WITH LARGE R_m INCREASES

Patient No.	Age	Sex	History	R_m (cmH ₂ O/l/sec)		Systolic BP Fall mmHg	Flush	Rhonchi
				Control	After Curare			
5	53	M	Chronic bronchitis	9.3	13.0	30	Yes	Increased
17	66	M	Chronic bronchitis	9.5	13.8	40	No	None
18	69	M	Chronic bronchitis	8.5	23.3	40	No	None
23	53	M	Chronic bronchitis	15.8	17.5	50	No	Unchanged
24	49	F	Previous Mendelson's Syndrome	13.8	20.0	10	No	None

The consequence of a high flow resistance are not just a requirement for higher ventilatory pressures. Bronchospasm is characteristically non-uniform¹⁵ and this will alter the distribution of inspired gas and could create severe impairment of gas exchange.

In complete contrast to curare, pancuronium appears to have no tendency to increase flow resistance, even in patients with severe pre-existing airways obstruction; in fact, respiratory flow resistance tends to fall in these patients. We have no adequate explanation for this effect.

We have concluded from this study that curare should be avoided during anaesthesia in any patient with a history suggestive of, or pulmonary function tests showing significant airways obstruction. This study suggests that pancuronium is the agent of choice.

We have also concluded from the anaesthetic experience that the use of curare to paralyze patients requiring ventilation for respiratory failure is probably undesirable. This applies particularly to patients with status asthmaticus, but may well apply to all patients with airways obstruction. If paralysis is necessary this study suggests that pancuronium is a more suitable agent.

SUMMARY

The method of forced oscillations was used to examine the effect of curare on respiratory flow resistance and to compare it to the effect of pancuronium. The results indicate that curare has a bronchoconstrictor effect that is significant in those with pre-existing airways obstructive disease. In contrast, pancuronium has no such effect. It is concluded that curare should be avoided in any patient with significant airways obstruction. The data suggests that pancuronium is the agent of choice.

RÉSUMÉ

Nous avons utilisé la méthode des oscillations forcées pour étudier l'effet du curare sur la résistance du courant respiratoire et comparer cet effet à celui du pancuronium. Les résultats démontrent que le curare exerce un effet bronchoconstricteur qui devient significatif chez les porteurs de maladies obstructives des voies respiratoires. Par contre, le pancuronium ne produit pas un tel effet.

Il faut conclure qu'il est préférable d'éviter l'utilisation du curare chez tous les porteurs d'une obstruction importante des voies respiratoires. Nos données font croire que le pancuronium est l'agent de choix.

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