VARIABILITY OF HAEMOGLOBIN CONCENTRATION DURING ANAESTHESIA

A Statistical Investigation of three Anaesthetic Methods

BY

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SUMMARY

Changes in haemoglobin concentration and systolic blood pressure were measured for fifty-six patients receiving three different methods of anaesthesia. One group received anaesthesia comprising a relaxant with nitrous oxide and oxygen and controlled respiration: no significant changes occurred. A second group received halothane inhaled spontaneously with oxygen: significant decreases in mean (integral) operative blood pressure and Hb concentration were observed. A third group had lumbar epidural block, spontaneous respiration and halothane inhalation. There was a statistically significant fall in blood pressure and Hb concentration. The fall in Hb concentration correlated significantly with the blood pressure decrease occurring some 5 minutes before. The possible sources of an increase in plasma volume during anaesthesia accompanied by peripheral vasodilatation are discussed.

The phenomenon of the variability of the haemoglobin concentration [Hb] of venous blood occurring during some types of anaesthesia is presented. The study was commenced when it was observed that the hypotension occurring with lumbar epidural blockade was apparently associated with falls in the concentration of haemoglobin in venous blood. This may be due to a physiological haemodilution of the blood occurring during periods of hypotension due to vasodilatation. The phenomenon has been investigated statistically and the results are given below.

METHODS

Selection of cases.

A total of fifty-six patients was investigated. None received any kind of medication for at least a week pre-operatively. All were judged to be free from serious pathology (apart from their indication for surgery) by pre-operative clinical examination.

Blood pressure and haemoglobin concentration determinations.

Upon arrival in the anaesthetic room, systolic blood pressure recordings were made until three equal, consecutive results were obtained at 5-minute intervals. This value was taken as the pre-operative level of blood pressure. Venepuncture was now performed and a sample of venous blood obtained for haemoglobin estimation. Induction of anaesthesia was now achieved by thiopentone injection through the same needle. Frequent blood pressure recordings were made throughout surgery; if the pressure was stable these were taken at 5-minute intervals; if unstable, as frequently as once a minute. The time of each recording was noted.

Specimens of venous blood were taken from the same vein as used for the initial venepuncture or from its contralateral fellow. Specimens were taken as frequently as practicable, usually every 10 or 15 minutes; in all cases venepuncture was made with a sterile dry syringe and needle and the time noted. Major postural changes were avoided whilst measurements were being made (Eisenberg, 1963).
Anaesthesia.

Group 1. Twenty-three patients received anaesthesia comprising premedication with opiate and atropine; induction was with thiopentone and a relaxant and an oral cuffed endotracheal tube was inserted. Anaesthesia was maintained using a relaxant (gallamine or tubocurarine), nitrous oxide, oxygen and, frequently, a supplement consisting of small increments of pethidine. Respiration was controlled. The operations undertaken are shown in table I.

<table>
<thead>
<tr>
<th>Operation</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correction of squint</td>
<td>1</td>
</tr>
<tr>
<td>Aural microsurgery</td>
<td>2</td>
</tr>
<tr>
<td>Tonsillectomy</td>
<td>2</td>
</tr>
<tr>
<td>Minor e.n.t.</td>
<td>5</td>
</tr>
<tr>
<td>Pyelolithotomy</td>
<td>2</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>4</td>
</tr>
<tr>
<td>Vaginal hysterectomy and repair</td>
<td>2</td>
</tr>
<tr>
<td>Laparoscopy</td>
<td>2</td>
</tr>
<tr>
<td>Other intra-abdominal operations</td>
<td>3</td>
</tr>
</tbody>
</table>

Group 2. Fourteen cases received anaesthesia comprising premedication with opiate and atropine. Induction was achieved with thiopentone and where indicated suxamethonium was injected and a cuffed endotracheal tube inserted. Anaesthesia was maintained by the spontaneous respiration of halothane and oxygen, using a closed circle system with carbon-dioxide absorption, basal fresh-gas flow and a Goldman vaporizer placed in the inspiratory limb of the circuit. The operations undertaken are shown in table II.

<table>
<thead>
<tr>
<th>Operation</th>
<th>No. of cases</th>
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<tbody>
<tr>
<td>Excision of sarcoma of foot</td>
<td>1</td>
</tr>
<tr>
<td>Urogential</td>
<td>5</td>
</tr>
<tr>
<td>Tonsillectomy</td>
<td>1</td>
</tr>
<tr>
<td>Excision of varicose veins</td>
<td>2</td>
</tr>
<tr>
<td>Plastic operations</td>
<td>2</td>
</tr>
<tr>
<td>Repair of inguinal hernia</td>
<td>1</td>
</tr>
<tr>
<td>Vaginal repair</td>
<td>1</td>
</tr>
<tr>
<td>Repair of undescended testis</td>
<td>1</td>
</tr>
</tbody>
</table>

Group 3. Nineteen patients received anaesthesia similar to that used for the latter group. However, for these patients, the injection of suxamethonium followed by the passage of an oral endotracheal tube was a constant feature. Further, following the establishment of spontaneous respiration, lumbar epidural block was performed through a convenient interspace and mepivacaine 1.5 per cent injected, roughly according to the dosage schedule for lignocaine established by Bromage (1962). In each of these patients the operation of vaginal hysterectomy and repair was carried out.

Haemodilution.

It was necessary to ensure that haemodilution occurred only in association with anaesthesia. Consequently, records were kept when the following conditions could be fulfilled:

1. For operations involving negligible blood loss; for example, middle ear microscopic surgery or repair of inguinal hernia.
2. For those operations associated with more than minimal blood loss, records were kept for the initial time fraction only, when haemorrhage was seen to be small in volume.
3. In the absence of any intravenous infusion or transfusion.

No record was kept after the loss of 175 ml of blood as determined by a modification of the haemoglobin extraction-dilution technique (e.g., Moir and Wallace, 1967; Roe, Gardiner and Dudley, 1962). However, it is reasonable to assume that physiological haemodilution due to haemorrhage very much in excess of 175 ml would have been insignificant. Thus Keele and Nell (1961) tabulate results showing that haemodilution due to even massive acute haemorrhage takes many hours to become apparent. Furthermore, it will be subsequently noticed that in those subjects receiving the halothane-lumbar epidural block technique, the major fall in haemoglobin concentration occurred during the first 40 minutes following the induction of anaesthesia. By this time, the surgery was invariably only just commencing. However, subsequently there was little further fall.

It may therefore be concluded that fluctuations in haemoglobin concentration were due to factors unassociated with blood loss or the administration of intravenous fluids or blood.
Haemoglobin determinations.
The method used was the cyanhaemoglobin technique; the same laboratory and technician undertook all the determinations. The error for this method by the Commonwealth Health Laboratory is between 0.5 and 1 per cent, but since this includes calibration error and the series depended upon comparisons of blood samples from individuals, each set being analyzed at the same time, the error was negligible.

Presentation of results.
A graphical mean of systolic blood pressure and haemoglobin concentration was obtained for each patient and plotted against time. These were compared statistically against the pre-operative values. Correlation coefficients were obtained where any linear relationship was revealed by plotting scattergrams of systolic blood pressure versus haemoglobin concentration. Since the fall in systolic pressure and in haemoglobin concentration were not necessarily simultaneous, the temporal relationship between them was also investigated in the group of patients who had halothane-oxygen with epidural anaesthesia, because these were all subjected to the same type of operation and sufficiently lengthy surgery for it to be a useful procedure.

RESULTS
A significant fall in systolic blood pressure and haemoglobin concentration occurred during anaesthesia produced by certain drugs and techniques. In Group 1 there was a significant mean fall in systolic blood pressure of 13.3 mm Hg (P<0.02), and a mean fall in haemoglobin concentration of 0.12 g/100 ml which was not statistically significant (P<0.2).

In Group 2 there was a highly significant mean fall in both haemoglobin concentration and systolic pressure (fall in [Hb]=0.505 g/100 ml (P<0.001); fall in pressure=40 mm Hg (P<0.001)). However, comparing mean falls in haemoglobin concentration and systolic pressure for the total period of anaesthesia there was poor and insignificant correlation between them (for fourteen cases: r=0.24; SE=0.277).

In Group 3 there was a highly significant fall in mean haemoglobin concentration during anaesthesia (0.826 g/100 ml; P<0.001) and in mean systolic blood pressure (52.53 mm Hg; P<0.001).

The correlation for the fall in haemoglobin concentration with the fall in pressure was given by r=0.41 (SE=0.268) for fifteen cases and r=0.39 (SE=0.236) for nineteen cases. Whilst the significance of correlation is thus in doubt, by increasing the series to N>25 significance would probably be achieved.

With Group 3 patients, the time relationship between changes in haemoglobin concentration and systolic pressure was investigated. By dividing the time following the induction of anaesthesia into increments of 10 minutes and determining, graphically, the mean concentration and pressure during each increment for each patient, it was possible to show the mean falls per time increment. With lumbar epidural block occurring about 20 minutes after the induction of light general anaesthesia, maximum falls in systolic pressure and haemoglobin concentration occurred by the beginning of the fourth 10-minute increment of time and certainly before any blood loss due to surgery.

By subtracting the haemoglobin concentration and systolic pressure in the second, third, fourth and fifth 10-minute increments from the corresponding pre-operative values for each of thirteen cases, the falls in each parameter were obtained. Using these falls, various correlation coefficients were obtained for falls in concentration and systolic pressure. However, the only significant value was that obtained for haemoglobin concentration in the second, third, fourth and fifth increments of time with the blood pressure being the mean of the preceding and coexistent time increment (r₃=0.64; SE=0.289). This suggests that falls in blood pressure precede falls in haemoglobin concentration by some 5 minutes and perhaps implies a causal effect.

When scatter-diagrams are drawn of four points for each of thirteen patients for fall in haemoglobin concentration with systolic pressure fall (mean of coexistent and preceding time increments) (fig. 1) it can be seen that there is a linear relationship between the concentration and pressure falls. In general, the coefficients of correlation are low because of wide individual variance. The general expression, using r₃=0.64, is given by: [Hb] fall g/100 ml=0.0135 (systolic
DISCUSSION

With some combinations of anaesthetic drugs, notably halothane used in conjunction with lumbar epidural blockade by mepivacaine (Carbocaine), there are highly significant falls in both blood pressure and haemoglobin concentration. Significant correlation occurs when the falls in haemoglobin concentration are compared with the blood pressure falls occurring some 5 minutes previously \((r=0.64; \text{SE}=0.289)\). Under these conditions there is a linear relationship between individual falls in blood pressure and haemoglobin concentration; the coefficient of correlation is rather low because of wide difference between individuals.

For the other combinations of drugs no such relationship could be demonstrated. With halothane and oxygen there were significant falls in blood pressure and haemoglobin concentration but correlation was insignificant.

That haemodilution due to vasodilatory hypotension might occur may be inferred from a recapitulation of the physiology of such hypotension. First, there may be a generalized decrease in intracapillary hydrostatic pressure (Starling, 1898). Second, the fall in perfusion pressure in the renal afferent arterioles results in the release of renin; consequently plasma angiotensin is formed. Angiotensin is a potent stimulant of aldosterone release (de Bono et al., 1963) and this causes water, Na\(^+\) and Cl\(^-\) retention whilst K\(^+\) is lost; further, anaesthesia and surgery are accompanied by the liberation of antidiuretic hormone. Third, the effect of anaesthesia may be an alteration in the relative quantities of intravascular and interstitial plasma proteins. Large amounts of extravascular plasma protein exist (Adamson and Hill, 1968; Skillman, Awwad and Moore, 1967). Extravasation of plasma protein occurs through capillary walls, at a rate which varies inversely with molecular size (Jones and Peters, 1966). Youlten (1968) has shown that the rate of capillary transmural protein extravasation in resting rat cremasteric muscle is very great (500 mg/hour/100g muscle). Hyman and Steinfeld (1967) postulated blood volume regulation by a central volume sensing system the efferent response of which is adjustment of plasma protein concentration. Anaesthesia of the type received by Group 3 patients may augment plasma volume by causing an increase in the ratio of intravascular to interstitial plasma protein. There are four ways in which this may be effected:

1. A decrease in the rate of plasma protein extravasation.
2. An increase in the rate at which plasma proteins are returned to the circulation from the lymphatics.
(3) An increase in plasma protein production. (However, following haemorrhage in man (Adamson and Hill, 1968) and dogs (Liljedahl and Rieger, 1967) there is an increase in plasma volume and the total amount of intravascular protein. Almost all the increase is derived from extravascular plasma protein sources and little new production of plasma protein occurs.)

(4) A loss of interstitial fluid plasma proteins into the lymphatic system or the cells. Kent (1967) showed that underperfused myocardial cells contained plasma protein which had diffused into them from the interstitial fluid.

If induced hypotension is associated with impaired perfusion of some cells their plasma protein content is increased. The colloid osmotic pressure of the interstitial fluid falls and the plasma volume increases. Although the concentration of the protein in the plasma decreases, its osmotic effect, in relation to that of interstitial fluid, is increased.

Shires, Williams and Brown (1961) and Shires (1965), using tagged sulphate ions, demonstrated a contraction of the extracellular fluid volume during surgery. Using non-hypotensive pentobarbitone anaesthesia in dogs, they were unable to show any alteration in the volume of the plasma compartment. It would seem that increases in the volume of the plasma are partly dependent on blood pressure falls but also upon drugs and techniques used to produce such falls.

ACKNOWLEDGEMENTS
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REFERENCES


Youlten, L. J. (1968). The permeability to plasma protein of skeletal muscle (rat cremaster) blood vessel walls. J. Physiol. (Lond.), 194, 63P.

Respiratory failure has a different emphasis in different specialties. The chest physician thinks primarily of obstructive airway disease; in the accident unit crushed chest is the main cause of respiratory failure; while for the neurologist the scene was, until recently, dominated by poliomyelitis. The anaesthetist may have a special association with any of these conditions but his own expertise is with drug-induced respiratory failure. This prepares him to contribute to the management of respiratory failure in any branch of medicine.

The strength of Respiratory Failure is that authors from different disciplines have tackled an interdisciplinary subject, giving it the broad coverage which it requires. The book progresses from the theoretical to the practical and its value rises steadily in the process. The introductory chapters giving the theoretical background provide yet another brief review of lung function and seem to possess no unique qualities. However, the second part is concerned with the general principles of treatment of respiratory failure and here the breadth of experience and the sound theoretical background of the authors becomes apparent. One may take exception to isolated points such as the statement that oxygen therapy is usually not essential when the arterial Po$_2$ is between 30 and 50 mm Hg but in general it is clear that the combined expertise of the authors is immense and their authority will seldom be challenged. Practical details are there in plenty and even include precise arrangements of trays of equipment. Valuable appendices include a list of addresses and telephone numbers of manufacturers of respiratory equipment.

This book should prove invaluable, if not essential, for those setting up an intensive care unit. It is likely to become a bench book, particularly for those who are only intermittently treating patients in respiratory failure. The book goes as far as possible to make the practical expertise of the authors available to a wide public.

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