Significance of changes in cerebral electrical activity at onset of cardiopulmonary bypass

P. E. KRITIKOU AND M. A. BRANTHWAITE

From Brompton Hospital, London SW3 6HP, UK

Kritikou, P. E., and Branthwaite, M. A. (1977). *Thorax*, 32, 534–538. Significance of changes in cerebral electrical activity at onset of cardiopulmonary bypass. A study of 100 patients requiring open-heart surgery has been undertaken to ascertain whether prophylactic measures designed to minimise cerebral damage have influenced the incidence or severity of changes in cerebral electrical activity recorded at the onset of cardiopulmonary bypass. The incidence of change in cerebral electrical activity remains high but the severity of the disturbances has diminished as compared with a series investigated before prophylactic measures were introduced. Changes suggestive of cerebral depression were particularly notable in children under 10 years of age. The significance of these findings is discussed in the context of factors which might influence cerebral electrical activity at the onset of bypass.

Changes in cerebral electrical activity are common at the onset of cardiopulmonary bypass and can be recorded easily using a heavily filtered electroencephalograph or cerebral function monitor (Maynard *et al.*, 1969). In a previous survey from this unit (Branthwaite, 1973a) an alteration in the cerebral function monitor (CFM) record was noted during the first few minutes of bypass in 88 of 140 patients (62.9%), and these changes were classified into four arbitrary categories—no change; elevation, either abrupt or gradual; a biphasic response; immediate depression. Ten patients sustained cerebral damage and there was evidence which suggested that this had occurred at the onset of bypass in seven cases.

In a separate study (Branthwaite, 1973b) it was shown that the arterial blood pressure during the first five minutes of perfusion is significantly lower when the pattern of change on the CFM suggests cerebral depression, and evidence was obtained subsequently (Branthwaite, 1974) to support the view that cerebral blood flow can fall at the onset of bypass if there is severe, sudden hypotension, even though the systemic flow rate is high. It was argued that this decrease in cerebral blood flow might be responsible for cerebral damage occurring at the onset of bypass, although microemboli from the perfusion apparatus could also contribute.

After prophylactic measures had been introduced to control these two hazards, the incidence of neurological damage fell from 19.2% to 7.4%

(Branthwaite, 1975). If it is indeed true that changes in cerebral electrical activity at the onset of bypass indicate some form of cerebral damage, and that excessive hypotension and microemboli are responsible, at least in part, the reduction in incidence of clinically apparent damage should have been accompanied by a comparable reduction in the incidence or severity of abnormal findings in the CFM records. A further study has been undertaken to explore this hypothesis.

Material and methods

The study was carried out on 100 consecutive patients requiring surgery in 1976 or 1977, for whom one of the authors (PEK) was a member of the anaesthetic team. Coronary artery vein grafting was undertaken in 22 patients and valve surgery, with or without coronary artery vein grafting, in 55 (aortic valve 19; mitral valve 30; multiple valves 5; tricuspid valve 1). Left-to-right shunts were closed in eight patients, right-to-left shunts in 11, and miscellaneous operations were carried out on four patients (excision of left ventricular aneurysm; isolated pulmonary valvotomy; relief of coarctation of the aorta with mitral valve plication; tricuspid valve repair with closure of coronary arterial fistula).

CFM tracings were recorded at 30 or 50 cm h⁻¹ from two intradermal needle electrodes placed 2.5 cm on either side of the midline, a little behind

the level of a line joining the external auditory meati. The impedance across intradermal electrodes is low and virtually constant (less than 2 k Ω), and it was not recorded on the second channel of the CFM. This was used instead to record the arterial blood pressure, the signal being derived from a radial arterial catheter attached to a Consolidated Electrodynamics pressure transducer and SE Laboratories amplifier.

Patients were premedicated with papaveretum and scopolamine, trimeprazine or diazepam being used as well in a few cases. Anaesthesia was induced with thiopentone and continued with nitrous oxide, oxygen, and supplements of either morphine sulphate, papaveretum, or, very occasionally, 0.5% halothane. Pancuronium bromide was used to ensure muscle relaxation and permit controlled ventilation. A note was made of all drugs given to the patient within the last 15 minutes before, and the first five minutes after, the onset of bypass, and of all drugs added to the pump prime.

Cardiopulmonary bypass was established using a membrane oxygenator (Teflo or Landé-Edwards) in 80 cases, a 'Rygg' bubble oxygenator in five, and a disc oxygenator in the remaining 15; a Pall 40 micron filter was used on the arterial line in all cases. The circuit was primed with a mixture of plasma protein fraction and electrolyte solution, both at room temperature, except for perfusions in infants or small children when fresh whole blood was used as well. It is essential for gas to flow through the membrane oxygenator during priming to avoid condensation of water vapour in the gas channel, and a low flow of oxygen and carbon dioxide was also supplied to both disc and bubble oxygenators before perfusion began. The circuit was not flushed with carbon dioxide before priming.

Bypass was initiated slowly but 'full flow' (at least 80 ml kg⁻¹ min⁻¹) had been reached in all cases by the end of five minutes. Gradual cooling was started with the onset of bypass in most cases. Artificial ventilation (and hence nitrous oxide) was discontinued when the left ventricle ceased to generate pressure transients on the arterial waveform. Adrenaline or metaraminol was used to raise or sustain the arterial blood pressure during the first few minutes of bypass in 12 subjects. These pressor drugs were given prophylactically to patients with a history suggestive of cerebrovascular disease and were also used therapeutically if the arterial pressure fell abruptly at the onset of bypass, particularly in patients with coronary arterial disease. No value of the arterial pressure was regarded as an absolute indication for vaso-

pressor therapy, and no patients required a vasopressor because of dilatation of the pupils or depression on the CFM associated with hypotension.

The pattern of change occurring in the CFM tracing during the first five minutes of bypass was classified according to the criteria defined previously. The mean blood pressure before bypass was calculated from the formula—(diastolic pressure plus 1/3 $\times$ pulse pressure) and was compared with the mean pressure five minutes after the onset of bypass. If the heart was still ejecting at five minutes, the same formula was used to obtain the mean pressure.

Results

Three records were technically unsatisfactory and were discarded; the tracing recorded from a fourth patient, who sustained a cardiac arrest just before the onset of bypass, was also excluded.

A change in the CFM tracing was recorded during the first five minutes of bypass in 79 of the remaining 96 cases (82.3%). There was a step-like elevation in eight subjects, and a gradual rise occurring over three minutes or more in 36; a biphasic change was recorded in 28 subjects and immediate depression in seven.

The 35 patients who showed either a biphasic response or immediate depression on the CFM during the first five minutes of bypass were compared with the 61 who showed either no change or a sudden or gradual elevation. The arterial blood pressure at five minutes and the magnitude of the drop in blood pressure during the first five minutes did not differ significantly between the two groups (Table 1). The percentage of patients in whom the left ventricle was still ejecting at five minutes, hence generating pulsatile cerebral perfusion, was higher in the group showing either no change or some pattern of elevation on the CFM record (Table 1).

The mean blood pressure at five minutes was slightly lower in the 12 patients given adrenaline or metaraminol, and the fall in pressure was greater (Table 2), but these differences were not significant. The arterial pressure was still pulsatile at five minutes in two of these 12 patients (16.7%).

There were 13 patients who were less than 10 years of age; three were infants and two more were under 2 years old. Only one of the CFM records from these 13 children showed no change at the onset of bypass, and this tracing was already abnormal before bypass, probably as a result of hypotension. In the remaining children, abrupt elevation of the record occurred in two instances,

Table 1 *Haemodynamic findings during first five minutes of bypass correlated with pattern of change on CFM tracing*

CFM pattern	Mean arterial pressure 5 min after onset of bypass	Fall in mean arterial pressure during first 5 min of bypass	% with pulsatile arterial waveform 5 min after onset
No change or elevation (n=61)	58.7 mm Hg (7.8 kPa)	18.6 mm Hg (2.5 kPa)	22/61 (36.1%)
Biphasic or depression (n=35)	54.3 mm Hg (7.2 kPa)	17.1 mm Hg (2.3 kPa)	5/35 (14.3%)
	P > 0.05	P > 0.05	P < 0.05

Table 2 *Comparison of haemodynamic findings during first five minutes of bypass between patients given adrenaline or metaraminol and all other patients*

Patients	Mean arterial pressure 5 min after onset of bypass	Fall in mean arterial pressure during first 5 min of bypass	No. with pulsatile arterial waveform 5 min after onset
12 requiring vasopressors	50.0 mm Hg (6.7 kPa)	20.0 mm Hg (2.7 kPa)	2/12 (16.7%)
84 not requiring vasopressors	58.1 mm Hg (7.8 kPa)	17.8 mm Hg (2.4 kPa)	25/84 (29.8%)
	P > 0.05	P > 0.05	P > 0.05

a biphasic change in six and immediate depression in four.

Four patients died during or soon after the operation, and the state of the nervous system could not be examined. Two patients suffered neurological dysfunction within the first three days of operation: a child aged 1 year made a normal recovery for 18 hours but then suffered multiple cardiac arrests followed by convulsions and transitory blindness; a 62-year-old woman regained consciousness normally but developed a left hemiplegia on the second postoperative day. This was of sudden onset and was presumed to be embolic in origin.

Discussion

The reduced incidence of neurological damage reported previously from this unit (Branthwaite, 1975) has been sustained. Only two patients showed signs of gross neurological dysfunction within the first three days after operation, and in both cases the aetiology was almost certainly unrelated to the operative procedure. In spite of this, the incidence of sudden change in the CFM record at the onset of bypass remained high and was, in fact, greater than the figure reported in the first series (Branthwaite, 1973a)—82.3% in 1977, 62.9% in 1973; $P < 0.05$. However, the proportion of patients showing immediate depression of the CFM record at the onset was lower (7 of 96 in 1977; 20 of 140 in 1973; $P < 0.05$). When depression did occur, it was mild and transitory (Fig. 1) and in no case was there depression lasting more than two to three minutes. Similarly, the downward phase of the trace in patients with a biphasic

Fig. 1 *Mild depression on cerebral function monitor at onset of bypass. In this and subsequent illustrations the upper panel is the CFM tracing and the lower panel the arterial blood pressure.*

change at the onset of bypass was often slight and did not fall below the baseline level recorded pre-bypass (Fig. 2). The apparent alleviation of the severity of change seen at the onset of bypass in a series of patients in whom gross damage related to bypass did not occur supports the hypothesis that the onset of bypass can be a time of hazard, and that manoeuvres directed towards the elimination of undue hypotension and microemboli are useful prophylactically.

A feature of particular interest was the high incidence of abnormal changes in the CFM records at the onset of perfusion in children. Four of the seven patients showing immediate depression on the CFM at the onset of bypass were

Fig. 2 A biphasic change in cerebral electrical activity at onset of bypass, the downward component never falling below the mean level established before bypass.

children, and a biphasic change was recorded in six more children. The reason for this is difficult to determine. Whole blood formed at least part of the prime in all these cases and hence the chance of microembolus formation may have been higher. Alternatively, hypothermia may have contributed in some cases. Surface cooling to a core temperature of approximately 30°C had been used before surgery in several of the youngest children, and further cooling followed the onset of bypass. Below 30°C , depression of the CFM record is common (Branthwaite, 1973b). Over-rapid cooling has been identified as a possible cause of cerebral damage in children (Björk and Hultquist, 1960) but great care was taken to maintain a temperature gradient of not more than $2\text{--}3^{\circ}\text{C}$ between the child and the circulating blood, and the fall in body temperature did not exceed $1^{\circ}\text{C min}^{-1}$.

Apart from the findings in children, an explanation is required for the high incidence of sudden change in cerebral electrical activity at the onset of bypass in adults, a change which appeared to be benign in that there were no obvious neurological sequelae attributable to the procedure. Some degree of arterial hypotension was recorded but bore no consistent relationship in this series to the pattern of change seen on the CFM in the first few minutes of bypass. This lack of correlation may be because the blood pressure at five minutes, rather than the lowest pressure reached during the first five minutes, was used in the analysis. The loss of a pulsatile component to the arterial waveform was associated with a higher incidence of changes

suggesting cerebral depression, an observation which is consistent with experimental work demonstrating that the incidence of neurological damage related to bypass is decreased when a pulsatile flow is maintained throughout perfusion (Sander-son *et al.*, 1972). In the circumstances of the present study, the preservation of a pulsatile component to the arterial waveform indicated that at least some proportion of the arterial supply was derived from well-filtered blood entering the left ventricle from the lungs. This might lessen the risks of cerebral embolism but the protective effect is likely to be fairly slight because the left ventricular output can be only a small fraction of the total systemic flow when the pump flow rate is high ($80\text{ ml kg}^{-1}\text{ min}^{-1}$ or more in all cases).

An alternative hypothesis has been advanced by Bethune (1976), who suggested that the pressure difference between free and dissolved gases in the circulating blood favours the growth of gaseous microemboli at the onset of bypass, particularly if nitrous oxide has been continued until perfusion begins. Nitrous oxide is a highly soluble gas and will tend to leave the patient's blood and enter microbubbles composed of air and oxygen until there is gaseous equilibrium between the nitrous oxide in the blood and in the bubble. As a result, the size of any infused bubble will increase. Bethune (1976) suggested that this hazard could be eliminated by flushing the circuit with carbon dioxide before introducing warmed liquids, by avoiding any gas supply during the period of recirculation, and by discontinuing the nitrous oxide 10 minutes before the onset of bypass, so allowing about 90% of the nitrous oxide to be eliminated. However, in a separate series of 10 patients investigated here, there was still a change on the CFM at the onset of bypass in seven patients, even though nitrous oxide had been discontinued at least 10 minutes previously (Fig. 3). The pattern of change seen was similar to that observed in the other 96 patients, and none of these 10 cases suffered neurological damage. In all of them, perfusion had been carried out with a Teflo membrane oxygenator. The priming technique differed from that recommended by Bethune (1976) but the chances of bubble formation with membrane oxygenators are probably low, and it seems unlikely that bubble formation or growth during the first few minutes of bypass could have been responsible for the changes in cerebral electrical activity which were detected.

It is concluded that the onset of cardiopulmonary bypass can be a time of potential hazard to the brain and that measures to control hypotension and eliminate particulate and gaseous

Fig. 3 Further change in cerebral function within first five minutes of bypass, even though nitrous oxide had been discontinued for more than 10 minutes. The gradual rise in mean level of the tracing after withdrawal of nitrous oxide is a common finding.

microemboli confer a considerable degree of protection. There must be other factors which influence cerebral function at this time, a change in the nature of the perfusion waveform probably being one of the most significant.

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Requests for reprints to: Dr. M. Branthwaite, Brompton Hospital, Fulham Road, London SW3 6HP, UK.