Cerebral Resuscitation with Barbiturates

To the Editor.—In a recent Editorial, Michenfelder discussed a study by Nussmeier et al. on the pretreatment of incomplete ischemia. Unfortunately, Michenfelder used the Editorial format to give an unbalanced view of our past studies on resuscitation after complete ischemia in monkeys and patients.

The rhesus monkey study by Bleyaert et al. was the first long-term (7-d) study of outcome after complete global brain ischemia with intensive care. Michenfelder initially criticized our model, and then later invited a member of the Pittsburgh group to introduce it into his laboratory. The study by Bleyaert et al., published in ANESTHESIOLOGY after peer review, was based on a rationale that is still valid today: 1) Barbiturates, which had been shown to ameliorate incomplete focal ischemia and incomplete global ischemia, might also favorably alter the secondary multifocal, incomplete ischemic mismatching of oxygen supply and demand that we and others have demonstrated occurs after complete global ischemia and reperfusion. 2) Barbiturates exert many potentially beneficial short-term effects beyond their ability to reduce brain metabolism.

The subsequent pigtail monkey study by Gisvold et al. with the same model could not duplicate the results of Bleyaert et al. This does not necessarily mean that the study by Bleyaert et al. was “flawed”; rather, it reveals how difficult it is to achieve consistently effective cerebral resuscitation after complete ischemia. Many factors not appreciated by us or others at the time might have influenced the outcome: the use of different subspecies; reperfusion pressure patterns; duration of controlled ventilation; and details of intensive care. The only valid criticism of the study by Bleyaert et al. now is the fact that some of the control experiments were not performed concurrently with the thiopental experiments.

The Brain Resuscitation Clinical Trial was initiated in 1979 as a National Institutes of Health–supported multicenter program. It was not designed to “thrust on the medical community prolonged barbiturate coma with evangelistic zeal,” but rather to establish an ongoing mechanism for clinical study and evaluation of novel treatment potentials for coma after cardiac arrest. The rationale for having chosen thiopental loading as the first novel treatment to be tested was based on more than the results of the Bleyaert et al. study; it included many other demonstrated beneficial effects of barbiturates and the widespread clinical use of thiopental loading after cardiac arrest at the time.

Our clinical study showed that thiopental loading, started in comatose patients 10–50 min after restoration of spontaneous normotension, is safe, i.e., does not increase reaerst or mortality, but also does not significantly improve cerebral or overall outcome. We have concluded, therefore, that this treatment should not be used routinely after cardiac arrest. This does not negate the possibility that some beneficial effects might be achieved with barbiturates after milder insults with earlier or more prolonged administration, or with a barbiturate used as one of a combination of treatments. Until such possibilities are proven in the laboratory, we agree with Yatsu that barbiturates should be used after cardiac arrest only in selected cases for selected indications. These include prevention or control of seizures, sedation, and normalization of elevated intracranial pressure.

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REFERENCES

Position of Proximal Orifice Determines Electrocardiogram Recorded from Multiorificed Catheter

To the Editor:—Johans\(^1\) reported that the intravascular electrocardiogram (ECG) monitored with a multiorificed catheter depends on the position of the proximal orifice, and that further work is needed to explain this finding. Examination of the electrical principles involved make this finding predictable.

The saline-filled catheter is a conductor with a different voltage source at each orifice provided by the summed electrical activity of the heart at that orifice. The electrocardiograph is electrically connected to the proximal orifice by a column of saline with impedance \(Z_c\). The voltage measured by the electrocardiograph, \(V_{ECG}\), is related to the voltage at the proximal orifice, \(V_p\), by the following equation:

\[
V_{ECG} = V_p - I_c Z_c
\]

where \(I_c\) is the current flowing from the orifice to the electrocardiograph. Because the electrocardiograph has a high-input impedance compared with \(Z_c\), \(I_c\) approaches 0, and \(V_{ECG}\) must nearly equal \(V_p\). Johans’ observation that this relationship is true confirms the expectation that the summed electrical activity of the heart at the proximal orifice provides an independent voltage source unaffected by voltages at more distal orifices.