Correlation of Cerebral Blood Flow with Outcome in Head Injured Patients

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In order to determine the relationship of cerebral blood flow (CBF) to the clinical outcome of head injury, serial determinations of CBF were performed by the intravenous Xenon technique in 24 patients. The patients were of mixed injury severity and were classified into four groups depending on the neurological exam at the time of each CBF study. All eight patients who were lethargic on admission demonstrated increases in their minimally depressed CBF as they improved to normal status. Eleven patients in deep stupor or coma ultimately recovered. Ten of these patients initially had moderate to profound decreases in CBF which improved as recovery occurred. The single exception was an adolescent whose initial CBF was high but became normal at recovery. Five comatose patients died. In four of these, already depressed CBF fell even lower, while one adolescent with initially increased CBF developed very low CBF preterminally. The data presented in this report demonstrated a good correlation between CBF and clinical outcome. In every one of the adult survivors, depressed CBF increased as the patient recovered to normal status. All adults who died showed a deterioration of CBF as the neurological status worsened. The only exceptions were two adolescents who initially showed high CBF values. In the adolescent who died, CBF dropped to low levels while in the survivor a normal CBF was achieved. Thus in adults a traumatic brain injury was associated with depressed CBF which increased with recovery or decreased further with deterioration while the reaction to injury was quite different in the younger brain.

ONE OF THE PRINCIPAL REASONS for measuring cerebral blood flow (CBF) in head injured patients is to determine if a correlation exists between the level of CBF and brain function and between CBF at the time of admission and the clinical outcome.

The study described in this report is based on 24 patients with varying degrees of head injury in whom multiple regional cerebral blood flow (rCBF) studies were performed from shortly following the head injury to recovery or death. In the adult head injured patients CBF was nearly always below normal in the initial study, then increased toward normal in patients who recovered and decreased toward cerebral circulatory arrest in patients who subsequently died. Of particular interest were two adolescents who were unconscious at the time the first CBF study was performed but had a marked elevation of CBF in spite of their coma.

Materials and Methods

The population for the study consisted of 24 patients ranging in age from 14 to 76 years. At the time of admission to the hospital each patient was classified into one of four grades based upon the initial neurological examination. Using the Glasgow Coma Scale,[11] Grade 1 equals 14; Grade 2, 12–13; Grade 3, eight to 11; and Grade 4 seven or less points. Stated in approximate terms, the Grade 1 patient is alert and oriented, the Grade 2 patient is lethargic but responds appropriately when aroused, the Grade 3 patient is difficult to arouse and disoriented, and the Grade 4 patient is comatose with inappropriate motor responses to painful stimulation or no response at all.

Following admission to the Emergency Ward and the initial neurological examination, arterial blood gases were measured in all patients classified Grade 3 or Grade 4. Endotracheal intubation was performed in all Grade 4 patients and in Grade 3 patients in whom

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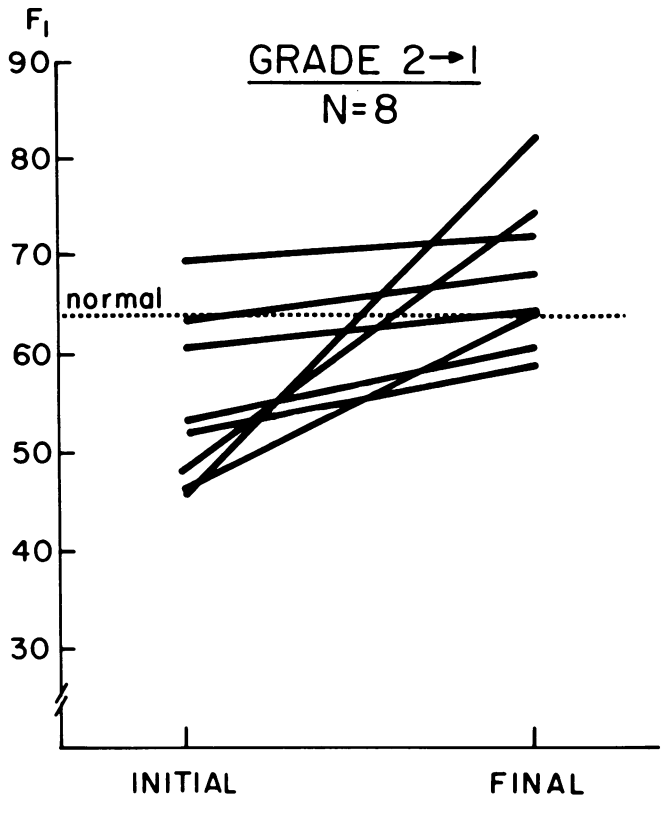

FIG. 1. Fast compartment blood flow (F_1) in ml/100 gm/min on the initial test (Coma Grade 2) and on the final test (Coma Grade 1) in patients who recovered. Average rCBF from 16 regional detectors is shown. The "normal" rCBF value has been corrected to a Pa_{CO_2} of 33.4 mm Hg, the mean for all patients in the study.

there was concern about their respiratory status or in whom sedation or anesthesia was necessary to perform computerized axial tomography (CT scan). Appropriate diagnostic and therapeutic procedures were carried out in patients with multiple injuries. Intracranial pressure was recorded continuously with an intraventricular cannula or subarachnoid bolt in 11 patients.

rCBF was recorded from the clearance curves of ^{133}Xenon using 16 scintillation detectors mounted in individual lead collimator tubes arranged as a crown about the patient's head. Eight detectors were arrayed over each hemisphere. The ^{133}Xenon was administered by intravenous injection of a bolus of ^{133}Xenon in saline. The method has been described by Obrist and colleagues[7,8] and by Austin and colleagues.[1]

Since changes in arterial P_{CO_2} (Pa_{CO_2}) have a profound effect on CBF, the blood flows were adjusted for differences in Pa_{CO_2} among studies in the same patient. In order to minimize the adjustment, we chose to correct the blood flows to the median Pa_{CO_2} value for all studies in each patient, rather than to some arbitrary normocarbic value. Fortunately for our purposes, Pa_{CO_2} differences between patients did not vary greatly, since most of them showed mild spontaneous hyperventilation in the acute stage of their illness as well as in follow up studies when they tended to be anxious about the test.

In normal subjects the clearance curve of ^{133}Xenon from the brain is biexponential consisting of a fast compartment which represents the clearance of the isotope from gray matter and a much slower compartment which represents white matter flow. The latter also includes a small extracerebral component. The volume of blood flow through gray matter is approximately four times the blood flow through white matter. By convention CBF is expressed as milliliters of blood flow per 100 g of brain per minute (ml/100g/min). We compute a number of flow parameters from each clearance curve but have concentrated our attention on gray matter flow (F_1) and on mean flow (MF), which is the average blood flow for all of the tissue seen by a detector (gray, white and extracerebral). At normocarbia in normal subjects, the present method yields a mean value for F_1 of approximately 80 ml/100g/min, and for MF of approximately 40 ml/100g/min. In the illustrations that follow only F_1 values are presented, because in every patient MF paralleled changes in F_1. The normal value for F_1 given in the illustrations has been corrected to the average median Pa_{CO_2} value for all patients, which was 33.4 mm Hg.

Results

Eight patients were Grade 2 on admission, and all of them recovered to Grade 1 (Fig. 1). In each patient CBF increased between the initial study which was performed following admission and the final study which was performed when the patient had achieved Grade 1. The increase in CBF, albeit a slight increase in five of the eight patients, occurred even when CBF was normal or slightly elevated at the time of the initial study. In the two patients in whom the increase in CBF was steepest, the final value was above normal.

Sixteen patients were classified Grade 3 or Grade 4 on admission and either recovered to Grade 1 or died. Figure 2 illustrates the initial and final CBF values in the 11 patients who recovered. Ten of these patients had a depressed CBF, and in several of the patients CBF was half normal or less. In each of the ten cases CBF rose toward normal with clinical improvement, although as in Figure 1, the final CBF values varied greatly even though all of the patients were declared to be Grade 1 at that time.

Figure 3 illustrates the CBF data in the five patients who died. In four of the five patients CBF was markedly reduced on the first examination, and then declined to even lower values in the final study made prior to death. In one of the patients CBF was virtually un-

recordable at a value of 10 ml/100g/min six hours before death.

The patients in Figures 2 and 3 labeled "S" and "P" are of special interest. They were adolescents 14 and 15 years old, respectively, and were the only patients under the age of 19 in this series. Patient "S" made a complete recovery, and as he did, CBF fell from a value of 100 ml/100g/min to normal. Patient "P" also had cerebral hyperemia on admission despite profound coma, and as she deteriorated to clinical brain death, CBF fell from a value of 90 to 10 ml/100g/min. Both patients had severe brain swelling on CT scan, and we postulate that diffuse brain swelling in children following head injury, which has long been described as "malignant edema", in fact is due to severe cerebrovascular congestion, not edema.[3]

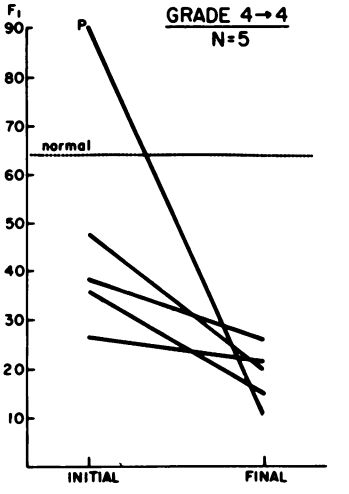

FIG. 3. Fast compartment blood flow (F_I) in ml/100 gm/min on the initial and final tests in patients who remained in deep coma (Grade 4) and died. Case P is an adolescent who presented with diffuse brain swelling (CT scan) and hyperemia.

Discussion

In recent years the method that has been used most commonly to study the cerebral circulation in head injured patients is the ^{133}Xenon intracarotid injection technique in which the isotope is injected through a catheter inserted into the internal carotid artery under fluoroscopic control. Several rCBF studies may then be performed over a period of hours under different conditions such as changing Pa_{CO_2} or systemic arterial pressure to test cerebrovascular reactivity. Probably it is unsafe to leave the catheter in the artery for more than a few hours, and because repeat catheterization of the internal carotid artery also carries some risk, most investigators have been reluctant to repeat the rCBF studies at another time unless carotid angiography was indicated for diagnostic purposes. Soon after we began to do CT scans in head injured patients, it became apparent that cerebral angiography was no longer needed in the large majority of patients. It was clear then that we would be justified in performing rCBF studies using the intracarotid technique only in the rare patient in whom the CT scan provided incomplete information on the nature of the injury. Therefore, further studies of the brain circulation in head injury were dependent on the application of a noninvasive method of introducing the ^{133}Xenon into the general circulation or on the development of an altogether different method for measuring rCBF.

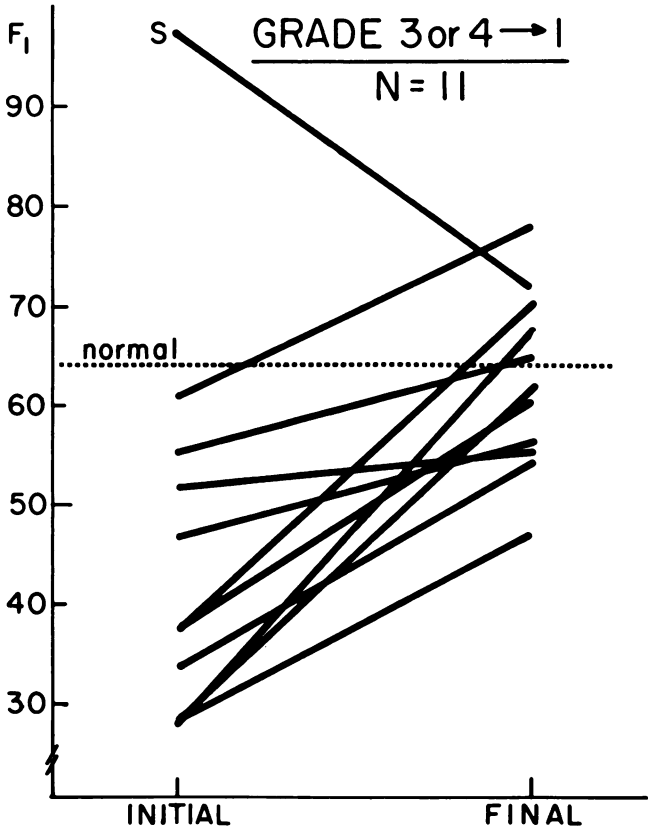

FIG. 2. Fast compartment blood flow (F_I) in ml/100 gm/min on the initial test (Coma Grade 3 or 4) and on the final test (Coma Grade 1) in patients who recovered. Case S is an adolescent who presented with diffuse brain swelling (CT scan) and hyperemia.

A discussion of the principles and the limitations of the noninvasive inhalation and intravenous methods for measuring rCBF is beyond the scope of this report. It is enough to say that we are confident of the accuracy of the method except in patients with severe pulmonary pathology, where the use of expired air to correct for isotope recirculation may lead to inaccurate results. The method is safe; radiation exposure to the lungs is approximately the same as obtained from a routine chest x-ray.

The intracarotid ^{133}Xenon method has provided much useful information in head injured patients on the relationships between CBF and cerebral perfusion pressure, which is defined as the difference between the mean arterial and intracranial pressures; the

responsivity of cerebral vessels to changes in Pa_{CO_2} and the status of cerebral autoregulation following head injury; the relationships between brain edema and CBF, between CBF and the acid-base balance of the cerebrospinal fluid and a number of other aspects of intracranial dynamics.[2–4,9,10] Several types of information are missing, mainly because of the limitations of performing serial studies over a long period of time. Information of particular interest in the management of head injured patients includes: the relationship between CBF and brain function assessed by the neurological examination; CBF values on admission as predictors of clinical outcome; and the responses of CBF to therapeutic agents (*e.g.* steroids, hyperventilation, hypertonic mannitol) as a guide to the selection of specific therapies.

The data presented in this report demonstrated a good correlation between CBF and clinical outcome. In every one of the 18 adult patients who were Grades 2 to 4 on admission and recovered, CBF increased as the patient recovered to Grade 1. It is not clear why the final values varied so much among these patients all of whom were alert and well oriented at the time of the last rCBF study. Perhaps the clinical designation is not fine enough to detect significant differences in performance among the patients. Currently we are engaged in a psychosocial evaluation of the patients in search of evidence of residual brain damage which might explain the large differences in the final CBF values.

In contrast to the increase in CBF that occurred in the adult patients as neurological status improved, all of the patients who were in coma at the time of the first study and subsequently died had a particularly marked depression of CBF initially compared to the group of patients who recovered, and invariably CBF continued to fall as the patient's neurological status deteriorated even further.

The exceptions to these observations were the two adolescent patients who presented with a marked dissociation between CBF and level of consciousness. These limited observations suggest that the young brain responds very differently to acute trauma than does the older brain.

The patients in this series received a variety of therapies, some according to protocols established in our head injury program and others on an ad lib emergency basis. The principal purpose of the therapy was to reduce intracranial pressure, and the effort was successful in all of the cases. None of the patients had marked intracranial hypertension at the time of the rCBF studies. This is an important point, since increased intracranial pressure does reduce CBF in head injured patients independent of neurological status.[6]

In the long run the most important contribution of the noninvasive ^{133}Xenon technique to head injured patients may be in the identification of those patients who will respond to therapy which improves brain function before that response is evident from the neurological examination.

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