Dimethyl Sulfoxide in the Management of Patient with Brain Swelling and Increased Intracranial Pressure after Severe Closed Head Injury

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Summary

The results of a prospective study on the effects of dimethyl sulfoxide (DMSO) in patients with severe closed head injuries causing brain edema and increase in intracranial pressure (ICP) are presented. 10 patients were selected and carefully analyzed according to Glasgow coma scale (GCS) scores and severity of brain edema. The results demonstrate that DMSO rapidly reduces the raised ICP, increases the cerebral perfusion pressure (CPP) and improves the neurological course and outcome without affecting the systemic blood pressure and patient responsiveness except only in one patient. We also point out that the rebound effect does not occur.

Dimethylsulfoxid zur Behandlung von Patienten mit zerebraler Raumforderung und erhöhtem Intrakranialdruck nach schwerer geschlossener Kopfverletzung

Die Ergebnisse einer prospektiven Studie über die Wirkung von Dimethylsulfoxid (DMSO) bei Patienten mit schwerer geschlossener Kopfverletzung und daraus resultierendem schwerem Hirnödem und erhöhtem Intrakranialdruck (ICP) werden mitgeteilt. 10 ausgewählte Patienten wurden einer sorgfältigen Analyse nach der Glasgow-Komaskala hinsichtlich des Schweregrades des Hirnödems unterzogen. Die Ergebnisse zeigen, daß der erhöhte ICP durch SMSO schnell verringert wird. Gleichzeitig wird der zerebrale Perfusionsdruck (CPP) erhöht, der neurologische Verlauf und das Ergebnis gebessert, ohne den systemischen Blutdruck und die Ansprechbarkeit des Patienten zu beeinträchtigen (mit Ausnahme eines Patienten). Der sogenannte „Rebound"-Effekt trat nicht auf.

Key-Words

Severe head injury – Glasgow coma scale – Raised intracranial pressure – ICP-monitoring – Dimethyl sulfoxide

Introduction

The prognosis of severe head injury is still almost as poor as it used to be, although the rapidity of emergency care and diagnosis has been dramatically improved. Despite distinct progress in the field of intensive care, including the monitoring of intracranial pressure (ICP) the neurosurgeon is often faced with the problem of attempting to interrupt a vicious circle, stemming from brain swelling causing raised intracranial pressure leading to cerebral hypoxia and so further brain edema. The mortality of severe head injury with this situation still remains 30 to 50% (3) as surgical and non-surgical therapy are often inappropriate and of no avail.

At the present time these therapeutic measures rely on a combination of therapies, many of which are directed to prevent elevated intracranial pressure (ICP) or to normalize ICP. In previous studies it was possible to demonstrate the beneficial membrane stabilizing effect of steroids (11, 29) and barbiturates on brain edema and intracranial pressure in clinical (10) and experimental head injury (21, 28). The Aescin was proved to be an agent immediately decreasing the cerebral pressure by insulation of the vascular wall in patients with acute brain edema after severe head injury (18). Hyperventilation is well known to cause cerebral vasoconstriction, thereby decreasing cerebral blood flow (CBF) and cerebral blood volume (CBV), and hence ICP (23, 26). The dehydrating effect of osmotic diuretic agents such as mannitol (1, 27), glycerol (15, 22), sorbitol and urea (14) was widely used during neurosurgery and neuroanesthesia to decrease brain bulk and intracranial pressure in patients with elevated CSF pressure. Local anesthetics are known to be one of the most patent membrane stabilizing agents decreasing and/or preventing raised intracranial pressure (2, 8, 9, 30).

All of these measures have been tried and tested; all have advantages and disadvantages, and no single measure is ideal. Management should evolve by adding new drugs or procedures to existing therapies when there is reason to believe that they would be effective.

Our study will aim to suggest that Dimethyl sulfoxide (DMSO) may find a place as a further nonoperative therapeutic measure in the management of patients with brain swelling and increased intracranial pressure.

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Table 1 Summary of data

Patient	GCS	Changes in SBP (mmHg)	Max. changes in ICP after injection (mmHg)	The mean highest ICP (mmHg)	Duration of infusion (Day)	Total dosage of DMSO (cc)	Outcome
1	4	Ø	37	53	6	305	Survived with deficits
2	5	Ø	26	38	8	500	Survived without deficit
3	6	Ø	19	60	2	700	Survived without deficit
4	3	Ø	24	98	1	135	Exitus (2nd day) ICP 98 mmHg at the time of death
5	6	Ø	23	38	4	200	Survived without deficit
6	6	Ø	36	36	4	275	Survived without deficit
7	4	Ø	26	37	2	250	Survived without deficit
8	3	Ø	24	95	2	200	Exitus (2nd day) ICP 58 mmHg at the time of death
9	5	Ø	20	56	2	250	Survived without deficit
10	3	Ø	Ø	75	7	400	Exitus (2nd day) ICP 75 mmHg at the time of death
			mv = 23,5				

mv: mean value

Material and method

We studied 10 patients, all of whom had a severe closed head injury (other than gunshot wounds) having presented within 6 hours of injury to the Neurosurgical Clinic of Dicle-University School of Medicine and having a Glasgow Coma Scale (GCS) score of 6 or less at the time of admission. The mean age of all patients was 22 years (range 11 year to 50 years). Seven patients were male. A CT study was performed on admission. A patient was considered to have marked brain swelling when the CT showed diffuse homogeneous swelling of the cerebral hemispheres with isodensity and the perimesencephalic cisterns could not be visualized. Patients with haematomas were excluded from the study due to their mass effect. Arterial and intracranial pressure were measured using a two-channel Hewlett-Packard system connected with a solid state Gaeltec ICP transducer inserted into the epidural space on the right frontal side through a burr hole. Cerebral perfusion pressure (CPP) was calculated (CPP = mean arterial blood pressure [MABP]-ICP). All patients were given an intravenous bolus infusion of DMSO (50 cc DMSO in 5% Dextrose) when ICP was 25 mmHg or more until ICP has been lowered to 15 mmHg or less. Therapeutic interventions in severe head injury were based on the level of ICP; for ICP of greater than 25 mmHg, an initial intravenous bolus (50 cc) of DMSO was rapidly administered and it was interrupted when ICP decreased up to 15 mmHg or more less.

Results

Death occurred in 3 of the 10 patients which was deemed secondary to head injury causing increased ICP. In no case there were medical complications. Highest ICP was greater than 100 mmHg in a nonsurvivor who died with ICP reading of 98 mmHg at the time of death the day after admission. His admission GCS score was unchanged at 3.

The highest ICP reading for patients who survived was 60 mmHg in whom application of DMSO lasted only 2 days with total doses of 700 cc. That patient presenting with initially GCS score of 6 survived without gross neurological deficit.

In most cases the ICP showed a marked decrease within 10 minutes after beginning of infusion, up to 41 mmHg. It returned to starting level or under initial level of ICP reading within 50 to 150 minutes which ranged from initial 25–98 mmHg. In no case was there a rebound effect and increasing during the administration of DMSO. Less marked changes in ICP were observed in patients with higher values of ICP. Only in a female patient was there no change of ICP after the administration of DMSO. She had an unchanged GCS of 3. Cerebral perfusion pressure increased within a few minutes after the start of DMSO infusion and this increase paralleled the decline in ICP because there was no decrease in arterial blood pressure. There were no cardiac problems or circulatory disturbances after injection of DMSO.

The continuous administration of DMSO did not prevent the ICP from returning to the raised starting level. The data are summarized in Table 1.

Discussion

The main cause of raised ICP in patients with severe closed head injury is brain edema which is an increase in brain volume caused by an accumulation of water, and not brain enlargement due to increased blood volume. Therefore a treatment may be effective by a direct effect on the water content, by tightening the blood-brain barrier, enhancing the resolution of brain edema and by decreasing the ICP (19, 20). ICP monitoring has been proven to have prognostic value and to be of benefit as an early-warning system of neurological deterioration or catastrophe and has become common in the management and study of the head-injured patient (10, 27).

DMSO has been reported to have three properties that are highly desirable in an agent used for treatment of head or spinal cord trauma; it provides strong diuresis (12), protection of cells from mechanical damage and reduction of edema in tissue by means of its ability to stabilize cell membrane (13, 16) or by its action as a free radical scavenger (17).

De la Torre et al. (1975) have tested DMSO in various experimental injuries of the central nervous system in relation to other therapies. They have shown that DMSO appears to be a useful and more generally effective drug than other comparable treatments to reduce ICP and increase CBF in acute extradural mass-forming lesions, middle cerebral artery occlusion, respiratory anoxia and spinal cord injuries, in rhesus and squirrel monkeys, dogs and rats (6) in accordance with a number of other studies in various experimental injury models (4, 5, 25, 31) and in clinical subjects (24, 32).

Another hypothetical explanation of DMSO effect is the increased tissue perfusion, thus affecting the microcirculation, platelet stasis and blood flow due to activity on prostaglandin synthesis. With increased tissue perfusion, cell oxygenation improves, metabolic acidosis in neutralized and intracellular fluid retention is diminished. Cardiac output increases after DMSO. This increase is probably caused by DMSO activity on myocardial contractility and tissue perfusion. Systemic arterial pressure is either slightly increased or remains unaffected. DMSO appears to neutralize the cellular damage caused by circulating hydroxyl radicals (7).

Our study demonstrates that DMSO is able to decrease acutely raised ICP for about 50–150 minutes when given intravenously as a bolus. The decrease ranges about 23.5 mmHg. Systemic blood pressure is not involved. Arterial blood pressure was not affected by administrating DMSO., whereas ICP was reduced significantly; therefore CPP is increased. Hyperosmolar solutions have been widely used and are of value particularly to gain time. However, in the presence of a blood-brain-barrier disturbance the agents used (mainly urea and mannitol) will pass over into the brain and therefore no long-lasting effect can be expected. The fact that urea enters the cells makes this drug particularly prone to a rebound effect as seen also in using mannitol. We have not seen a rebound effect in treatment with DMSO. The possible effect of barbiturate treatment is still controversial. The initial optimism has by and large been replaced by a critical attitude. Comparing barbiturate and DMSO there is an advantage in using DMSO because of its non depressing effect on systemic blood pressure. Another advantage is that DMSO does not interfere with the response of the brain injured patient to examination stimuli. A disadvantage of DMSO is the failure to prevent the ICP from returning to the raised starting level if it is continuously administrated.

There is no hard evidence that steroids, even in high doses, have any favorable effect on the edema in connection with trauma (19).

In order to explain the efficacy of DMSO in our study we may assume and summarize its membrane stabilizing effect (13) and improving the tissue perfusion with cardiac output (7, 19) and providing strong diuresis (12). According to *de la Torre* and our results we may conclude that increase in cardiac output caused by DMSO activity on myocardial contractility and tissue perfusion should be the circulatory effect that keeps the level of the arterial blood pressure unchanged whereas ICP decreases.

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