Success of heparin use in intraventricular haematoma treatment

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Abstract
Objectives: Prevent closure of an external intraventricular drainage with the use of heparin.

Methods: A patient with intraventricular haemorrhage presented with repetitive closure of intraventricular drainage tube. A trial of heparin infusion directly into the ventricle was attempted to prevent further closure of the catheter.

Results: The heparin used at a dose related of 340 units per 10 ml of intraventricular haematoma was effective in dissolving the clot and maintaining the external drainage patency.

Conclusion: Thrombolytic therapy with intraventricular infusion of heparin may be life saving in intraventricular haemorrhage. *(p118-121)*

Key words: *Hydrocephalus, intraventricular haemorrhage and heparin thrombolytic agent*

Introduction

A 66-year-old female patient, known to be on Coumadin post heart valve replacement was admitted to the emergency room in a comatose state. A Glascow Coma Scale (GCS) evaluation was assessed to be 6. An urgent brain computed tomography (CT) scan showed a large intraventricular haemorrhage, extending from the lateral ventricle to the cisterna magna (Fig. 1). Patient's INR was 4.5.

Methods and results

Brain CT scan was done one hour after the vascular accident and it showed a large intraventricular haematoma. Focus of bleeding was estimated to be in the right lateral ventricle. Blood was occupying 62% of the volume of the right lateral ventricle, 13% of the volume of the left lateral ventricle and 50% the volume of the third and fourth ventricles. Moreover, the blood was extending to the cisterna magna, where a quantity of some millilitres of blood was found in the perimedullary space.

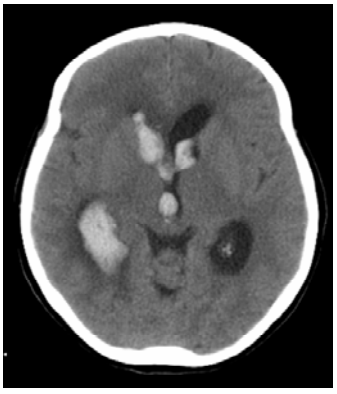

Figure 1 - Acute intraventricular haemorrhage.

Urgent left ventriculostomy with external drainage was performed. The patient clinically improved following the left frontal horn puncture with drainage of a large quantity of blood. The ventricular tube presented a spontaneous closure 10 hours post drainage and the patient clinically deteriorated. The ventricular tube was changed as it was found to be closed due to a blood clot at the tip of the tube. The following day, a decision to repeat the ventricular puncture was taken. Almost 15 minutes after the insertion

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of a new ventriculostomy, the second ventricular tube spontaneously closed. Five-thousand units of heparin were dissolved in 10 cc of normal saline and after precise calculations of the external ventricular drainage tube length and capacity, 4 cc (2000 units) of the prepared solution was injected into the system: only 1 cc of the solution (500 units) reached the ventricle. Twenty minutes later, a flow of a pinkish liquid drained through the external ventricular drainage. Thirty minutes later, the tubular system clotted again.

A similar trial of drain opening was done with double the dose of heparin solution that reached the ventricle (1000 units). This second trial was more effective, where the heparin effect was faster and lasted longer; it started after approximately 10 minutes and ended after one hour. After this one hour, the tube again clotted, spontaneously. Based on the same concept, 1500 and 2000 units were subsequently tried.

In the case of injection of 1500 units of heparin, a favourable course of unclotting lasting 4 hours was noted. Whereas in the case of injection of 2000 units of heparin, re-bleed from the lateral ventricle with blood in the external drainage occurred. During the entire time of this trial the higher loop of the external derivation was at the level of Monroe. After the definition and delineation of doses and their respective effects, 5 injections of 1500 units of heparin were given. Two injections in the 2nd day post trial, 2 further doses on the 3rd day and one last dose on the 4th day. After this, no spontaneous clotting was observed in the external derivation tube and a control brain CT scan showed the presence of blood inside the ventricular system; 10 - 20% less than the previously measured quantity (Fig. 2b). The patient was kept in the ICU for care and control of her diencephalic on-and-off symptoms.

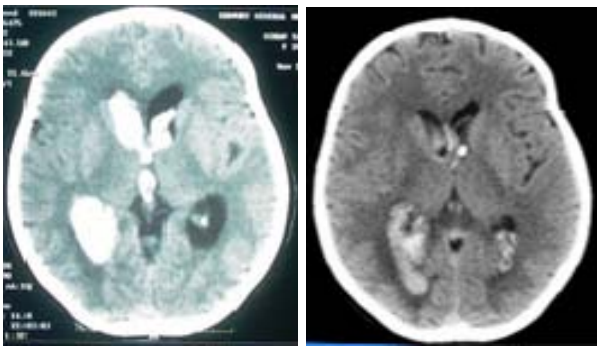

Figure 2a - Acute intraventricular haemorrhage with minor dilatation of the ventricular system prior to external derivation. **Figure 2b** - Fifth day post trial initiation.

After a period of 10 - 11 days of progressive decrease of blood output in the external drainage, the draining liquid became almost clear. At that time two isolated episodes of high body temperature were registered. Adequate antibiotics were started and on the 14th day post bleeding, and after a lumbar puncture was done to rule out cerebrospinal fluid (CSF) infection, an internalization of the external ventricular drainage with a VP shunt was done. Normal pressure valve of 110 mmHg was fixed.

Three weeks after the incident, the patient regained full consciousness, having only residual sluggish speech and movement deficits. She was transferred to the surgical ward on the fourth week, where she was rehabilitated during the next month.

The brain CT scan done 2 months later showed complete resolution of the intraventricular bleed (Fig. 2c)

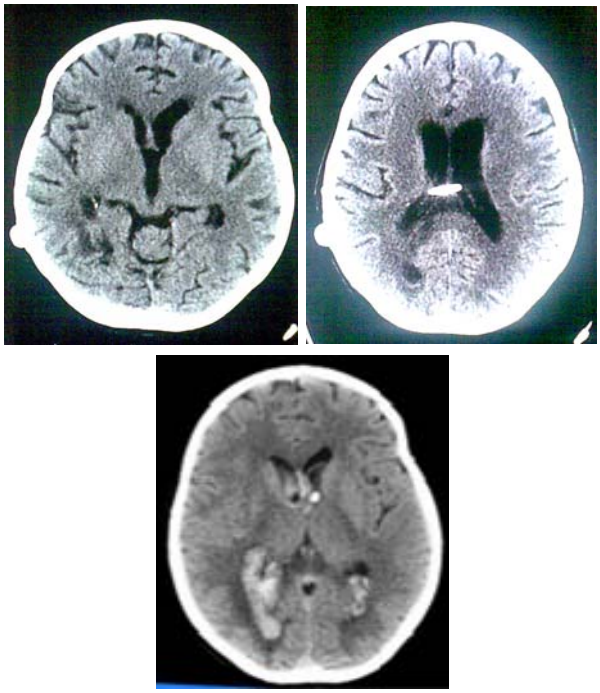

Figure 2c - Bain CT with a VP shunt 2 months post haemorrhage showing complete resolution of blood.

Discussion

Intraventricular haemorrhage presents a challenge to neurosurgeons. This event is always accompanied by significant morbidity and mortality because of the blood that remains in the ventricles for weeks after haemorrhage. Up to 50% of cases of "primary" intraparenchymal haemorrhage and "aneurysmal" subarachnoid haemorrhage are associated with intraventricular haemorrhage.[4]

Intraventricular haemorrhage was always correlated with high mortality rate. In some reports, it has been reported up

to 80%.[3] This poor prognosis is partially due to the continuing mass effect of the blood clots on the ventricular walls.[2] The relatively longstanding clots that remain in the ventricles for months after a haemorrhage derive from the inefficient and limited fibrinolytic system of the CSF.[2] Usually CSF drainage is required and permanent CSF shunt is required in 40%.[3]

The purpose of this paper is to present a case of intraventricular haemorrhage treatment, describing our experience in this case using intraventricular infusion of heparin. In the medical literature, heparin was never used as intraventricular injections. Due to its fast and short acting effect, heparin was carefully tried in our comatose patient (GCS 6) with a massive intraventricular pressure and a recurrent spontaneous closure of the external ventricular drainage by clots.

Mechanism of action of heparin is well known. It binds with antithrombin-III. This complex inactivates many thrombotic factors, mainly Xa and IIa.

The volume of blood in the ventricular system was equal to 43.77 ml as calculated by using the volume analysis tool available on our 16 multidetector CT scan (Fig. 3)

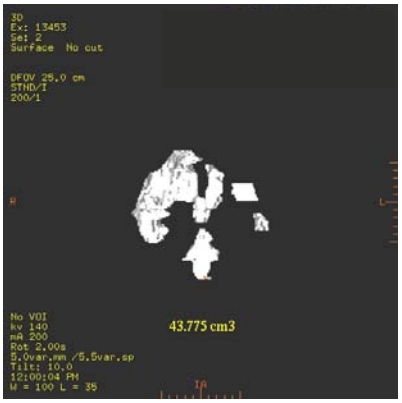

Figure 3 - Intraventricular blood volume calculated by the volume analysis technique on CT scan.

By trial and error method, approximately 44 ml of intraventricular blood necessitated 1500 units of heparin. Thus, 10 ml of blood inside the ventricle requires about 340 units of heparin to be dissolved.

Patients with intraventricular haemorrhage of aneurysmal or arteriovenous malformation origin should be excluded to prevent re-bleeding events.[3]

Other agents were previously used by us in other patients intraventricularly; rt-PA (Alteplase) a fibrinolytic agent, should be infused within 24 hours after the event with a dose of 3 mg every 24 hours.[3] Some authors gave rt-PA after ruling out or treating the possible source of further bleeding, such as an unsecured aneurysm.[2] Alteplase administration was bounded to a clear involvement of more than 30% of the volume of one lateral ventricle and/or the third or fourth ventricle by the haemorrhage. Animal models showed marked losses of the ependymal covering of the ventricular walls in the placebo-treated group, while the ependymal layer was largely intact in the animals treated with t-PA.[4]

Having had two previous cases treated with 2 mg of Alteplase injection intraventricularly (Fig. 4), no difference in outcome was noted between patients treated with heparin versus Alteplase. However, these interventions may increase the rates of re-bleeding and infection; the result in patient in whom clot-prevention strategy is evidently better.[5,3]

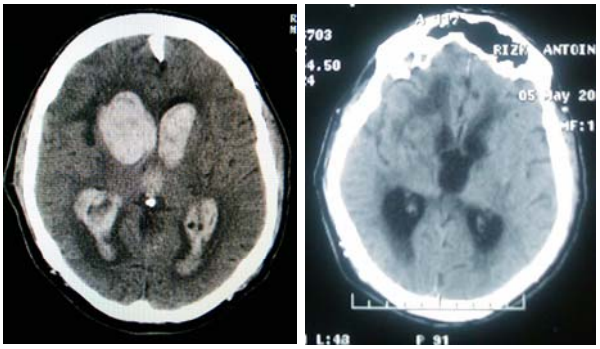

Figure 4 - Intraventricular haemorrhage pre and 2 weeks post intraventricular injection of Alteplase.

Many issues remain unresolved regarding theses agents, such as the optimal dose, frequency, rate, method, timing and duration of administration.[1]

Conclusion

The use of heparin has not been previously reported in clinical series in intraventricular haemorrhage settings. It offers significant improvement in the outcome. However, intraventricular infusion of heparin may increase the rate of re-bleeding. Our results indicate that heparin administered intraventricularly significantly enhances the drainage of the external ventricular derivation, preventing the occurrence of acute post-haemorrhagic hydrocephalus, through binding with antithrombin-III, inactivating many thrombotic factors.

We found that 10 ml of intraventricular haematoma necessitated 340 units of heparin to be dissolved. Above this amount rebleeding occurred.

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