Original Research Article

Management of spontaneous large intra cerebral hematoma with minimal invasive procedure (twist drill burr hole) with fibrinolytic therapy

Karla Ravi[1], Nandigama Pratap Kumar[2*], Ginjupally Dhanunjaya Rao[3], Savarapu Sai Kalyan[4], Gollapudi Prakash Rao[5]

[1,2]Assistant Professor, [3,4]Senior Resident, [5]Professor and Head, Department of Neurosurgery, Gandhi Medical College, Secunderabad, Telangana, India
[*]Corresponding author email: **npratapkumar@gmail.com**

International Archives of Integrated Medicine, Vol. 4, Issue 11, November, 2017.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 15-07-2017 **Accepted on:**28-07-2017
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Karla Ravi, Nandigama Pratap Kumar, Ginjupally Dhanunjaya Rao, Savarapu Sai Kalyan, Gollapudi Prakash Rao. Management of spontaneous large intra cerebral hematoma with minimal invasive procedure (twist drill burr hole) with fibrinolytic therapy. IAIM, 2017; 4(11): 229-240.

Abstract

Background: Spontaneous intracerebral haemorrhage (ICH) is associated with the high mortality among cerebrovascular events, and most of the survivors end with significant morbidity. Spontaneous intracerebral haemorrhage (ICH) is the second most common cause of stroke comprising 7.5-30% of all strokes. Surgery mainly helps in decrease in secondary injury and early rehabilitation.

Aim: To analyse the outcome and advantages of minimal invasive surgery i.e., burr hole or twist drill craniostomy with intraclot streptokinase injection to dissolve clot and aspiration to reduce mass effect in primary intracerebral hematoma, this help to prevent secondary injury and recovery of salvageable brain.

Materials and methods: Prospective study was done over from November 2014 to January 2017 in our department for the patients of spontaneous large intra cerebral hematoma > 80ml who underwent clot evacuation with fibrinolytic therapy with minimally invasive procedure with twist drill burr hole. Total 62 patients were included in the study. All the patients were followed with CT sequential scans to see for the clot size and followed with clinical status.

Results: Our analysis of 62 patients was consistent with the hypothesis that hematoma evacuation leads to improved neurological outcome, the outcome has been correlated with the rate of clot reduction.

Conclusion: Minimally invasive surgery is a safe and effective option in the management of spontaneous ICH especially in the patients whom major surgical procedures pose a significant risk. MIS is associated with lower mortality and better outcomes compared to surgical evacuation or conservative management. Our study have clearly shown an improved outcome after minimally invasive surgery and still there is some emptiness to determine the exact protocol to insist these type of studies to deal with bed occupancy and a burden to the society.

Key words

Spontaneous large intra cerebral hematoma, Minimal invasive procedure, Fibrinolytic therapy.

Introduction

Spontaneous intracerebral haemorrhage (ICH) is associated with the high mortality among cerebrovascular events, and most of the survivors end with significant morbidity. Spontaneous intracerebral haemorrhage (ICH) is the second most common cause of stroke comprising 7.5-30% of all strokes [1, 2]. Spontaneous ICH is classified as either primary or secondary. Primary ICH mainly due to chronic hypertension or cerebral amyloid angiopathy. Secondary causes of ICH may be secondary to tumours, haemorrhagic transformation of cerebral infarcts, aneurysms, vascular malformations, coagulopathy. Non-traumatic ICH accounts for 80% of ICH.

The annual incidence of ICH ranges from 10 to 30 cases per 100,000 population and is most common among elderly patients [3]. A systematic review examining published data from 2000 to 2008 demonstrated the incidence of ICH was doubled in low-income countries compared with high-income 22 per 100,000 persons vs. 10 per 10,000 persons [4]. Incidence is slightly more in females than males.

Advancing age, heavy alcohol intake, chronic hypertension and anticoagulant therapy are the well-established risk factors for ICH. Two-fold increase in incidence of ICH was noticed in every decade after 50 years. The predictors of early death of patients mainly depends on clinical and radiological severity of illness which include age, volume of hematoma, presenting Glasgow Coma Scale score, and extent of IVH. Volume of ICH is single most important, been shown to be a powerful predictor of poor outcome [5]. Many clinicians believe that effective therapies are lacking for patients who have ICH; however, this perception is changing in light of new data on the pathophysiology and treatment of this disorder in early intervention and decompression aimed at protecting the vulnerable brain from secondary injury.

Minimally invasive surgery (MIS) to reduce clot size is discussed, with the goal of decreasing morbidity through reduction in secondary neuronal damage. Fundamental questions regarding the pathophysiology of secondary injury following ICH still evolving. Nevertheless, recent studies suggest that reduction of clot burden is an important factor in limiting brain edema and additional neuronal injury, and in reducing the severity of neurologic morbidity following ICH. Some study demonstrated an improvement in the level of consciousness, and an improvement in the motor scores. No increase in the perihematomal edema was reported. Surgery mainly helps in decrease in secondary injury and early rehabilitation.

Aim and objectives

To analyse the outcome and advantages of minimal invasive surgery i.e, burr hole or twist

drill craniostomy with intraclot streptokinase injection to dissolve clot and aspiration to reduce mass effect in primary intracerebral hematoma, this help to prevent secondary injury and recovery of salvageable brain. This study mainly looked at hypertensive ICH, as ICH secondary to amyloid angiopathy had different management policy and prognosis in comparison to HTN ICH.

Primary Objective

- To look at treatment modality in intracerebral haemorrhage with poor general and neurological status where regular surgical intervention is not feasible or highly risky.
- Short term advantages
- Analyse the outcome at the end of discharge and at 5 months.

Secondary Objective

- To study the pre-operative factors determining the final outcome.

Materials and methods

Type of study: Institutional based Intradepartmental Prospective study over a period of 2 years

Period of study: November 2014 to January 2017

Study population: All the patients attending Department of Neurosurgery at Gandhi medical college and hospital, secunderabad. Total 62 numbers of patients were included in the study.

Study methods: Study includes all the patients of spontaneous large intra cerebral hematoma > 80ml who underwent clot evacuation with fibrinolytic therapy with minimally invasive procedure department of Neurosurgery in Gandhi Hospital, Secunderabad.

Plan of study: Study the factors considered for minimally invasive surgery, clot dissolution with fibrinolytics and evacuation, measurement of the clot size. Follow-up

Inclusion criteria

- Large supratentorial spontaneous ICH 80 mL diagnosed by using CT, CTA, with a GCS of 5-10. Deep and lobar ICH is allowed.
- Associated IVH is allowed and may receive a separate EVD (but thrombolysis is used in the ICH catheter).
- Clot stability, 6-hour clot size equal to the most previous clot size (within 5 mL) as determined by additional CT scans at least 6 hours apart.
- Symptoms less than 24 hours before diagnostic CT scan.
- First dose can be given within 76 hours after diagnostic CT.
- SBP <180 mmHg sustained for 6 hours recorded closest to the time of randomization.
- Age >18 and <80.

Exclusion criteria

- Infratentorial hemorrhage.
- Thalamic bleeds with apparent midbrain extension with third nerve palsy or dilated and nonreactive pupils.
- Irreversible impaired brainstem function (bilateral fixed, dilated pupils and extensor motor posturing), GCS < 5.
- Ruptured aneurysm, AVM, vascular anomaly, Moyamoya disease diagnosed with radiographic imaging.
- Platelet count <100,000, INR >1.4, or an elevated prothrombin time (PT) or activated partial thromboplastin time (aPTT), any irreversible coagulopathy, bleeding disorder, or known clotting disorder.
- Pregnancy
- Allergy/sensitivity to fibrinolytic agents.
- Previous enrollment in the study or any other interventional or surgical ICH studies.
- Complicating medical comorbidities.
- Active drug or alcohol use or dependence.
- In the investigator's opinion, the patient is unstable and would benefit from a

specific intervention rather than supportive care plus or minus MIS removal of the ICH.

- Inability or unwillingness of the subject or legal guardian/representative to give written informed consent.

Twist drill Craniostomy

- The procedure was performed at bedside with the patient supine position.
- A linear incision is made over the most prominent part of the hematoma.
- A single burr hole or 0.5 x 0.5 cm craniostomy done by guarded craniotome. Cruciate incision is given over the dura.
- The dura is opened and irrigation catheter is inserted into the hematoma.
- Hematoma is aspirated and 6000IU of streptokinase in irrigated into the hematoma and catheter is closed and secured. Skin incision is closed.
- Every 6 hour the catheter is opened and liquefied hematoma is evacuated and similar dose of streptokinase is irrigated and catheter closed.
- Aspiration Irrigation was repeated every 6th hourly for 72 hours and CT scan of brain was done to look for decrease of hematoma.
- Blood pressure of patient was adequately maintained at optimal level.
- The patients were adequately hydrated and post-operative CT scan was obtained on the 1st or 2nd day of surgery. (**Figure - 1** and **Figure - 2**)
- Catheter was removed after confirming adequate evacuation of hematoma on CT scan.

The following outcomes were analysed.

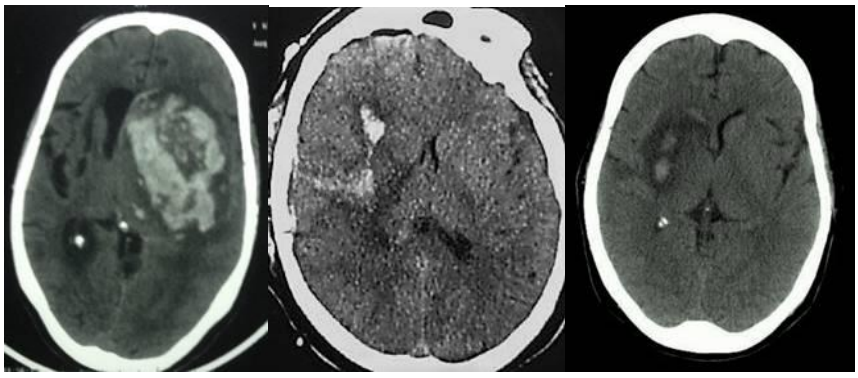
a. Primary outcome:

- Rebleeding
- Change in neurological state

b. Secondary outcomes:

- Cure rate (defined as complete symptomatic relief and adequate clearance of hematoma)
- Mortality (defined as death occurring during the hospital stay)
- Residual collections
- Complications (both medical and surgical)
- GOS at 5 months.

Figure - 1: CT Scan Head with sequential scans showing resolution of clot.



Results

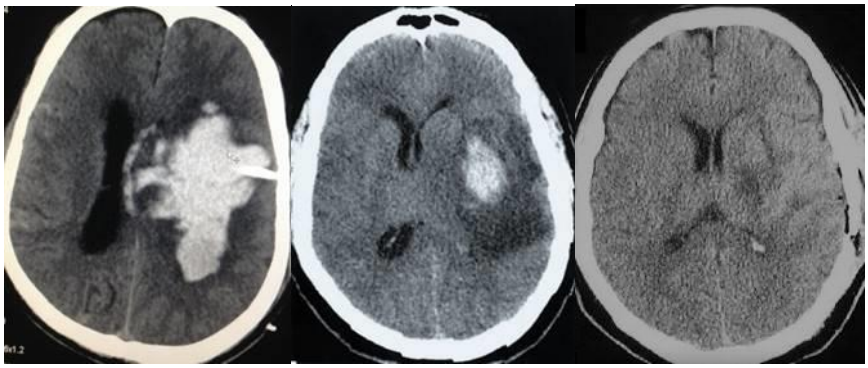
Total 62 patients were included in the study. Mean age of the study population was 57.94 with standard deviation of 12.8, 45.1% of the study fall between age 50-64 years. The study population had got 53.2% of right sided hematoma at presentation in which males were 2 times more common than females. Out of 62 patients 2/3rd of patients presented along with hypertension and nearly 60% of study population presented along with Diabetes mellitus. 14.5 percent of patients had comorbidities like renal

failure, coronary artery disease, and usage of antiplatelets.

56.4% of the study population presented with blood pressure greater than170 mmHg.

Study population of size 4.8% only were in the normotensive range at the time of presentation.19 patients out of 62 patients with blood pressure greater than 170mmHg out have achieved clot reduction greater than 25%.

Figure - 2: CT of head with placement of a catheter, thrombolytic dose with sequential scans showing resolution of clots.



Mean Clot reduction at the end of 72 hours of the study population was 32.92 with standard deviation of 8.7 with overall reduction greater than 25% was seen in 79.03%.

81.81% of the study falls in clot reduction greater than 25% at the time of discharge, in which 54.54% of the study falls in attaining GCS 5-7.

Out of total 62 patients, 19 patients achieved >25% clot reduction were out of coma, whereas when the clot reduction was less than 25% only 1 patient (10%) GCS was 8 i.e., out of coma.

After admission 45.16% of study population had underwent clot evacuation within 7-12.99 hours, 20.96% of study population had underwent clot evacuation within 13-18.99 hours, none underwent after 24 hours.

69.3% of the study population fall in severe disabled patients, who requires constant nursing care and attention, bedridden, incontinent and19.3% of study population fall in moderately to severe disability category who are unable to attend to own bodily needs without assistance, and unable to walk unassisted.

The total incidence of complications in the study population was 11%, and the overall incidence of patients with signs of disseminated intravascular coagulation were 9.6%.

Epistaxis (1.6%), haematuria (3.2%), Gl bleed (1.6%), re bleed (3.2%) and pulmonary complications (6.4%) were seen.

Mean Modified Rankin score at the time of discharge of the study population is 4.24 with standard deviation of 1.57.
At the end of 5 months the percentage patients with moderate disability was 30.65, severe disability was 27.41 who needs continuous need for help in daily activities.

The overall mortality at end of 5 months in study population was 41.94%.

Discussion

Spontaneous intracerebral hemorrhage (SICH) is the most devastating illness of all strokes. It was estimated that SICH affects over 1 million people worldwide every year [6, 7]. The case fatality rate of SICH at 30 days is about 30%-55%, and only 12%-39% of the survivors could live independently after 6 months [1, 8, 9].

Despite large amount of literature on the management of intracerebral hematoma, there has not been any concrete evidence for the management of spontaneous intracerebral hematoma. Many clinicians believe that effective therapies are lacking for patients who have ICH; however, this perception is changing in light of new data on the pathophysiology and treatment of this disorder, in particular, research establishing the role of surgical therapies to promote good outcomes. A series of MISTIE trials have gained popularity in the recent times and to pave way for minimally invasive strategies in the management of spontaneous ICH.

The decision regarding clot evacuation is controversial. It's always a matter of debate whether to go for medical management or surgical management. Taking into consideration the existence of an area of penumbra surrounding the hematoma area and of a non-living tissue, the removal of the hematoma would lead to a local decompression with the preservation of a viable parenchyma.

In the patients with intracranial hypertension and signs of herniation, surgical decompression and removal of the lesion with effect of mass is necessary. On the other side, it is supposed to be taken into consideration that most of the intraparenchymatous hemorrhages occur in elderly patients, already severely stricken by various co morbidities; making surgical evacuation riskier.

After a decade the results of STICH II trial has confirmed that early surgery does not increase the mortality or morbidity at 6 months and might have an overall benefit in survival with spontaneous intra cerebral hematoma without IVH [10]. Our study included only the patients with supratentorial intracerebral hematoma without IVH.

Many studies regarding minimally invasive surgery for clot evacuation have showed that removing clots helped to reduce the mortality in the early stages of onset but whether helped to improve the long term quality of life still have to be studied. Large craniotomies have been associated with high morbidity and longer duration of procedure time and anaesthetic complications. This is evident from the no. of studies published in the recent decades. A recent meta analysis, which included large series of studies, have confirmed that associated factors related with large craniotomies like procedure time, anaesthesia complications, poor general condition, can be overcome with minimally invasive surgery with fibrinolysis and clot evacuation.

Though there are over 10 randomised studies aimed at best treatment for patients with SICH it is still very difficult to select which treatment modality is better for each patient.

With the evolution of modern stereotactic and image guided surgical techniques, several case series of thrombolysis and catheter aspiration of ICH were published in the 1980's and 1990's suggesting that minimally invasive interventions are feasible, safe, and may avoid major surgical morbidity and offer improved outcome for selected patients with ICH [11-14].

In 2000, Montes et al demonstrated that CT-guided thrombolysis and aspiration appears safe and effective in the reduction of ICH volume and this experience helped motivate the subsequent phase II MISTIE trial [15]. The minimally invasive surgery and thrombolysis in intracerebral hemorrhage (MISTIE) trial explored an aggressive scenario of treating ICH by combining minimally invasive surgery and local delivery of rtPA [16].

MISTICH is the first large-scale randomized, parallel-group clinical trial to provide robust evidence for clinical practice by assessing the

safety and efficacy of different minimally invasive surgical methods for SICH.

MISTIE II was a phase II trial conducted from 2006 to 2011 evaluating safety, efficacy and dose escalation of rtPA in combination with minimally invasive surgery. In this trial patients with ICH volume of ≥20 cc and stable for 6 hours were treated with either 0.3 mg or 1 mg of rtPA every 8 hour to either final volume of <10 cc or 72 hours. They demonstrated reliable safety and feasibility of minimally invasive ICH clot removal. Based on these findings, a phase III trial is being planned, with sufficient power to delineate the treatment effect, which was seen in MISTIE II.

The MISTIE trials have been going on for the last 2 decades. Now the clinicians are considering minimally invasive surgery for intracerebral hematoma for better outcome in neurological status.

Enhancing the confidence in the MISTIE approach, a recently completed trial from china reported better outcome with minimally invasive thrombolytic evacuation of ICH with urokinase thrombolysis, as compared to open craniotomy [11]. But this study was limited by the absence of a cohort treated without any surgical intervention.

In our study twist drill craniostomy and catheter were used for thrombolytic evacuation of ICH with streptokinase thrombolysis. Our analysis of 62 patients is consistent with the hypothesis that hematoma evacuation leads to improved neurological outcome. In our study, the outcome has been correlated with the rate of clot reduction. The patients with less than 25% reduction in clot volume had poor prognosis compared to those with greater than 25% reduction.

In our study, clot reduction of greater than 25% was achieved in 45 patients. Out of these 19(42.22%) patients were out of coma, where as in the patients with clot reduction less than 25%, only 1 (10%) had a GCS more than 8 i.e. out of coma, Therefore Volume of clot reduction have consistently proved to be a powerful predictor of outcome.

Several factors like clot organisation, less local action of thrombolytic agent, misguided catheter, catheter blockage, longer duration between stroke and procedure, can lead to less rate of clot reduction. All these factors have to be considered while opting for minimally invasive procedures for evacuation of spontaneous ICH. Measures to overcome these limitations should be sought to improve rate of clot reduction.

None of the systemic reviews have studied about the factors limiting the rate of reduction of the clot size. As a result, the complete clot reduction is not achieved in any of the previous studies.

In our study the rate of clot reduction less than 25% is seen in 21% of patients and greater than 25% seen in the rest of the patients. The mean rate of clot reduction is 32.9 and SD of 8.69.Surprisingly, higher rates of clot reduction are achieved with the higher systolic blood pressure at presentation in our study. In patients with blood pressure greater than 170 mmHg, adequate clot reduction is achieved in 43.5% of patients.

In the study by Mahua Dey, et al., 90 patients were enrolled and followed for 180 days. Patients responded favourably to the surgery plus rtPA compared with just medical management. 20% of the clot was removed through surgical aspiration alone. With Surgical aspiration combined with rtPA, the average clot size was reduced by nearly 50% of initial volume; whereas patients randomly assigned to medical management showed only a 6% reduction of clot [17]. Nevertheless, there were no significant differences between the two cohorts in the quality of life of patients who had large (>50 ml) hematomas. In patients who had smaller hematomas (<50 ml), quality of life was

improved with MIS, without a noticeable impact on mortality.

Rebleed

Data from previous literature suggests that evacuation of blood clot on initial go, if very large would lead to reopening of the ruptured artery due to abrupt decline in the ICP.

Our study data showed the rate of rebleed during hospital stay was significantly lower, which is similar to most of previous published data.

Rebleed in our study was seen only in two patients with a percentage of 3.2, which include one female and one male. In both patients procedure has been abandoned and both died. Rebleed is one of the most serious complication of ICH and the decline in percentage of rebleeding rates may partly account for the significant decrease in mortality. In Mahua Dey cohort, 8% of patients had symptomatic rebleeding, which is higher when compared to our study [17].

Mortality

Many studies have showed that removing clots helped to reduce the mortality in the early stages of onset but data on long term quality of life still have to be studied.

Though the volumes of clots were very high in our study, mortality in the hospital is 11.29% and the overall mortality at end of 5 months in study population is 41.94%.At the end of 5 months the patients with moderate disability is (n= 19) 30.65% and with severe disability (n=17) 27.41%.

Mortality has been the primary end point of therapeutic studies in most published studies, and it has ranged from 30% to 70% in previous studies. This reflects in part patient inclusion and exclusion criteria, and to a lesser extent the treatment rendered in individual studies [17].

In our series, there was 41.94% mortality at end of 5 months. The other studies had a mortality ranging from 30-70%. However, it has to be noted that all the patients in this study had large hematoma volumes (>80 ml) and poor GCS (GCS=5-10) compared to other studies.

Mario Zuccarello, et al. showed that with power of 80%, a 2-sided significance level of 0.05, a 3-month mortality or poor outcome (GOS of #3) of 44% is noticed in the surgical treatment group [18]. When compared to this study, our study has noticed significant difference between GCS at admission and GCS at Discharge with 2-sided significance level of 0.05 and a 5 month moderate disability (GOS of #4) of 30.5%.

Complications

In our series, the 7 deaths within the hospital were due to complications; one with epistaxis, two with rebleed, one with haematuria, one with upper GI bleed, one with pulmonary complication.

The unusual complication experienced during study is bleeding diathesis, which have to be studied in detail to increase the outcomes.

Minimally invasive surgery

The role of minimally invasive surgery in the treatment of ICH has gained importance over the past decade. Surgical therapies have been unable to improve the neurologic outcome of these patients, as evidenced by the results of the international study of the treatment of intracranial hemorrhage. It failed to demonstrate a significant benefit of aggressive surgical treatment over conservative medical treatment for the acute care of ICH.

Additionally, fundamental questions regarding the pathophysiology of secondary injury following ICH remain to be investigated. Nevertheless, recent studies suggest that reduction of clot burden is an important factor in limiting brain edema and additional neuronal injury, and in reducing the severity of neurologic

deficits following ICH. If MIS with or without thrombolytic therapy were capable of achieving safe and efficient clot reduction, it might modify patient outcomes positively. In our study, it has been shown that there is significant decrease in mortality and complications when compared to conventional surgical decompressive craniotomy.

Regarding morbidity, the outcome scores were not so satisfying but the overall improvement in the GCS at the time of discharge has played a role in maintaining the patient status in medium outcome scores.

In our study, among surviving patients, 30.65% achieved a meaningful level of functional recovery at 5 months when compared to other studies, it was only 20% [1, 6].

Many case-control and cohort studies have identified clot volume and Glasgow coma scaleat admission are the main prognostic factors affecting the survival and neurologic outcome of these patients [19].

In our study the mean clot reduction at the end of 72 hours of the study population is 32.92 with standard deviation of 8.7 with overall reduction greater than 25% is seen in 79.03%.

81.81% of the patients in this study had clot reduction greater than 25% at the time of discharge, in which 36.3% of the patients attained a GCS >8.

In our study the rate of clot reduction is mean of 32.92 with sd of ± 8.7 and rate of GOS > 3 was 30.65%.

The rate of clot reduction noticed in Tang et al study was mean of 40 with SD of ± 16.5 and rate of GOS > 3 was 42.5%.

Reduction of clot size directly reduces local mass effect, which decreases the risk for fatal complications, such as brainstem compression. In addition, minimizing hematoma volume also could lead to a decreased risk for elevated ICP that is due to obstructive hydrocephalus.

To minimize brain tissue injury by surgical manipulation, minimal invasive and aspiration have emerged as treatment alternatives.

Approaches to hematoma evacuation studies that tested the safety and efficacy of MIS techniques in the treatment of ICH have centered on two different procedures: minimally invasive with aspiration of the hematoma, and stereotactic placement of a flexible catheter in the core of the hematoma followed by the administration of thrombolytic agents.

In Morgan, et al. study clot was evacuated through MIS and fibrinolytic therapy alone, whereas patients randomly assigned to medical management showed only a 6% reduction of clot [20].

A study by Marquardt and colleagues focused on a novel, multiple target aspiration technique in 64 patients to aspirate a ‘‘sufficient proportion’’ of the hematoma with minimal risk for the patient [21]. More than 80% of the hematoma volume was aspirated successfully in 73.4% of the patients, with only one episode of rebleeding.

In 2017 our study of a case series, 62 patients underwent minimally invasive surgery plus catheter insertion and evacuation followed by scheduled streptokinase infusion, supratentorial clot volume of >80 ml, followed up for 5 months, 41.94% mortality at 5 months, 32% clot reduction SD ± 8.69 in acute phase and 3.2% of rebleed.

And our study shows rate of clot reduction greater than 25% was achieved in 45 patients, out of these 19(42.22%) patients were out of coma, whereas when the clot reduction was less than 25% only 1 patient (10%) had a GCS more than 8 i.e. out of coma.

Fibrinolysis with clot aspiration, stereotactic clot aspiration is similar to endoscopic aspiration, but clot resolution is enhanced by thrombolytic agents, such as streptokinase, urokinase, or rt-PA. Clot evacuation combining the use of fibrinolysis with clot aspiration has emerged as a promising surgical modality in the acute care of ICH. Studies with animal models of ICH and IVH have demonstrated the efficacy of thrombolysis in reducing clot volume. Furthermore, the increase in perihematomal edema observed when ICH develops a complication of rt-pa for ischemic stroke has not been observed in trials of spontaneous ICH [11].

This observation suggests that rt-pa may be used safely to accelerate hematoma volume resolution. The testing of rt-pa in the treatment of ICH has moved into clinical trials.

Clot lysis using Urokinase as a thrombolytic agent, combined with stereotactic aspiration, was compared with best medical treatment alone in the stereotactic treatment of intracerebral hematoma by means of a plasminogen activator trial [22].

The optimal dosing of rt-pa for the treatment of ICH remains unknown. Different groups of investigators have empirically used different regimens. Dose escalation studies from thrombolytic therapy in the treatment of IVH that aimed to clarify this subject are close to completion. Schaller and colleagues used a novel method to calculate the initial rt-pa Dose. The amount of rt-pa was directly proportional to the maximal diameter of the initial hematoma volume. The dosage was recalculated daily based on clot diameter as measured by daily CT scans [23].

Our study have used twist drill craniostomy, catheter placement and irrigation with streptokinase and aspiration of deep ICH, suggested that this procedure was safe and linked to improved neurologic outcomes that correlated well with the degree of hematoma removal.

Our study also demonstrated an improvement in the level of consciousness, and an improvement in the motor scores. No increase in the perihematomal edema.

Similar beneficial effects have been observed with the use of thrombolysis in IVH in systemic reviews. Based on early data showing a trend toward improved 30-day outcomes in patients who received intraventricular Urokinase, a randomized double-blinded pilot trial by Naff and colleagues showed accelerated clot resolution with intraventricular Urokinase. These results reinforce the multifactorial nature of the proposed therapeutic effect of rapid clot removal in different paradigms of intracranial haemorrhage [24].

In a recent cochrane database review, it was concluded that endoscopic evacuation has not been shown to significantly decrease the odds of death and dependency among patients who have ICH [25]. Reports of treatment benefits in patients who were treated with endoscopic aspiration of ICH in japan have led to the routine use of this modality as an alternative to craniotomy in that country. In the United States, this treatment modality has been restricted to research protocols in academic stroke centers, and it is not advocated widely as an option for the treatment of ICH.

Thrombolytic therapy is an attractive therapeutic option that has the potential to modify the natural history of ICH.

A dose escalation trial also is needed to identify the fibrinolytic dose that has the optimal risk/benefit ratio. The end points should be determined to measure the improvements in function and to establish optimal clinical efficacy.

Conclusion

Minimally invasive surgery is a safe and effective option in the management of spontaneous ICH especially in the patients whom

major surgical procedures pose a significant risk. MIS is associated with lower mortality and better outcomes compared to surgical evacuation or conservative management.

The unusual complications during the course of the treatment like bleeding diathesis shall further progress the acute phase and could be fatal. These types of complications have to be extensively studied to decrease the mortality during the treatment to substantiate for a better outcome.

Our study have clearly shown an improved outcome after minimally invasive surgery and still there is some emptiness to determine the exact protocol to insist these type of studies to deal with bed occupancy and a burden to the society.

Further studies are required to establish the dosage of fibrinolytic agent, therapeutic window for procedure, any other alternative method better than MIS.

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