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Original Article

External Ventricular Drainage Reduces Mortality in Spontaneous Intraventricular Hemorrhage of Brain: A Comparative Study

Chowdhury SMNK[1],Rashid HM[2], Hossain NM[3], Ara SA[4], Bhuiyan MS[5], Sarker T[6], Saha K[7], OhiMS[8]

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Contribution of Author: Principal Investigator- Dr. S.M. Noman Khaled Chowdhury

Manuscript Preparation- Dr. Mohammad Humayun Rashid, Dr. Mohammad Nazrul Hossain

Data Collection- Dr. Syeda Asfiya Ara, Dr. Md. Sharif Bhuiyan, Dr. Tapas Sarker

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Abstract:

Introduction: *External ventricular drain (EVD) usage in patients with intraventricular hemorrhage (IVH) is variable in current practice and clinical trials, and its impact on outcome remains controversial. Aim of this study was to see the outcome of EVD in management of spontaneous IVH of brain assessing by Glasgow outcome scale (GOS) and modified Rankin scale (mRS) score compared with conservative management.*

Materials and Methods: *Between July 2018 and June 2019, a consecutive 125 admitted patients with spontaneous IVH were enrolled in this quasi-experimental study. Among them 56 patient's relative agreed to surgery who were accepted as case group and had EVDs. Remaining 69 patient's relative declined authorization for surgery and were accepted as control group and underwent conservative management. Baseline demographics, clinical presentation, and hospital course, Glasgow coma scale score (GCS) for level of consciousness and modified Graeb score (mGS) for severity of ventricular haemorrhage were recorded at baseline and postoperatively. Admission Computed tomography (CT) scans performed within 24 hours of admission were reviewed for IVH type and hydrocephalus. Patients were followed up for 3 months post operatively and assessed using the GOS score and mRS score.*

Results: *Both the groups were similar at baseline in terms of age (mean±SD: 59±14 vs 60±14, p = 0.645), sex and comorbidity distributions. However, patients who received EVDs had lower mean GCS score (p=<0.001) and higher mean mGS score (p= 0.015) than those who did not receive an EVD. Incidence of hydrocephalus was similar in both groups (57.4% vs 46.7%, p = 0.268). Among the 77 survivors at 3 months, there were 23.1% (6/21) patients scored mRSd"2 in case group, while 38.2% (13/34) in control group (P=0.211). After binary logistic regression analysis, EVD placement was independently associated with reduction of 90 days mortality than conservative management (OR: 3.982; 95% CI: 1.3-12.19) but no effect on morbidity and functional dependence. Other independent predictors for mortality were higher age (p=0.002), lower GCS at admission (p=<0.001) and presence of hydrocephalus (p= <0.001) on CT scan.*

Conclusion:*These results suggest that EVD placement may be beneficial for patients with IVH, who have particularly poor prognosis at admission, but our results must be validated in future randomized clinical trial with larger cohorts and longer follow-up periods that are sufficiently powered to control for the heterogeneity of the study population and managements.*

Keywords: *Intraventricular Hemorrhage, External Ventricular Drainage, Acute Hydrocephalus, Spontaneous IVH*

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1. Dr. S.M. Noman Khaled Chowdhury, Professor & Head, Department of Neurosurgery, Chittagong Medical College Hospital, Chattogram
2. Dr. Mohammad Humayun Rashid, Chief Resident, Department of Neurosurgery, Chittagong Medical College Hospital, Chattogram
3. Dr. Mohammad Nazrul Hossain, Associate Professor & Head, Department of Neurosurgery, Ibrahim Cardiac Hospital & Research Institute
4. Dr. Syeda Asfiya Ara, Assistant Professor, Department of Pathology, Chittagong Medical College Hospital, Chattogram
5. Dr. Md. Sharif Bhuiyan, Resident, Department of Neurosurgery, Dhaka Medical College Hospital, Dhaka
6. Dr. Tapas Sarker, Chief Resident, Department of Neurosurgery, Chittagong Medical College Hospital, Chattogram
7. Dr. Kamalesh Saha, Registrar, Department of Neurosurgery, Khulna Medical College Hospital, Khulna
8. Dr. Sirajul Munir Ohi , Chief Resident, Department of Neurosurgery, Chittagong Medical College Hospital, Chattogram

Correspondence to: Dr. S. M. NomanKhaledChowdhury, Professor and Head of the Department, Department of Neurosurgery, Chattogram Medical College Hospital, Phone: +8801819019415, E-mail: ncdmc1971@gmail.com

Introduction:

Intraventricular hemorrhage (IVH) is acute neurosurgical condition. The incidence of intraventricular hemorrhage (IVH) is increasing nationwide, correlating with an aging and vasculopathic population coupled with widespread use of anticoagulant and antiplatelet medications among which primary IVH occurs in 30% and secondary IVH occurs in 70% patients.[1,2] Intraventricular hemorrhage (IVH), hydrocephalus, and herniation syndromes are of particular importance in ICH as they may be lethal to patients with a mortality rate ranging from 45% to 80%. IVH are classified as either primary, involving the ventricular system and adjacent ependymal lining, or secondary to intracerebral hemorrhage or subarachnoid hemorrhage with extension into the ventricular system. When IVH is large enough to impede normal cerebrospinal fluid (CSF) circulation, acute obstructive or non-communicating hydrocephalus can occur.[3] There are four mechanisms that explain the pathophysiology of this event: acute obstructive hydrocephalus, the mass effect exerted by the blood clot, the toxicity of blood breaking products on the adjacent brain parenchyma, and lastly, the development of a chronic hydrocephalus. It is thus obvious that the clearance of blood from the ventricles should be a therapeutic goal.[4] The primary objective of IVH treatment is to reduce increased intracranial pressure (ICP), limit hemorrhagic mass effect and associated edema thereby halt development of obstructive hydrocephalus by the prompt removal of irritant blood and blood products from the ventricular system. There is an association between Intraventricular blood volume and poor outcome. Patient with ventricular blood volume more than 20 ml in general had poor outcome.[5] But it is not always possible to measure intraventricular blood volume radiologically. Computed tomography scan with software is required to calculate intraventricular blood volume which is not always available. Simple and rapid measure of intraventricular hemorrhage volume are lacking. But Timothy et al.[6] developed 'The modified Graeb Score' (mGS). In their study they found mGS and IVH volume were highly correlated. Baseline mGS was predictive of poor outcome.

Hydrocephalus resulting from ICH is generally treated with external ventricular drainage (EVD) and it is one of the treatment option despite fatal compliance.[6,7,8] The clinical response to EVD and its effects on hydrocephalus are not known in detail. The efficacy of ventricular drainage can be evaluated by knowing the patients who will benefit from the treatment by clinical improvement and reversal of the hydrocephalus.[9]

Management of Intraventricular hemorrhage started with the conventional therapy which include emergency care and resuscitation of the patient. Patient should be treated in neurointensive care if possible with endotracheal intubation, mechanical ventilation where necessary. Sedatives, neuromuscular blocking agents that do not elevate ICP should be selected. Those who do not required ICU, care should be assured for control of ICP including resuscitation with intravenous fluids, placement of the head of bed at 30°, correction of fever with antipyretics, control of blood pressure, hyperglycemia and deep venous thrombosis prophylaxis, seizure prophylaxis.[10]

Although the conservative treatment is available but ventricular drainage, craniotomy and surgical evacuation of IVH, minimally invasive drainage of IVH have limited experience in the literature. Recent progress in neuroendoscopy allows minimally invasive surgery for patients with cerebral hemorrhage and use of technique for IVH can safely achieve reliable decompression and improvement of non-communicating hydrocephalus in acute phase.[11,12] Other option for treating IVH is EVD with administration of fibrinolytic agent, i.e.: r-tPA and urokinase (UK). Some authors show that administration of low doses of intraventricular UK in patients with IVH is safe with careful screening.[13,14] In most centers, EVD use remains at the discretion of the treating neurosurgeon while further decisions on medical and surgical treatment are guided by clinical decision making tools such as the ICH score.[15]

Considering all these information, the decision of EVD in the treatment of IVH with hydrocephalus has always been challenging to neurosurgeons. Accepted neurological deficit with quick recovery is the key concept of EVD. Conservative treatment has always been a choice to avoid surgical procedure but with the development of modern techniques and reviewing recent literature, it is difficult to establish proper treatment modalities for intraventricular hemorrhage. Due to the paucity of the relevant literature and lack of conclusive evidence to guide optimum treatment protocol, this quasi experimental study was designed to compare the outcome, assessing by modified rankin scale and Glasgow outcome scale of the patients undergoing external ventricular drainage or conservative treatment for spontaneous intraventricular hemorrhage.

Methods:

This was a quasi-experimental study conducted in the Department of Neurosurgery, Chattogram Medical College and Hospital, Chattogram, Bangladesh for a period of 1 year from July 2018 to June 2019. After detail history and clinical examination, CT scan of head, 150 consecutive patients were selected for this study. Based on inclusion and exclusion criteria, 25 patients were excluded among them 11 patients had GCS 3 with non reacting pupil, 7 patients needed surgical evacuation of haematoma and 5 patients legal guardian did not want to continue with the study procedure, 2 patient were dropped out due to not attend to follow up schedule and their contact numbers were switched off. So 125 patients with spontaneous intraventricular hemorrhage were enrolled to this study. Among them 56 patient's relative agreed to surgery who were accepted as case group and had EVDs. Remaining 69 patient's relative declined authorization for surgery and were accepted as control group and underwent conservative management. Modified graeb score was calculated from the CT scan and documented. On admission GCS score was recorded. In case group, all patients were treated with external ventricular drainage after resuscitation and proper counseling to legal guardian. In control, patients were managed conservatively.Patient presented with intraventricularhaemorrhage, either primary or secondary and presence of obstructive hydrocephalus was our inclusion criteria. Traumatic intraventricular haemorrhage, Intraventricular haemorrhage with ICH that requires surgical evacuation of haematoma, patients with GCS score 3 with non-reacting pupil and patient whose legal guardian does not intend to include in the study was excluded from study.

Results:

Both the groups were similar in terms of age and sex distribution. Overall mean age was around 60 years with age range from 15-85 years. More than three fourth of the patients in both group were from the age group of >50 years (73.83%). Male to female ratio was almost equal in both groups (p = 0.374).

There were no differences between EVD and no EVD groups regarding medical comorbidities. Most prevalent comorbidity among the patients of both groups was hypertension (p=0.151), followed by diabetes (p=1.0) and previous ischemic stroke (p=0.892) . Distribution of other predisposing factors and risk factors were also similar in both groups but these are not statistically significant.

Overall the most frequent symptoms in the studied patients were vomiting, followed by loss of consciousness, headache and convulsion. There were no significant differences between two groups regarding presenting symptoms. On the contrary, preoperative GCS score was significantly lower (p<0.001) and mGS was significantly higher (P=0.001) among the patients had EVD compare to the patients treated conservatively.

Baseline CT findings were similar in both groups (Table I). Majority of the patients in both groups had ICH with VE. Proportion of the patients had hydrocephalus on CT was 57.4% and 46.7% respectively in EVD and conservatively treated group respectively.

The overall correlation between baseline GCS score and mGS score is presented in the Figure 1 and it depicts that, as the mGS score increases the GCS score decreases. Moreover, there was increased likelihood of EVD requirement with decreasing GCS score and increasing mGS score.

Table-I

Baseline CT scan findings of the study participant (n=125) with spontaneous IVH with or without EVD

CT findings	Had EVD (n=56)	Treated conservatively (n=69)	p value
Type of hemorrhage			
Intraventricular hemorrhage	12 (19.1%)	7 (5.7%)	
Intracerebral hemorrhage with ventricular extension	41 (76.6%)	60 (91.7%)	0.095*ns
Subarachnoid hemorrhage with ventricular extension	3 (4.3%)	2 (1.7%)	
Hydrocephalus			
No	24 (42.6%)	36 (53.3%)	0.268*ns
Yes	32 (57.4%)	33 (46.7%)	

*p values were derived from Chi-square test, ns = Not significant

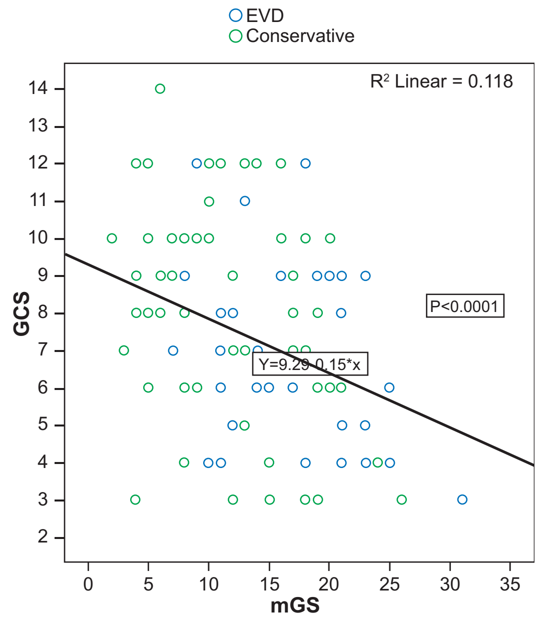


Fig.-1: *A plot comparing baseline mGSscore and GCS score.*

To compare the outcome of EVD and conservative treatment following spontaneous IVH, GOS score were assessed at discharged and after 3 months. Among the patients underwent EVD at discharge most of the patients (93.3%) were either severely disable (p=0.006) or moderately disable (p=0.004). On the contrary, after 3 months majority of the patients (81.5%) were either moderately disable or had mild disability. These changes were statistically significant. Besides GOS score, Modified Rankin Scale score (mRS) was also used to evaluate the functional outcome after 3 months among the study patients. Table **II** indicate that, severe disability was significantly reduced (from 50.0% to 3.7%) after 3 months among the patients underwent EVD.

There was no significant difference in survival curves between the groups (Log Rank p=0.628). In EVD group 59.6% patients survived for at least 3 months following onset of symptoms and the corresponding value in conservatively treated group was 56.7%.

Table-II

Change in mRS score from discharge to after month 3 of the patients with spontaneous IVH with EVD

Modified Rankin scale score	At discharge(n=30)	At 3 month (n=27)	p value*
0 (No symptoms)	0 (0%)	2 (7.4%)	0.219^{ns}
1 (No significant disability)	1 (3.3%)	2 (7.4%)	0.598^{ns}
2 (Slight disability)	1 (3.3%)	2 (7.4%)	0.598^{ns}
3 (Moderate disability)	2 (6.7%)	7 (25.9%)	0.070^{ns}
4 (Moderately severe disability)	10 (33.3%)	12 (44.4%)	0.426^{ns}
5 (Severe disability)	15 (50.0%)	1 (3.7%)	<0.001^{s}
6 (Dead)	1 (3.3%)	1 (3.7%)	1.0^{ns}

*P values were derived from either Chi-square test or Fisher's Exact test as appropriate.ns = not significant, s = significant

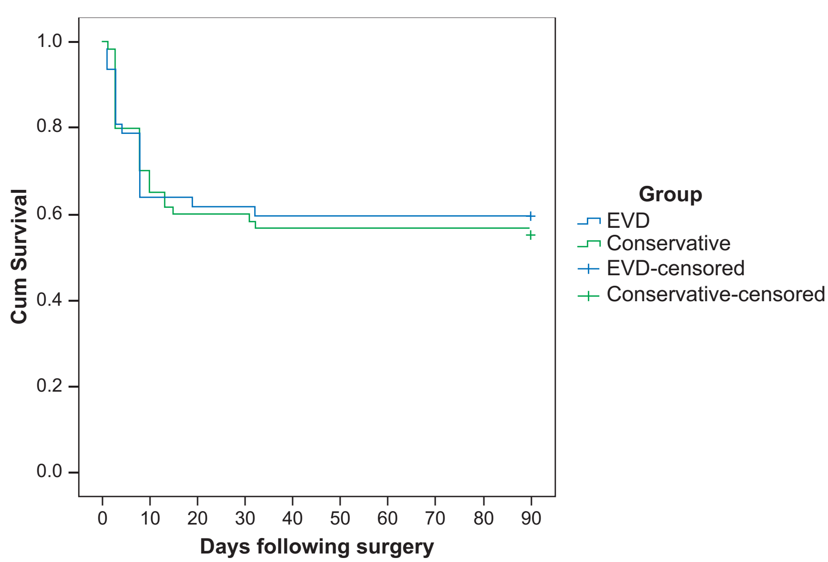


Fig.-2: *Comparison of cumulative survival in two groups during 3 months following surgery or conservative management*

Treatment modality had no effect on survival (p=0.635). However, patients who died within 90 days of their IVH were significantly older, had lower GCS score and higher mGSscore than the patients who survived. Patients with hydrocephalus died significantly more than the patients without hydrocephalus.(Table III)

Binary logistic regression analysis was done to determine the independent predictor of 90 days mortality following spontaneous IVH. The variables which had significant association in univariate analysis (Table III) were entered in the model. Table IV depicts that, after adjustment patients who were treated conservatively were 3.98 times more likely to die within 90 days than the patients who had EVD. Other independent predictors were higher age, lower GCS at admission and presence of hydrocephalus on CT.

Binary logistic regression analysis was done to determine the independent predictor of favorable outcome at 90 days following spontaneous IVH. The variables which had significant association in univariate analysis (Table III) were entered in the model. Table V depicts that, after adjustment patients treatment modalities either EVD or conservative did not revealed as an independent predictor. Age, GCS score at admission and hydrocephalus were the independent predictors of 90 days favorable outcome.

Treatment modality had no effect on functional dependency among survivors at 3 month after the event (p=0.211). However, patients who had functional dependency had significantly lower GCS than the patients who were functionally independent among the survivor (p<0.001).Binary logistic regression analysis was done to determine the independent predictor of functional dependency at 90 days following spontaneous IVH among the survivors (Table VI). It depicts that, after adjustment patients treatment modalities either EVD or conservative did not revealed as an independent predictor. Only GCS score at admission was the independent predictors of 90 days functional dependency.

Table-III

Association of different predictive variables with 90 day mortality of the study participants (n=125) with IVH

Variables (unit)	Survived (n=77)	Died (n=48)	p value
Age (years)			
Mean ±SD	55.93±15.40	65.00±10.89	0.001^{†s}
Sex			
Male	30 (49.2%)	23 (50.0%)	0.931^{*ns}
Admission GCS			
Mean ±SD	7±2	5±1	<0.001^{†s}
Admission mGS			
Mean ±SD	12±5	15±7	0.015^{†s}
Hydrocephalus			
Present	17 (27.4%)	38 (84.4%)	<0.001^{*s}
Hemorrhage type			
IVH	10 (16.1%)	3 (6.7%)	0.246^{*ns}
ICH with VE	51 (82.3%)	40 (88.9%)	
SAH with VE	1 (1.6%)	2 (4.4%)	
Group			
With EVD	26 (45.9%)	21 (41.3%)	0.635^{*ns}
Without EVD	34 (54.1%)	26 (58.7%)	

*p values were derived from Chi-square test; †: p values were derived from independent sample t test.; ns = not significant; s= significant

Table-IV

Independent predictor of 90 day mortality of the study participants (n=125) with IVH

Variables	Odds ratio (OR)	95% C.I.for OR		p value
		Lower	Upper	
Treated conservatively	3.982	1.300	12.194	0.016^{s}
Age in years	1.066	1.024	1.110	0.002^{s}
Female	0.705	0.268	1.858	0.480^{ns}
GCS score on admission	0.538	0.398	0.726	$<0.001^{s}$
mGS score on admission	1.072	0.985	1.168	0.108^{s}
Hydrocephalus	12.46	5.24	21.32	$<0.001^{s}$

ns = not significant, s = significant

Table-V

Independent predictor of favorable outcome after 3 months of the study participants (n=125) with IVH

Variables	Odds ratio (OR)	95% C.I. for OR		p value
		Lower	Upper	
Treated conservatively	0.404	0.128	1.273	0.122^{ns}
Age in years	0.944	0.906	0.983	0.005^{ns}
GCS score on admission	2.03	1.45	2.85	$<0.001^{s}$
Hydrocephalus	0.114	0.038	0.338	$<0.001^{s}$

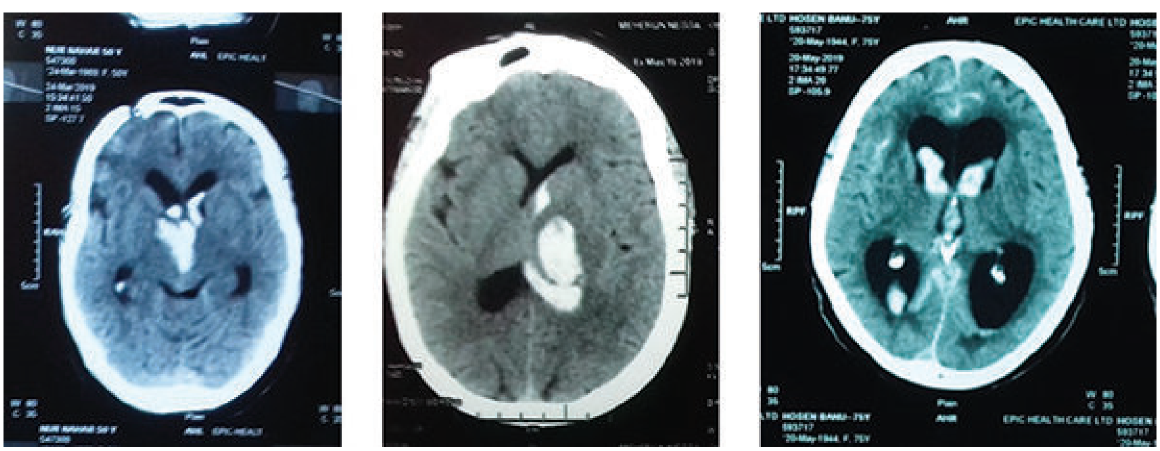
ns = not significant,s = significant

Table-VI

Independent predictor of functional dependence (mRS>2) of the 60 survivors with IVH after 3 months

Variables	Odds ratio (OR)	95% C.I. for OR		p value
		Lower	Upper	
Treated conservatively	1.427	0.271	7.501	0.675^{ns}
Age in years	1.043	0.995	1.093	0.075^{ns}
GCS score on admission	0.598	0.428	0.836	$<0.001^{s}$
Hydrocephalus	0.910	0.204	4.056	0.901^{ns}

ns = not significant,s = significant



A B C

Fig.-3: *Type of Intraventricular hemorrhage according to CT scan. A. Intraventricularhemorrhage ; B. Intracerebral hemorrhage with ventricular extension ; C. Subarachnoid hemorrhage with ventricular extension*

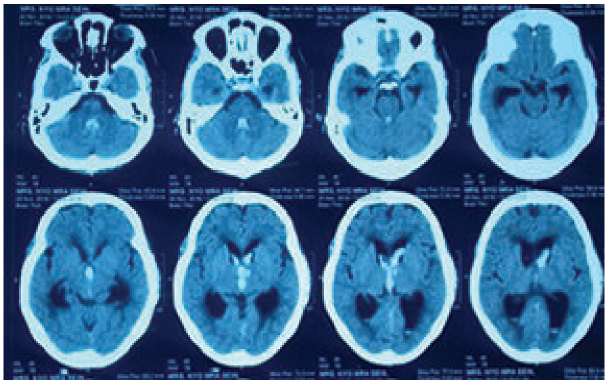


Fig.-4: *Pre-operative CT scan of spontaneous IVH with hydrocephalus*

Fig.-5: I*ncision at Kocher's point*

Fig.-6: *Burr hole and insertion of external ventricular drainage*

Fig.-7: *Ensuring cerebrospinal fluid drainage*

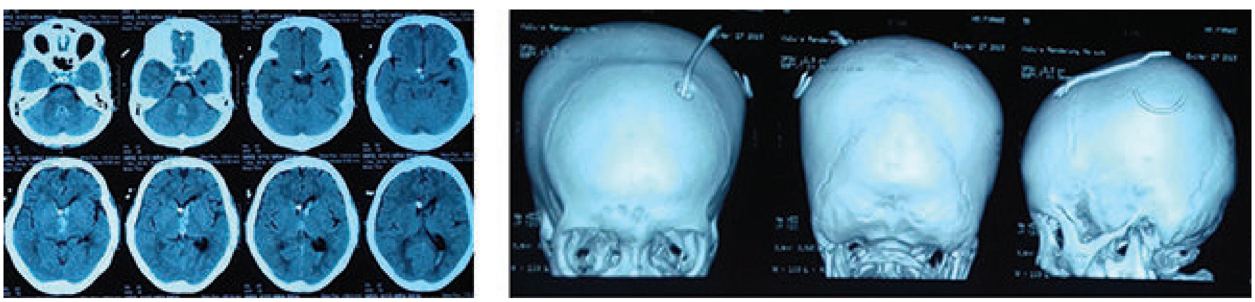


Fig.8: *Post-operative CT scan same patient with EVD in situ*

Discussion:

We hypothesized that, EVD improves the outcome in patient of spontaneous IVH significantly more than the outcome achieved by conservative treatment. The study revealed that, after adjustment for known predictors of IVH outcomes EVD had significantly reduced 90 days mortality compared to conservative treatment but had similar effect in terms of favorable outcome (GOS>3) after 90 days. Our finding was in accordance with the findings of a recent RCT by Bhaskar et al.[16] where mortality following medical management for IVH was 100% compared to 75% in surgically managed group (p=0.02). In the present study, in unadjusted analysis EVD utilization was not associated with significant reduction of mortality (p=0.635); however, in the adjusted analysis the odds ratio showed a significant protective effect of EVD utilization in IVH (OR: 3.98; 95% CI: 1.3-12.94; p=0.005). Similar observation was observed by Brendan et al.[7,17] Although various treatment protocols including supportive medical treatments, steroids, antihypertensive agents, and EVD methods are in use, there is still controversy surrounding the effects of these methods[14]. Considering that EVD was conducted primarily in those who had poor consciousness levels with significant hydrocephalus, which might be associated with a poor prognosis, it is difficult to judge the effects of the treatment modality by itself. In the present study, the patients underwent EVD had significantly poor consciousness level and more hydrocephalus compared to patients treated conservatively. To assess the independent impact of treatment modalities in our binary logistic regression analysis it was revealed that, after adjusting the other predictive variables (age, GCS, hydrocephalus) patients who were treated conservatively were 3.98 times more likely to die within 90 days than the patients who had EVD. On the contrary EVD had similar effect in terms of favorable outcome (GOS >3). Recently Lee et al.[18] reported that, many of their patients received EVD, of whom the majority (78%) displayed unfavorable outcomes (GOS <4). Interestingly, Liu et al.[19] retrospectively investigated the discharge outcome of EVD in severe IVH with a control group matched by intraventricular hemorrhage volume and age received conservative treatment. Their findings demonstrated that, the mortality rate of treatment group was 13.3% (10/75), much lower than that of the control group 41.1% (31/75, *P*<0.001). Considering the result of present study and the above mentioned studies it could be stated that, compared with conservative treatment, EVD treatment significantly improved the outcome of patients with IVH.

In the absence of specific treatment (i.e., EVD), IVH irrespective of etiology is associated with a 78 % risk of death and a 90 % risk of poor outcome[20]. In our study, the overall mortality was 43.9%, with 68% of these occurring within the first 48 hours. Mortality correlated with age, admission GCS score, and presence of acute hydrocephalus. This was in agreement with the findings of El-Saadany et al.[21,22] who reported the overall mortality was 44.4%, with 50% of these occurring within the ûrst 48 hours, but much higher than that of the Lee et al.[18] who reported the overall mortality rate was 19%. The probable reason for this dissimilarly could be explained by much lower baseline GCS of the patients of the present study in comparison to that of the Lee et al.[18] Among the survivors at 3 months majority of them (56.7%) had moderate disability and 36.7% had mild disability. Similarly Lee et al., (2017) reported that, majority of survivors (80%) had no deficits or mild deficits (GOS ≥4). The reported rate of poor outcome following a large series of intracerebral hemorrhages ranges from 49% to 78%[22-25]. Therefore, the neurological prognosis of PIVH is likely superior to that of intracerebral hemorrhage. This relatively favorable neurological course for PIVH might be associated with comparatively little brain parenchymal damage.

Within the IVH literature, indications for EVD use is compelling: Nieuwkamp et al.[20] demonstrate a 26% decrease in IVH mortality associated with EVD utilization (78% vs. 58%) through a meta-analysis, but no difference in functional outcomes (poor outcomes 90% vs. 89%).Nieuwkamp et al.'s[20] findings are consistent with the results of the present analysis, demonstrating trends toward positive mortality benefit without overall positive functional outcomes benefit. Logistic regression analysis was done to determine the independent predictor of functional dependency after 3 months following spontaneous IVH among the survivors. It revealed that, after adjustment patients treatment modalities either EVD or conservative did not revealed as an independent predictor. Only GCS score at admission was the independent predictors of 90 days functional dependency (mRS>2). This discrepancy between mortality and functional outcome and morbidity may suggest that there are other concomitant physio-pathological mechanisms that influence the final outcome other than initial age, GCS, hydrocephalus.Nieuwkamp et al.[20] in their meta analysis reported that, in cases of SAH with IVH, the prognosis seems even more dismal, with risks of death and severe handicap of 84% and 93%, respectively, in patients treated without EVD and risks of 67% and 87 %, respectively, in patients treated with EVD. In the present study this trend is supported but probably due to small representation of such cases might prevent us to get a significant association. The majority of our patient, 79 (73.83%) were from > 50 years age group and 28 (26.16%) patient from ≤50 years age group whereas study done by Lee et al.[18] found among 112 patient, 55 (49%) were from >50 years age group and 57 (51%) were from ≤50 years age group. Male to female ratio was almost equal in our study (49.53% male and 50.46% female) which is consistent with Nieuwkamp et al.[20] study where in eight reported study, they found 51% were man. But Lee et al.[18] found 57% male and 43% female. But these demographic characteristics are not statistically significant in our study (p= 0.374).

We found that natural course of the IVH is one of the main reason for mortality. We observed five causes of death among the patients. Raised ICP is one of the reason that explained brain herniation and death in 2 (4.25%) patients in EVD group whereas 12 (23.40%) death in conservatively managed group. Other causes are dyselectrolytaemia [7(14.89%) vs. 6 (12.76%)], aspiration pneumonia [5(10.63%) vs. 7(14.89%)], septicaemic shock [4(8.51%) vs. 1 (2.12%)] and rebleeding [3(6.38% vs. 1 (2.12%)]. But we failed to compare these data with other literatures as there is very limited resource available that discussed cause of mortality of IVH patient although Nieuwkamp et al.[20] and El-Saadany et al.[21] discussed 78 % risk of death irrespective of aeitology of IVH.

Granting the prognosis of IVH was poor, compared with conservative treatment, EVD treatment significantly improved the outcome of these patients. To our knowledge and based on our review of the literature, no previous reports have been published that compare the outcome of EVD with conservative treatment following IVH in our context. Strength of our study is that with our limited resource and time we were able to enrol a reasonable number of patients and to observe their outcome for a reasonable time period. We hope that, our findings will be helpful for the neurosurgeon of this country in their decision making during management of IVH cases.

Conclusion:

EVD is an effective interventional modality in the armamentarium of the neurosurgeon to rapidly reduce life threatening mass effect. In multivariate adjusted analyses, EVD use showed a trend towards lower overall mortality, with significantly lower mortality in patients with hydrocephalus and lower initial GCS. There was no benefit to improved morbidity or reduced functional dependency patients receiving an EVD. This data can be used to develop evidence-based protocols for EVD use. However, a randomized study recruiting a large number of patients is required to clarify our findings and to establishing a protocol and a recommendation, which can assist in the formulation of universally acceptable guidelines.

Limitations of the study:

It was a single center study. The number of patients enrolled in this study was relatively small. We could not provide ICU support to all critical patients. Follow up after discharge was short, a longer follow up might bring a better result. Different surgeons with different treatment preferences undertook the patient's care, adding to between patient variability. Other immeasurable underlying differences between the groups may have confounded our results.

Conflict of Interest:

None to disclose.

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