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RESEARCH ARTICLE

"Do not cause harm" by Advising Clot Removing Surgery for Moderate to Large Size Deep Supratentorial Intracerebral Hemorrhage (SICH): A Randomized Study

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ABSTRACT

Background: Deep seated supratentorial spontaneous intracerebral hemorrhage (ICH) of large size (> 30 ml size) has poor outcome and high mortality even after best treatment. Clinicians have inclination towards surgical intervention with clot removal surgery to improve outcome. In available literature only few articles available which included large size deep seated supratentorial ICH patients to assess effect of surgical techniques.

Aims and objectives: To compare outcome of clot removing surgery versus best medical treatment in patients with large (> 30 ml) deep supratentorial ICH.

Methods: Study design was experimental study (randomized control), Total 60 patients were planned to enrolled in two groups; group 1 – subjected to surgical treatment; Group 2 – subjected to conservative treatment. Simple random sampling using computer generated randomized table was applied for sampling. All patients aged above 18 years, presenting with supra-tentorial SICH within 6 - 72 hours of onset and having hematoma volume of 30 - 80 cc and ICH score of 2 or more were selected.

Statistical analysis was done through IBM SPSS Version 25. Both frequency and crosstab analysis was done to find out any significant association of various clinical parameters with mortality or functional outcome.

Results: Need for Intensive care unit and total duration of hospital stay was significantly high in surgical group ($p = 0.000$ and 0.019). The mortality and neurological outcome was not statistically different between two groups.

Conclusion: Best medical treatment is better and cost effective option than surgical treatment in patients with large deep seated supratentorial ICH.

Introduction

Spontaneous intracerebral haemorrhage (SICH) accounts for 10-30% of all strokes and is associated with high mortality (up to 40%) or severe disability in most of the survivors [1]. For treatment purpose patients of SICH can be broadly classified into two types supratentorial or infratentorial and supratentorial further classified into superficial (lobar) and deep (basal ganglia/thalamus). Main stay of medical treatment is management of hypertension, raised intracranial pressure, prevention of re-bleeding or hematoma expansion and seizure control. Surgical treatment of SICH can be in form of clot removal surgery (conventional or minimally invasive techniques), Decompressive craniotomy and extra-ventricular drainage/shunt surgery depending on patient's profile [2].

The rationale for the clot removal surgery in SICH is to reduce the impact of primary and secondary brain injury. Clot removal surgery commonly recommended in patients of infra-tentorial SICH when size of haemorrhage is more than 3 centimetres in diameter [3]. Although, the recommendation is based on observational studies and surgery is found effective in preventing death but no effect on disability [4].

In supratentorial hemorrhage none of the definitive medical or surgical treatment is found effective in alteration of outcome in different trials. Patients with large supratentorial SICH are frequently subjected for surgical treatment but the type and time for surgery is controversial especially for supratentorial SICH [1]. In patients with supra-tentorial SICH, evidences collected from 17 randomized controlled trials addressing surgical evacuation of supra-tentorial SICH, other large studies and meta-analysis suggested neutral results on primary outcomes [5]. Although, subgroup analysis in these studies suggested that patients with large and superficial hematoma with GCS (Glasgow Coma Scale) of 10-13 on admission might have better outcome from surgical treatment [6].

Most studies on supratentorial ICH included both superficial and deep haemorrhages and we could not found any randomized study which has included only deep (ganglionic or thalamic) hemorrhage of > 30 ml size for the surgical versus medical treatment. One single center observation study on 60 patients of hypertensive basal ganglia hemorrhage showed improved outcome with surgical treatment but there was no control group to compare [7]. Thus the current study was done in selected Indian patients of large (> 30 ml) deeply situated supra-tentorial SICH to compare 3 months outcome of patients subjected to medical verses surgical (clot removal) treatment groups.

Methods

The current study had approval of institutional ethical committee after obtaining patients consent for the data collection on SICH patients. Study design was experimental study (Randomized control). Total 60 patients were planned to enrolled in two groups; group 1 – subjected to surgical treatment; Group 2 – subjected to conservative treatment. Simple random sampling using computer generated randomized table was applied for sampling.

All patients aged above 18 years, presenting with supra-tentorial SICH having hematoma volume of 30 - 80 cc and ICH score of 2 or more were subjected to surgery at the earliest after randomization. Surgery was done between 6 hours to 72 hours of onset.

Hematoma volume was measured on CT (computerized tomography) Scan by using formula of ('a' x 'b' x 'c')/2, where "a" was greatest diameter, "b" was longest perpendicular diameter to "a", and "c" was number of axial slices having parenchymal hemorrhagic lesion multiplied by slice thickness. Intracerebral hemorrhage (ICH) scoring was done according to standard method [8]. Patients with secondary intracerebral hemorrhage were excluded.

Following enrolment, demographic information of all patients was recorded in standard Proforma. Along with it, following parameters were recorded at the time of admission, date and time of first symptom, date and time of hospital admission, known hypertension or not, past usage of blood thinners before ICH, Glasgow coma scale (GCS) at the time of admission, systolic and diastolic blood pressure, random blood sugar, hematoma volume on CT scan, ICH score, presence or absence of mass effect on first CT scan after admission, The best conservative management of SICH started soon after admission and randomization. The patients in surgical treatment group were posted for surgery immediately after randomization as early as possible.

Surgical intervention included craniotomy and clot evacuation (by minimal operative injury method). After medical or surgical treatment, following parameters were recorded to assess outcome; long ICU care (> 7 days) required or not, Total duration of hospital stay, end result (discharged or death), and level of disability (decided by Barthel Index) at 90 days. Final analysis was done after 90 days of the follow-up.

Primary outcome was to see the difference in mortality rates among two groups and secondary outcome was to assess the functional outcome of patients surviving in two groups. Statistical analysis was done through IBM SPSS Version 25. Both frequency and crosstab analysis was done to find out any significant association of various clinical parameters (duration of illness, level of SBP & DBP at the time of admission, RBS at admission, GCS at admission and ICH score at admission) with mortality or functional outcome. Significant association was analysed by chi square test and the value of < 0.05 was considered to be significant.

Results

Total 60 patients (30 in each arm) were enrolled over a period of one year, with mean age of 55.6 years (range 30 -89 years) and 38 (62.3%) were male. Basic characteristics of patients at the time of admission, in two groups are shown in Table 1. It is clear that there is no significant difference in basic parameters of patients in two groups at the time of admission.

Parameters	Surgical treatment group (N = 30)	Medical treatment group (N = 30)	P value
Age less than 60 years Age More than 60 years	21 (70%) 9 (30%)	17 (56.67%) 13 (43.33%)	0.211
Male Female	21 (70%) 9 (30%)	17 (56.67%) 13 (43.33%)	0.211
Duration less than 12 hours More than 12 hours	22 (73.3%) 8 (26.7%)	20 (66.67%) 10 (33.33%)	0.389
Known hypertensive Not a known hypertensive	13 (43.33%) 17 (56.67%)	17 (56.67%) 13 (43.33%)	0.219
GCS < 8 GCS > 9	13 (43.33%) 17 (56.67%)	8 (26.7%) 22 (73.3%)	0.139
SBP > 160 mmHg on arrival SBP < 160 mmHg on arrival	14 (46.67%) 16 (53.33%)	13 (43.33%) 17 (56.67%)	0.5
DBP > 90 mmHg on arrival DBP < 90 mmHg on arrival	19 (63.3%) 11 (36.7%)	24 (80%) 6 (20%)	0.126
RBS > 200 mg/dl on arrival RBS < 200 mg/dl on arrival	6 (20%) 24 (80%)	9 (30%) 21 (70%)	0.276
ICH Score 2 ICH Score 3 ICH Score 4	11 (36.7%) 16 (53.3%) 3 (10%)	15 (50%) 10 (33.33%) 5 (16.67%)	0.284
Prior use of blood thinner – yes Prior use of blood thinner – no	22 (73.3%) 8 (26.7%)	22 (73.3%) 8 (26.7%)	0.614

GCS – Glasgow Coma Scale, SBP – Systolic Blood Pressure, DBP – Diastolic Blood Pressure, RBS – Random Blood Sugar, ICH – Intracerebral Hemorrhage

Table 1: Baseline characteristics of patients in surgical and medical groups

After surgical or medical treatment (according to group allocation), patients were followed in either ICU/Ward till death/discharge. The findings of parameters recorded for primary and secondary outcomes are shown in Table 2. Over all findings suggest that there was significantly high requirement of ICU care and longer hospital stay in surgical treatment group without any significant change in outcome. Two third patients in each group were having poor outcome at the end of 3 months.

Parameters	Surgical treatment group N=30	Medical treatment group N =30	P value
ICU Required for > 7 days– Yes	29 (96.7%)	8 (26.7%)	0.000
ICU Required for > 7 days– No	1 (3.3%)	22 (73.3%)	
Total hospital stay > 2 weeks	20 (66.67%)	11 (36.7%)	0.019
Total hospital stay < 2 weeks	10 (33.33%)	19 (63.3%)	
End result – discharge	23 (76.67%)	24 (80%)	0.5
End result – in hospital death	7 (23.33%)	6 (20%)	
Barthel index at 90 days			
0 – 20 (worst outcome)	8 (26.7%)	7 (23.3%)	0.726
21 – 60	10 (33.3%)	13 (43.4%)	
61 – 90	12 (40%)	10 (33.3%)	
91 – 99 (best outcome)	0 (0%)	0 (0%)	
Glasgow outcome scale (90 days)			
1 (death)	8 (26.7%)	7 (23.3%)	0.707
2 (vegetative)	0 (0%)	0 (0%)	
3 (severe deficit)	13 (43.4%)	16 (53.4%)	
4 (moderate deficit)	7 (23.3%)	4 (13.3%)	
5 (good recovery)	2 (6.6%)	3 (10%)	
Neurological status in 90 days			
Deteriorated/died	8 (26.7%)	7 (23.3%)	0.542
Remain same after discharge	8 (26.7%)	12 (40%)	
Improved after discharge	14 (46.6%)	11 (36.7%)	

ICU – Intensive Care Unit

Table 2: Outcome parameters of patients in surgical and medical treatment groups

Further subgroup analysis was done on the patients having GCS > 9 (GCS < 8 were excluded) to see the outcome of surgical versus medical treatment as shown in Table 3. Even subgroup (GCS 9 and above) also showed that no significant change in primary and secondary outcome among two groups.

Parameters	Surgical treatment group N = 17	Medical treatment group N = 22	P value
End result – discharge	15 (88.2%)	21 (95.5%)	0.402
End result – in hospital death	2 (11.8%)	1 (4.5%)	
Barthel index at 90 days			
0 – 20 (worst outcome)	2 (11.8%)	1 (4.5%)	0.104
21 – 60	3 (17.6%)	11 (50%)	0.094
61 – 90	12 (70.6%)	10 (45.5%)	0.183
91 – 99 (best outcome)	0 (0%)	0 (0%)	
Glasgow outcome scale (90 days)			
1 (death)	2 (11.8%)	1 (4.5%)	0.259
2 (vegetative)	0 (0%)	0 (0%)	0.888
3 (severe deficit)	6 (35.2%)	14 (63.6%)	
4 (moderate deficit)	7 (41.2%)	4 (18.2%)	
5 (good recovery)	2 (11.8%)	3 (13.5%)	
Neurological status in 90 days			
Deteriorated/died	2 (11.8%)	1 (4.5%)	0.665
Remain same after discharge	7 (41.2%)	11 (50%)	0.784
Improved after discharge	8 (47%)	10 (45.5%)	

GCS – Glasgow Coma Scale

Table 3: Outcome parameters of patients in surgical and medical groups with GCS > 9

Discussion

"Do not harm" is Hippocratic Oath of physician is important to remember while deciding for the best treatment plan [9]. Our data suggests that in deep supra-tentorial SICH patients will have more expenditure due to surgery cost, ICU stay and longer hospital stay without any extra benefit in outcome. Thus hematoma evacuation surgery in deep supra-tentorial SICH is not good option and patients should be given best medical treatment available.

One systemic review by Sondag et al 2020, focused on the surgical treatment in supra-tentorial SICH and had concluded that surgery can be beneficial if done early and with minimally invasive techniques [5]. Total 21 studies included in this review with 2091 patients in surgical arm and 2054 in medical arm. In this systemic review only four studies had included patients of deep hemorrhage only including thalamic hemorrhage along with superficial supratentorial ICH. In our study about 13% patients were pure thalamic hemorrhage and rest were having either putaminal or mixed type of deep hematoma. First study by Zuccarello M et al [10] included patients with hematoma volume of > 10 cubic cm and performed surgery in 3 hours of randomization. The primary outcome was percentage of patients achieving GOS > 3, and author showed that 56% of surgical group patients achieved GOS >3 as compared to 36% in medical treatment group (p=0.04). In our study almost same numbers (76% in medical group vs 73% in surgical group) had achieved GOS > 3. Since in current study we had taken patients with larger size (30-80 cubic cm) and surgery within 12 hours of randomization so results were not comparable. Small number of patients, inclusion of small size hemorrhage and superficial lobar hemorrhage might contribute to better outcome in the Zuccarello M study. The second study in above mentioned systemic review was by Juvela S et al in 1989 included 58 patients and this study similar to our findings author concluded that no benefit from surgical treatment [11]. Third study by Auer LM et al 1989 [12], concluded that The outcome of surgical patients with putaminal or thalamic hemorrhage was no better than for those with medical treatment; however, there was a trend toward better quality of survival and chance of survival in the operated group. The last study on deep ICH included in systemic review was by Luo JB et al (2008), included seventy-five patients with mild cerebral hemorrhage (10-30 ml) were randomly divided into two groups for aspiration treatment with minimally invasive directional soft tube placement (minimally invasive group, n=36) and conservative treatment (medication group,

n=39) [13]. Compared with conservative treatment, the minimally invasive treatment with soft tube placement can significantly shorten the hospital stay, promote neurological function recovery, lower the mortality rate, and reduce the cost of hospitalization.

European guidelines 2006 recommended that if hematoma is superficial and not reaching to deep basal ganglia, or there is deterioration in consciousness then surgery can be considered (Level C). European does not recommend surgery in deep seated hemorrhage [14]. On the other hand Japanese guidelines 2009 recommended evacuation of putaminal hematoma if volume is > 31 ml with moderate neurological findings and evidence of severe mass effect. For thalamic hemorrhage Japanese guidelines recommended for no hematoma evacuation required [14].

The role of clot removal surgery in supratentorial ICH, Two trials STICH & STICH II were designed to answer the question whether surgical treatment has benefit in supratentorial ICH [15, 16]. Both STICH and STICH II had shown no significant change in outcome after surgery in supratentorial ICH. The STICH II trial also confirm that early surgery has no role in superficial supra-tentorial spontaneous hemorrhages also as 59% of surgical treatment group and 62% patients of medical group had unfavorable outcome [16]. One recent meta-analysis on pooled patients of STICH, STICH II and STICH (Trauma), concluded that the data from 1541 patients of spontaneous ICH with an intermediate GCS at presentation (GCS of 9-12) may have benefits from surgery while higher or lower GCS may not [17]. Although, in our study patients having GCS of more than 9 at the time of admission failed to show any extra benefit from surgery. Therefore, altogether evidences from large trials showed that conventional clot removal surgery in deep supratentorial ICH is not having any impact on survival or neurological outcome.

In recent years, after failure of conventional clot removal surgery, few research centres had tried non-conventional methods of surgery including minimally invasive surgery in deep supratentorial ICH. In one Chinese study (n= 377) patients of basal ganglia ICH (size 25-40 ml) were randomized to either minimally invasive surgery (Craniopuncture and needle aspiration) or conservative treatment. At the end of 2 weeks and 3 months patients of surgical group showed significant neurological improvement without any change in mortality [18]. But the another large trial on catheter evacuation of hematoma followed by irrigation by alteplase (MISTIE III) found no clear benefit however found better neurological outcome in patients with < 15 ml sized hematoma [19]. Moreover, results of ongoing ENRICH trial is awaited to see the role of minimal invasive surgery in supra-tentorial ICH [20]. Till now it seems that better surgical results with minimally invasive techniques are limited to small size (10-30 ml) hematoma not in > 30 ml size of lesions.

Final statement by the AHA/ASA guidelines of ICH (2015) on all types of surgeries suggested clearly that; 1) for supra-tentorial hemorrhage usefulness of surgery is not established; 2) policy of early hematoma evacuation is not clearly beneficial; 3) evacuation in deteriorating patients can be considered as a life saving procedure without any change in neurological outcome ; and 4) effectiveness of minimally invasive clot evacuation with stereotactic or endoscopic aspiration with or without thrombolytic usage is uncertain [21]. Another recent review of all studies on clot removal and minimally invasive surgery in supratentorial ICH also concluded that no benefits of surgical treatment in neurological recovery and in lowering of death rates [22]. The major explanation for lack of benefit from surgical clot removal in supra-tentorial hemorrhage might be; 1) early onset of secondary injury cascade; and 2) secondary injury produced by surgery itself, leading to poor neurological recovery [23].

Thus, if we have to follow the rule **"To do Good and not to do harm"** then best medical treatment is a better option to deep supra-tentorial SICH patents as compared to surgery. If we analyze all currently existing evidences of randomized trials, meta-analysis and systemic reviews all types of clot removing surgeries (conventional or minimal invasive surgery) have no impact on mortality or morbidity after deep supratentorial ICH of > 30 ml. In future there might be evolution of minimally invasive techniques of surgery which can improve outcome of patients in deep supratentorial ICH.

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