Effectiveness of Coagulation Profile as a marker for blood loss in Elective Craniotomy patients

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Author’s Contribution
1 Conception of study
2 Experimentation/Study conduction
3 Analysis/Interpretation/Discussion
2.3 Manuscript Writing
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Abstract

Objective: The objective of this study is to determine the role of preoperative coagulation studies in predicting intraoperative blood loss, in patients undergoing elective craniotomy in our tertiary hospital setting.

Materials and Methods: This was a Quasi-experimental study conducted at the Department of Neurosurgery, Aga Khan University Hospital Karachi for the duration of 6 months. A non-probability consecutive sampling technique was employed. All admitted neurosurgery patients for elective craniotomy were enrolled and followed as part of the study. Laboratory values including baseline workup e.g. Complete Blood count, PT, activated Partial Thromboplastin Time (aPTT), Internationalized Ratio (INR) were taken preoperatively and postoperatively. A predesigned questionnaire for the collection of data was used, which included demographics and clinical information. Approval from the university ethical committee was obtained before starting the study. Data was entered and analysed into SPSS version 21. Effect modifier age, gender, co-morbidities, type, and duration of surgery, were controlled through stratification. Post-stratification paired t-test and independent-sample t-test were applied using P ≤ 0.05 as significant.

Results: In this study 57 patients who underwent elective craniotomy were included to assess the mean blood loss and to compare mean blood loss in patients with normal and deranged coagulation profiles. The mean age of patients included in the study was 39.36±13.94 years with 43 (75.4%) males and 14 (24.6%) females. The mean preoperative haemoglobin level amongst all patients turned out to be 14.10±3.98 gm/dl. The postoperative haemoglobin level showed a decrease with a mean of 12.68±3.98 gm/dl. Therefore the mean difference calculated between pre and post-operative haemoglobin levels turned out to be 1.42±0.99 gm/dl.

Conclusion: It is to be concluded that significant change was found in preoperative and post-operative Haemoglobin levels in patients undergoing elective craniotomy. There was also a highly significant difference in blood loss between patients having a normal versus deranged coagulation profile. However, there is a need to conduct more studies using a large sample size with multiple study sites in Pakistan to validate these results.

Keywords: Elective Craniotomy, coagulation profiles.
Introduction

One of the leading intraoperative complications is haemorrhage, and has significant implications in the outcome of the patient regardless of the underlying disease process. For bleeding to stop, either the continuity of the vessel has to be restored or the coagulation cascade has to kick in and plug the defect. Usually, the intraoperative blood loss is secondary to surgical defect but an inherent defect in coagulation may contribute as well. In one study, $81,942,000 were spent yearly on the pre-operative investigation of coagulation profile in neurosurgical patients. On average, the coagulation profile (PT/PTT) costs Rs. 1890/-(Rs18.62) in major cities of Pakistan. Pre-operative blood investigations are a general prerequisite before any surgical procedure; including the coagulation parameters which intuitively does make sense, rather than screening only the high risk or at risk patients, this is because even slight intra-operative or postoperative bleed may have devastating effects, therefore overemphasis on pre-operative coagulation profile for every patient undergoing craniotomy leads to exploitation and at times may produce false-positive results.

PT and aPTT are the basic measuring tools for evaluating a coagulation cascade. Although derangement of these parameters does equate well with spontaneous intracranial bleed, their value for assessing the risk of post-operative haemorrhage is not known. Universally, neurosurgeons advise Prothrombin Time (PT) and activated Partial Thromboplastin Time (aPTT) on all patients before operation. The significance and cost-effectiveness of this practice have not been questioned as such. In various other fields of surgery, studies have been conducted to look for the importance of pre-operative screening of PT, aPTT, but only a few such studies are available for neurological patients. Dutzmann et al. from Germany showed that this practice of pre-operative screening with PT and aPTT in elective neurosurgical patients is futile. B. Schramm et al. in a retrospective study over a year, showed similar results.

No previous studies have specifically evaluated the neurosurgical population, strictly speaking about craniotomy patients in Pakistan. This study aims to determine the effectiveness of pre-operative coagulation studies in patients undergoing elective craniotomy in our tertiary setting.

Materials and Methods

This was a Quasi-experimental study conducted at the Department of Neurosurgery, Aga Khan University Hospital Karachi. A non-probability consecutive sampling technique was employed. The inclusion criteria comprised of patients having either gender with ages between 18 years to 60 years undergoing elective craniotomy for intracranial space-occupying lesions e.g. meningiomas, ependymomas, glioblastomas, craniopharyngiomas, etc giving an informed oral and written consent with a baseline haemoglobin level cut-off of >1 l gm/dl. The patients excluded from the study were those who were admitted in intensive care units or underwent surgery for trauma (emergency procedures), those having known bleeding tendency (e.g. known traits of hemophilia, thalassemia), bleeding disorders (e.g. Idiopathic thrombocytopenic purpura, Hemophilia, von Willebrand Disease) assessed via past medical history, those having known drug history especially drugs known to cause thrombocytopenia (e.g. aspirin, warfarin, heparin, enoxaparin), patients with known co-morbid e.g. liver diseases also assessed via past medical history and patients with no or incomplete pre-operative and post-operative laboratory values or medical records.

All those neurosurgery patients that were given the admission form for elective craniotomy were enrolled and followed as part of the study. Laboratory values including baseline workup (e.g. Complete Blood count) taken pre-operative and post-operative, pre-operative coagulation profile including activated Partial Thromboplastin Time (aPTT), Internationalized Ratio (INR) with laboratory-specific reference ranges were noted and recorded. A predesigned questionnaire for the collection of data was used, which included demographics and clinical information. Approval from the university ethical committee was obtained before starting the study.

All patients admitted to the neurosurgery service undergoing elective craniotomy within the study period fulfilling the inclusion criteria, were enrolled using consecutive sampling technique after written informed consent and followed up prospectively for 6 months. Surgeons performing the surgery included greater than 5 years of neurosurgical experience. The pre-operative assessment for each patient was evaluated for haemoglobin levels (Hb) and coagulation workup and was recorded, post-operative haemoglobin levels were also observed and recorded, and coagulation derangements were determined.
Data was entered and analyzed into SPSS version 21. Descriptive statistics were calculated, mean and standard deviation were calculated for quantitative variables like age of the patients, duration of surgery, coagulation profile, blood loss (in terms of pre-operative and post-operative haemoglobin levels and their difference; whereas frequency and percentage were calculated for categorical data i.e. gender, type of surgery performed and co-morbid). The mean difference of haemoglobin (pre-operative and post-operative) was calculated as a marker for blood loss. Paired sample t-test was applied in finding the difference in the mean haemoglobin levels (Pre-operative and Postoperative) and independent sample t-test was applied to compare the difference in Hb levels between the normal and deranged coagulation profile group. Effect modifier age, gender, co-morbid, type, and duration of surgery, were controlled through stratification. Post-stratification paired t-test and independent-sample t-test were applied using $P \leq 0.05$ as significant.

**Results**

In this study, 57 patients who underwent elective craniotomy were included to assess the mean blood loss and to also compare mean blood loss in patients with normal and deranged coagulation profiles. The mean age of patients included in the study was 39.36±13.94 years with 43 (75.4%) males and 14 (24.6%) females. The mean pre-operative haemoglobin level amongst all patients turned out to be 14.10±3.98 gm/dl. The postoperative haemoglobin level showed a decrease with a mean of 12.68±31.98 gm/dl. Therefore the mean difference calculated between pre and post-operative haemoglobin levels turned out to be 1.42±0.99 gm/dl as shown in Table 1.

The blood loss varied amongst patients and it also depends on the type of surgery performed. The mean blood loss calculated in all patients turned out to be 422.10±299.93 millilitres with a mean coagulation profile investigated pre-operatively of 26.61±16.95. However, the mean duration of surgery for all patients was about 4.03±1.81 hours. When mean blood loss was compared amongst patients who had normal coagulation profiles versus those patients who had deranged profiles, a significant difference was found with a p-value of 0.0001 as shown in Table 2.

The co-morbid conditions with which the patients presented to us were also taken into account. Therefore out of 57 patients, the incidence of cardiovascular disease was found in 4 (7%) patients, diabetes mellitus in 11 (19.3%) patients, and 14 (24.6%) patients were found to be hypertensive as shown in Table 8. The patients who underwent craniotomy had different indications for it, however, the most common condition was intracranial tumours which were present in 50 (87.7%) patients followed by craniotomy for subdural hematoma removal and craniotomy for evacuation of brain abscess was the least common indication as shown in Figure 1.

### Table 1: Comparison of pre and post-operative haemoglobin level (N=57)

| Haemoglobin Level (gm/dl)          | Mean | SD  | Mean Change | 95% C.I  | P-Value |
|-----------------------------------|------|-----|-------------|----------|---------|
| Preoperative Haemoglobin Levels   | 14.10| 57  | 1.99        | 1.42     | 1.42-1.68 | 0.000  |
| Postoperative Haemoglobin Levels  | 12.68| 57  | 1.98        | 1.42     | 1.42-1.68 |        |

### Table 2: Comparison of blood loss in normal versus deranged coagulation profile (N=57)

| Coagulation Profile | Mean (aPTT) | N   | Mean Blood Loss in ml | SD  | 95% C.I  | P-Value |
|---------------------|-------------|-----|-----------------------|-----|----------|---------|
| Normal              | 25.20       | 53  | 345.3                 | 71.7| -24.93-15.15  | 0.0001  |
| Deranged            | 45.25       | 4   | 465.7                 | 82.4|         |         |

### Table 3: Frequency of Co-morbid

| CO-MORBIDS         | Frequency | Percent |
|--------------------|-----------|---------|
| Cardiovascular Disease | 4         | 7.0     |
| Diabetes Mellitus | 53        | 93.0    |
| Hypertension       | 11        | 19.3    |
|                     | 46        | 80.7    |
|                     | 14        | 24.6    |
|                     | 43        | 75.4    |
Figure 1: Frequency for the type of surgery

Discussion

Haemorrhage, whether it’s intraoperative or postoperative is a big area of concern for surgeons as it not only affects the outcome of the surgery but its replacement i.e., the blood products are a scarce commodity. Therefore it is understandable why surgery teams all over the world try to determine the amount of blood loss in particular surgery and cross matches the donors accordingly.\textsuperscript{15,16}

It is not uncommon to find a patient with a deranged coagulation profile. When faced with such a patient, the estimate of blood loss intraoperatively and postoperatively is very crucial to prevent complications and even mortalities. Many deranged coagulation parameters are easily detected, such as thrombocytopenia, prolonged global INR, diminished levels of coagulation inhibitors, or high levels of fibrin degradation products. Identification of such coagulation abnormalities is often required since each cause requires different management. PT, aPTT, and INR is often a basic lab test that is required to check a patient fit for any surgical intervention from a coagulation point of view. The role of this investigation is paramount in determining the risk of intraoperative bleeding however its role to detect the risk of post-operative bleeding is still not very clear. The intra-operative haemorrhage can be detected objectively by measuring the blood in suction bottles, soaked gauzes, amount of intravenous fluid required for replacement, and by checking haematocrit. Post-operative blood loss, however, will require some other means to detect ongoing blood loss. In neurosurgical patients, CT scan or MRI imaging modalities can offer help in detecting postoperative blood loss.

By segregating the elective craniotomies into those with normal coagulation profiles and those with abnormal coagulation profiles, we checked the blood loss and post-operative imaging between the two groups. The results showed that intraoperative blood loss was significantly affected by the deranged coagulation profile, being higher in those who were coagulopathic. However, post-operative imaging did not reveal any surgical bed or intracranial hematoma between the two groups.

In this study mean ± Standard deviation for the difference of pre-and post-operative haemoglobin level was 1.42±0.99 with C.I (1.15……1.68) mg/dl, and p-value found to be highly significant (P=0.000). In our study, we also found a highly significant difference in blood loss between normal versus deranged coagulation profiles i.e. (P=0.000). During the study period of six months, 57 patients were enrolled with a mean age of 39.36±13.94 years. The duration of surgery was 4.03±1.81 hours. Post-operative CT scan was done in 20 patients and MRI was done in 37 patients and neither imaging modality showed any hematoma in surgical bed or cranial cavity postoperatively, regardless of whether the patient had the normal or abnormal coagulation profile before surgery.
These findings are supported by the study conducted by Abbasi S, et al, who reported the mean age of patients was 41 years with a standard deviation of 12.5 and a range of 19 to 67 years. The 25th percentile was 32 years and the 75th percentile was 51 years. The duration of surgery was between 2 to 6 hours with a mean of three hrs (SD of 1 hr).

The strengths of our study were the use of consecutive sampling best suited for our study design and sample selection, as our inclusion and exclusion criteria were stringent. The use of objective definitions for predictor and outcome variables also minimizes the source of bias in our study.

The main limitations of our study were the use of a weak study design analysis and strength of evidence of which is limited and therefore the study design does not require any prior sample size calculation. Also, limited outcomes selected in our study affect the worth of our study. Many variables and factors have an association with our predictor and outcome variables that could have been included in our study. The use of non-probability sampling also limits generalizability; however, we had a small number of patients and besides the follow-up duration is short. This study was hospital-based; hence the figure does not reflect the true frequency and severity of the disease. Moreover, the study was conducted in one unit in the single hospital which further confines its generalization.

**Conclusion**

It is to be concluded that a significant decline can be seen in post-operative haemoglobin levels, when compared to the pre-operative levels, in patients undergoing elective craniotomy. There was also a highly significant difference in blood loss between patients with a normal versus deranged coagulation profile. However, there is a need to conduct more studies using a large sample size with multiple study sites in Pakistan to validate these results.

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