DVT Prophylaxis in head-injured patients: Current Concepts and Guidelines

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Abstract

Objective:

DVT prophylaxis is often delayed in head -injured patients because clinicians believe that the risk of bleeding from prophylaxis is more critical than the risk of venous thromboembolism.

Material & Methods:

All head injury admissions between September 2021 and September 2022 were selected for inclusion in this study. Patient data including age, sex, injuries, Glasgow Coma Scale, Injury Severity Score, were collected. Chemical prophylaxis, either heparin or enoxaparin, was started as soon as it was considered safe. Patients with traumatic intracranial hemorrhage were followed up with brain computed tomography to examine the safety of chemical DVT prophylaxis.

Results:

A cohort of 100 patients was studied during the one year study period. Their average GCS scores and Injury Severity Score scores were 11 and 14 respectively. Overall, 68% of patients suffered from mild to moderate head injuries. Fifty-nine percent of patients were poly-traumatized with different types of extracranial injuries. 60% were managed conservatively and 40% needed surgical intervention. Overall, 75% of patients received chemical DVT prophylaxis and 25% received mechanical prophylaxis. 50% received early chemoprophylaxis, that is within 72 hours, 25% received late prophylaxis, that is after 72 hours. The average delay in start of DVT prophylaxis was 2.9 days. 2.4% of patients developed DVT in spite of prophylaxis but no one developed any expansion of intracranial hemorrhage .

Conclusion:

This study concluded that early DVT prophylaxis in head-injured patients is safe and effective.

Introduction

The incidence of deep venous thrombosis (DVT) in polytrauma patients ranges from 6–60% [1]. Multiple injuries, male gender, lower limbs injury, prolonged hospital stay, old age, and immobilization are main risk factors for the occurrence of venous thromboembolism (VTE) in trauma patients[2]. Recently, traumatic brain injury (TBI) has been considered an important independent risk factor which increases the chances of venous thromboembolism by 3–4-fold [3]

There is a lack of consensus regarding deep venous thrombosis prophylaxis in trauma patients. No clear guidelines are available regarding the timing, dosage, frequency, or duration of prophylaxis. Therefore,

timing, agent of choice, and dose of prophylactic drug are based on the physicians' perceived risk for intracranial hemorrhage (ICH) progression[4]. DVT prophylaxis is often delayed because clinicians believe that the risk of bleeding from thromboprophylaxis is more critical than the risk of venous thromboembolism[5] .

Abundant evidence from multiple randomized clinical trials conclusively showed that use of thromboprophylaxis in trauma patients is a safe, and effective for decreasing VTE. However, despite these evidence-based guidelines, thromboprophylaxis remains either underutilized or suboptimal[6] .

With this background, we analyzed our own clinical practice regarding initiation of DVT prophylaxis in head-injured patients with or without polytrauma and to know how far our clinical practice is comparable with the existing guidelines.

Material & Methods

This is a prospective study conducted at PMAH from September 2021 to September 2022 with prior approval of the departmental academic committee. All trauma patients who presented to an emergency room within 24 hours after injury, with evidence of head injury regardless of their Glasgow Coma Scale, were included in this study. These patients were rapidly managed by the team of an emergency physicians and trauma surgeons according to Advanced Trauma Life Support (ATLS) protocols. After stabilizing the patients, detailed history, general physical and systemic examinations were recorded. Pan-computerized tomography (CT) scans along with complete laboratory investigations, were done in all cases to assess the nature and severity of any other organ injuries.

Patients became part of the study only if CT brain showed some cranial pathology like skull fractures, contusions, diffuse axonal injuries, and hemorrhages. Patients who suffered from concussions but were admitted for more than 48 hours, were also part of the study. Magnetic resonance imaging of the brain and spine was not a routine procedure but were done in a select number of cases whenever needed. Patients with past history of DVT, paedritic/pregnant cases, spinal cord injury, penetrating and sports injuries were excluded from the study.

Trauma and injury severity score (TRISS), was calculated for every patient at the time of presentation [7]. Caprini scoring system was used for initiation and selection of DVT prophylaxis for the prevention of venous thrombosis as per hospital policies[8].

Those patients who had low GCS, and needed intubation and mechanical ventilation, were admitted to the intensive care unit (ICU) for further assessment and management. Patients suffering from epidural, subdural or intracerebral hematoma needing surgery, were operated in an emergency as E1 (priority elective) cases. Stable patients with high GCS scores were managed in high dependency units with round the clock monitoring and neuro-observation. Follow-up brain CT scans were done after 24 hours or earlier in case of deterioration, in all head-injured patients. If follow up CT head scan showed no change or if

patient had no associated source of bleeding like other visceral injuries, DVT prophylaxis was started either with enoxaparin 40 mg subcutaneously once daily or heparin 5000 units intravenously twice daily as prophylactic doses depending upon the availability of drugs or physicians preference. However, heparin was exclusively prescribed for patients with renal impairment .

Those polytraumatized patients in whom there was any source of bleeding other than the brain, were also refrained from DVT prophylaxis. Similarly, DVT prophylaxis remained on hold in patients who were scheduled for any kind of surgery. Nevertheless, after planned surgical procedures, DVT prophylaxis was started after careful estimation of risk/ benefit ratio. In all post-craniotomy cases after hematoma evacuation, follow-up CT head was done within 24 hours. In case of stable CT head, DVT prophylaxis was started either soon after follow-up CT scans or some surgeons preferred to wait up to 72 hours after surgery. Regardless of TRISS or Caprini score, all patients were put on mechanical prophylaxis in the form of intermittent pneumatic compression devices until chemical prophylaxis was started. All possible efforts were made not to miss any type of prophylaxis in any patient.

No patient was routinely monitored for development of DVT either by means of venography or ultrasonography. Doppler ultrasound of legs and pulmonary CT angiography were performed in a select number of cases based on strong clinical suspicion and observation. If someone developed signs and symptoms of pulmonary embolism and/or deep veins thrombosis anywhere in the body, therapeutic doses of heparin were started with close monitoring of coagulation profile and follow-up CT scan studies of brain as well as other suspected part of body in order to check any progression of preexisting hemorrhages.

Isolated head trauma cases were discharged after a suitable period of observation. Polytrauma patients were discharged when their respective specialties cleared them after either conservative or surgical management. These patients were initially downgraded to high dependency units or regular wards before their discharge. Those patients who developed thrombosis during hospitalization, were discharged subsequently, either on enoxaparin or oral anticoagulant like Apixaban, for an extended period of time with strict advice for monthly follow-up in outpatients departments (OPD).

Results

A total of 100 patients were admitted during this twelve- month study period. Ninety three patients were male and seven patients were female. The age range of these patients, was between 15 to 82 years (mean age 34.8 -years). Seventy patients were involved in road traffic accidents (RTA), 22 suffered trauma due to fall, and eight cases were assaulted on the head.

Glasgow coma scores ranged from 3–15, average 11 .Fifty eight patients had mild TBI (GCS 13–15), 7 patients had moderate TBI (GCS 9–12), and 35 patients had severe TBI (GCS < 8) (Table 1). Overall, 68% of patients had mild to moderate head injuries. Our range of the Injury Severity Score (ISS) was between1 to 45 ; the average score remained 14 .The Injury Severity Score (ISS) relates to mortality, morbidity, and

hospitalization time after trauma. DVT scores based on Caprini criteria ranged between 0 to 20 (average 7.6).

Weight of our study population varied from 40 to 118 kg (average 74.9 kg). BMI (body mass index) ranged from18 to 40 kg/m^2 (average 26 kg/m^2). An ideal BMI ranges from18.5 to 24.9. BMI between 25 and 29.9 skews towards overweight range.

Fifty nine patients were polytraumatized with different types of extracranial injuries and 47 patients had isolated head injuries. Contusions, extradural hematomas and skull fractures were the most common pathologies on head CT scans, respectively (Table 2). Ribs, long bones, pelvic and maxillofacial fractures were commonly noted among extracranial injuries.

Out of 100 cases, 60 patients (60%) were managed conservatively; 40% patients needed some surgical interventions. Eighteen patients underwent neurosurgical procedures mainly craniotomy or decompressive craniectomies for epidural, subdural & intracerebral hematomas. Few other polytraumatized patients had undergone laparotomies, thoracotomies, and ORIF(open reduction & internal fixation) of long bones.

44 patients were put on enoxaparin and 31 received heparin, whereas 25 could not receive chemoprophylaxis, either because of their critical clinical condition or other compelling contraindications like thrombocytopenia, coagulopathy, occult bleeding or waiting for surgery. However, all of them remained on pneumatic compression devices throughout their stay.

Overall, 75% patients received chemical DVT prophylaxis and 25% received only mechanical prophylaxis. 50% received early chemoprophylaxis, that is within 72 hours, 25% received late prophylaxis that is after 72 hours (Table 3). Average delay in start of DVT prophylaxis was 2.9 days. Maximum delay was 20 days. Seven patients received chemoprophylaxis after 7 days. Hospital stay ranged from 2 to 95 days (average 15 days).

Seven patients expired, none were caused by pulmonary embolism or late hemorrhage: five patients are still admitted in critical and moribund condition and two have developed DVT; one in upper limb and other transverse sinus of brain.

Discussion

An explicit association between DVT and trauma was first proved by Geerts in 1994.He performed serial impedance plethysmography and lower-extremity contrast venography in a cohort of 716 patients who were not receiving any type of DVT prophylaxis and discovered that 57.6% of trauma patients developed deep-vein thrombosis [9]. In the Prophylaxis of Thromboembolism in Critical Care Trial (PROTECT), of 3764 critically ill patients who were receiving thromboprophylaxis medications, ultrasound screening revealed a proximal DVT rate of 5.1–5.8% [5]. Incidence of DVT in TBI patients is three to fourfold higher than those

patients without head trauma[1]. In a large multicenter trial, one in five patients with TBI developed VTE despite the use of chemoprophylaxis[10].

Therefore, it seem prudent that DVT prophylaxis should be started as soon as possible. But the paradox of VTE prophylaxis is that any agent that decreases venous clot formation has a corresponding tendency to increase bleeding .Therefore, it is important to know whether this prophylaxis is really safe and effective or not. In one study, the rate of DVT in the cohort with no routine chemoprophylaxis was 5.6%, while the rate of DVT after routine chemoprophylaxis was 0%[11]. Another study from a Level I Trauma Center of patients with TBIs receiving early (0–72 hours) or late (> 72 hours) chemoprophylaxis found no evidence that early prophylaxis increases the rate of hematoma progression[12]. The Delayed Versus Early Enoxaparin Prophylaxis I (DEEP-I) randomized control trial found that intracerebral hematoma (ICH) progression rates among TBI patients receiving early prophylaxis were similar to those in patients who had been treated with placebo[13]. In another systemic review, out of twenty-one studies, eighteen studies confirmed that VTE prophylaxis in patients with stable head CT scan does not lead to TBI progression. Fourteen studies revealed that VTE prophylaxis administration 24 to 72 hours post-injury is safe in patients with stable injuries. Four studies suggested that administering prophylaxis within 24 hours of injury in patients with stable TBI does not lead to progressive intracranial hemorrhage[14]. Most recently, Störmann et al presented findings in which patients with severe TBI were categorized into four groups by timing of prophylaxis initiation: <24 hours, 24–48 hours, > 48 hours and no therapy. They showed that early (< 24 hours) administration was not associated with ICH progression[15]. Similar reductions in VTE rates were also observed and reported by Scudday, Saadeh, Rivas, Shulkosky [16,17,18,19].

Although, many meta-analysis revealed that early initiation of DVT prophylaxis is safe but some studies also warned about the danger of progression of intracranial bleeding. Prospective, multicenter, observational study sponsored by the Eastern Association for the Surgery of Trauma (EAST) Multicenter Trial Committee, observed that nearly 10% of TBI patients developed neurologic deterioration after the introduction of DVT prophylaxis [20]. Another retrospective cohort study including 4951 patients who had neurosurgical interventions at trauma centers participating in the American College of Surgeons Trauma Quality Improvement Program between 2012 and 2016, noted that earlier initiation of prophylaxis was associated with increased risk of repeated neurosurgery and greater mortality. During the first 3 days, each additional day of prophylaxis delay was associated with a 28% decrease in odds of repeat neurosurgery. After 3 days, each additional day of prophylaxis delay was associated with an additional 15% decrease in odds of repeat neurosurgery. Each additional day of prophylaxis delay was also associated with decreased odds of death. These findings suggest that care should be taken in starting DVT prophylaxis during the first 3 days after the index procedure[21].

With these alarming and conflicting reports, clinicians are in ambivalence to decide the real timing of DVT prophylaxis. Ideally, practice should be based on some authenticated guidelines but since nothing is clear therefore clinical practice is typically experience-based and subjective.

The question of when to start anticoagulation is not straightforward. The Eastern Association for the Surgery of Trauma (EAST) strongly recommends use of LMWHs in all trauma patients [22]. American College of Surgeons Trauma Quality Improvement Project released guidelines in 2015, supporting consideration of VTE prophylaxis within the first 72 hours of hospitalization[15]. American College of Chest Physicians (ACCP) guidelines- published in 2012 & updated in 2016- also recommended the use of LMWH for major trauma patients as soon as it is considered safe[23]. National Institute for Health and Care Excellence (NICE) 2018 guidelines on preventing VTE in hospitalized patients endorsed interventions to reduce the incidence of VTE in the hospital and within 90 days after a hospital admission. American Society of Hematology Guidelines 2018 also advocate pharmacological prophylaxis for all ill patients[6]. Brain Trauma Foundation (BTF), simply states that anticoagulation should be used, but has not declared any timing of prophylaxis. BTF concluded that there is insufficient evidence to support recommended timing of VTE prophylaxis initiation following TBI[24]. Neurocritical Care Society recommends initiating LMWH or unfractionated Heparin for VTE prophylaxis within 24–48 h of presentation in patients with TBI. More recently, a systematic review from 2020 concluded that early chemoprophylaxis 24–72 hours is related to reduced VTE incidence without increasing the risk of intracranial hemorrhage[15]. But, in spite of all these guidelines, haziness still persists and precise timing for chemoprophylaxis remains uncertain.

Many options for anticoagulation are available but which medicine to choose is another puzzle. There are many controversies regarding drugs and the doses in DVT prophylaxis. Eastern Association for the Surgery of Trauma guidelines recommend use of low-molecular-weight heparin (LMWH) / enoxaparin as the preferred agent in patients with traumatic intracranial bleeding. Level one evidence also supports the use of LMWH in reducing the incidence of mortality and VTE events among trauma patients [25,26]. In randomizing 265 patients to receive either enoxaparin or unfractionated heparin, Geerts et al. demonstrated a significant reduction in DVT rates from 44–31%, as well as in proximal DVTs from 15–6%, with the use of enoxaparin. This study also proved that 30 mg of subcutaneous enoxaparin twice daily performed better than 5,000 U of subcutaneous heparin twice daily at reducing DVT in moderate to severely injured trauma[27]. Also, enoxaparin was shown to have a neuroprotective effect in animal models as well as in humans following traumatic brain injury .Animal studies showed that enoxaparin reduced brain edema and secondary brain injury due to its anti-inflammatory effects. Enoxaparin also prevents thrombosis in cerebral microcirculation and reduces related damage [28]. LMWH was shown to be superior to heparin in a double-blinded, randomized clinical trial among 344 trauma patients without frank intracranial bleeding[27]. The initial enoxaparin dose for trauma patients may also be based on weight like 0.5 mg/kg twice daily, or 30 mg for 50 to 60 kg patients, 40 mg for 61 to 99 kg patients, and 50 mg for patients greater than 100 kg [29,30]. The advantages of using LMWH compared to other modalities are its ease of administration, increased efficacy, improved specificity, and no monitoring requirement [31]. Therefore, enoxaparin 30 mg subcutaneously once or twice a day should be the preferred VTE prophylaxis agent for use in hospitalized trauma patients .

A judicious and appropriate use of DVT prophylaxis is another important issue. It has been noticed that if on one hand, DVT prophylaxis is being ignored than on the other hand it is either underutilized or

overutilized. A 2008 multinational study of 358 hospitals in 32 countries showed that patients who were considered low risk for VTE tended to be “overprophylaxed,” with about one-third of both low-risk patients receiving prophylaxis that was not indicated. A retrospective observational study of Canadian hospitals showed that fewer than one-quarter of acutely ill patients were prescribed any form of VTE prophylaxis. US hospitals with only 12.7% of medical patients and 16.4% of surgical patients prescribed appropriate prophylaxis according to accepted guidelines. A study of hospital discharge information for > 70 000 cancer patients showed that only 53.6% were prescribed prophylaxis. A consortium of hospitals in Michigan examined 44 775 patients and also found that 77.9% of low-risk medical patients were prescribed excess prophylaxis, suggesting the indiscriminate use of prophylaxis [6]. Therefore, it is important to ensure that high risk patients should not be missed for DVT prophylaxis but at the same time low risk patients should not be overexposed to DVT prophylaxis.

Our study showed that 65% of patients were suffering from mild to moderate head injuries based on GCS, ISS and DVT scores. Most of the patients were males with an average age of 35-years. Predominant cause of head trauma remained RTA. An average GCS of our patients was 11. Also, averages ISS was 14 whereas ISS > 15 is considered as severe trauma. Although there are several DVT scoring systems, the Wells DVT score, the Wells PE score, and the Geneva PE score are the most widely used and best validated scores[6]. We calculated DVT score on the basis of Caprini model as per hospital policy. The 2013 Caprini risk assessment model has been validated in over 250 000 patients in more than 100 clinical trials worldwide. It provides a consistent, thorough, and efficacious method for risk stratification and selection of prophylaxis for the prevention of DVT. As the numerical score increases, the clinical DVT rate rises exponentially. But cutoff score between risk groups varies depending on the surgical population[7]. Our average DVT score based on Caprini criteria was 7.7 which is tantamount to mild to moderate head injuries.

Our fifty-three percent patients were polytraumatized. Overall, 40% needed surgical intervention like neurosurgical/ orthopedic/ maxillofacial procedures. Neurosurgical procedures are classified as very high hemorrhagic surgical procedures, making the management of anticoagulation in neurosurgery one of the toughest challenges [32]. Therefore, it was natural to have a delay in prescription of chemoprophylaxis. We also noticed significant hesitancy among other surgical specialties in initiation of prophylaxis. No one shouldered this responsibility and ultimately neurosurgeons had to resolve when to start or resume prophylaxis. In spite of all these odds,

50% patients received early chemoprophylaxis that is within 72 hours; 25% received late prophylaxis and 25% patients received mechanical prophylaxis. Although literature supports the effectiveness of mechanical prophylaxis but compression devices are not effective for upper limb, pelvis and catheter-related venous thromboses, which all continue to be potential sources of pulmonary embolism in high-risk critically ill TBI patients[5].

We noticed that surgeons usually preferred heparin but due to shortage of supply finally most of the patients had to be shifted on enoxaparin. Patient remained on chemoprophylaxis until discharge or until

patients could ambulate independently. There was no interruption of DVT prophylaxis once it was started. Our average delay was 2.9 days which is unarguably acceptable. Similar results have been recently reported in a retrospective study from Kingdom of Saudi Arabia[33].

We did not observe any progression of intracranial hemorrhage in any patient after initiation of chemoprophylaxis. We also did not notice any cases of pulmonary embolism. Nevertheless, 2.5% developed some sort of thrombosis in the body. Our findings clearly show that our current clinical practice is commensurate with international standards and guidelines. This study also revealed that fear of ICH progression is unjustified, irrational and illogical. Initiation of chemoprophylaxis within 72 hours in head injuries even in polytraumatized patients is sagaciously advisable.

Our study has some limitations as well. Firstly, we were not able to record exact time interval between timing of injury/accident and arrival of patients at our institution in many patients but it was not more than 24 hours. This could result in a bias in calculating the exact time interval from the time of injury to the time of initiation of prophylaxis. Secondly, low GCS of patients at the time of admission was not accurate because of their sedation for intubation and ventilation from the referring hospitals. Their GCS improved when sedation was gradually tapered off. Hence, this subset of severe traumatic brain injury with GCS < 8 is not a representative sample. Thus, our judgement regarding timing of DVT prophylaxis in severely head injured patients may not be valid. Thirdly, our prescribed doses of heparin and enoxaparin were neither appropriate nor guided by anti-Xa levels and weight. We prescribed these medicines for all patients as standard and fixed doses whereas ideally these should be calculated on a weights basis. Because, obesity in Saudi Arabia is a growing health concern, and our average BMI has also tilted towards the higher side. Hence weight-based prescription of DVT chemoprophylaxis could be a sensible option to be practiced. Finally, we did not undertake any scrutiny for occult or asymptomatic DVT, either during hospitalization or after discharge proactively. Literature review indicates that DVT proportions are increased whenever routine surveillance techniques are used[34]. But routine screening of patients for DVT is logistically difficult and is not cost-effective. Also, currently, there are no explicit standards for ordering imaging tests to confirm or exclude a VTE outside of clinical judgment [6]. Strength of our study is that we mentioned BMI as an important covariable between DVT prophylaxis and TBI.

Our study lucidly shows that DVT prophylaxis is safe within 24 hours in head injured patients with or without polytrauma. There is neither any progression nor any development of new hemorrhages. Even after major neurosurgical procedures, initiation within 72 hours of DVT prophylaxis was found safe. Although, heparin is cost-effective but enoxaparin is more efficacious and neuro-protective[35].

Based on the available literature, we can cautiously conclude that early DVT prophylaxis reduces the risk of VTE without affecting progression of intracerebral hemorrhage[36]. Thromboprophylaxis should never be deferred on the basis of an irrational fear of its side-effects[37]. It provides an opportunity both to improve patient outcomes and also to reduce hospital costs .The International Society on Thrombosis and Haemostasis has recently put forward a call for risk assessment in all hospitalized patients and pledged to reduce hospital-acquired VTE by 20% by the year 2030 [6].

Conclusion

DVT prophylaxis is indeed a double-edged sword and needs a vigilant assessment before its commencement. It should be started no later than 72 hours post-injury or surgery by any means. Head injuries with stable CT brain post-injury, may be put on chemoprophylaxis in more or less than 24 hours without fail.

Abbreviations

DVT Deep Venous Thrombosis

GCS. Glasgow coma scale

TBI. Traumatic Brain Injury

ICU. Intensive Care unit

VTE. Venous thrombo-embolism

ICH. Intracerebral Hemorrhage

CT. Computerized Tomography

OPD. Outpatient department

BMI. Body. Mass index

LMWH. Low molecular weight heparin

Declarations

Conflict of interest

All authors of this manuscript have no Conflict of Interest.

Authors contributions:

Dr. Ahmed Bakhsh; has conceived the idea, collected the data, written the manuscript.

Dr. Hosam Ali Shatta was involved in surgeries

Dr. Aljuzair ; was main supervisor

Dr. Umair Ahmed & Dr Warda Rauf collected references, preparing the tables and editing and proof reading of manuscript.

Dr. Hany was involved in surgeries

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Tables

Tab.1 Glasgow Coma Score

GCS		No. of cases	
3—8	(Severe Head injury)	35	35 %
9—12	(Moderate Head Injury)	07	07 %
13—15	(Mild Head injury)	58	58 %

Tab.2 Head Pathology

Pathology	No. of cases
Diffuse Axonal Injury	03
Concussion	06
Contusions	21
Acute Subdural hematoma	11
Extradural hematoma	17
Traumatic SAH	15
Intracerebral hematoma	04
SAH/ Contusions	09
Skull fractures	14
Total	100

Tab.3 Timing of prophylaxis

Timing of DVT prophylaxis		No. of patients (75/100)
Within 24 hours	(0 day)	04
After 24 hours	(1 day)	15
After 48 hours	(2 days)	10
After 72 hours	(3 days)	19
After 96 hours	(4 days)	10
After 168 hours	(7days)	10
After 240 hours	(10 days)	07