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Desmopressin Is A Transfusion Sparing Option To Reverse Platelet Dysfunction In Patients With Severe Traumatic Brain Injury

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Abstract

Background: Platelet dysfunction (PD) is an independent predictor of mortality in patients with severe traumatic brain injury (sTBI). Platelet transfusions have been shown to be an effective treatment strategy to reverse platelet inhibition. Their use is contingent on availability and may be associated with increased cost and transfusion related complications making desmopressin (DDAVP) an attractive. We hypothesized that DDAVP would correct PD similarly to platelet transfusions in patients with sTBI.

Methods: This retrospective study evaluated all blunt trauma patients admitted to an urban, level one trauma center from July 2015 to October 2016 with sTBI (defined as Head AIS ≥ 3) and PD (defined as adenosine diphosphate [ADP] inhibition ≥60% on thromboelastography [TEG]) and subsequently received treatment. Per our institutional practice patients with sTBI and PD are transfused one unit of apheresis platelets to reverse inhibition. During a platelet shortage, we interchanged DDAVP for the initial treatment. Patients were classified as receiving DDAVP or platelet transfusion (PLT) based on the initial treatment.

Results: A total of 57 patients were included (DDAVP n=23; PLT n=34). Patients who received DDAVP were more severely injured (ISS: 29 vs. 23, p=0.045) but there was no difference in Head AIS (4 vs. 4, p=0.16). There was no difference between the two groups in admission platelet count (244 ± 68 $\times 10^3$/uL vs. 265 ± 66 $\times 10^3$/uL, p =0.24), or other coagulation parameters such at PT, PTT or INR. Prior to treatment both groups had similar ADP inhibition as measured

by TEG (ADP 86% vs. 89%, p=0.34). After treatment both the DDAVP and PLT groups had similar correction of platelet ADP inhibition (p=0.28).

Conclusion: In patients with severe TBI and PD, DDAVP may be an alternative to platelet transfusions to correct PD.

LEVEL OF EVIDENCE: IV, therapeutic

Keywords: Platelet dysfunction, TBI, DDAVP, TEG, Platelet transfusion

BACKGROUND

Traumatic brain injury (TBI) remains a major cause of mortality in the United States, affecting more than 1 million people each year[1]. In 2013, the Centers for Disease Control and Prevention (CDC) estimated that approximately 2.8 million of the country's emergency department (ED) visits, hospitalizations and deaths were related to TBIs[2]. Many studies suggest that an acquired coagulopathy develops in TBI patients[3–8]. In a recent systematic review, incidences of coagulopathy were reported as high as 33% in all TBI patients and up to 60% in those with severe TBI (sTBI)[9].

The degree of coagulopathy appears to be related to the severity of brain injury and identification of coagulopathy on admission in TBI patients is associated with worse outcomes[6,10–13]. Talving et al. found up to a 10-fold increase in mortality in TBI patients who develop coagulopathy during their hospital course[7]. Coagulopathy can be diagnosed with either conventional assays such as international normalized ratio (INR), partial thromboplastin time (PTT), fibrinogen level, and platelet count or[6,10–13] with more dynamic studies such viscoelastic assays which include thromboelastography (TEG). TEG analyzes the kinetics and stability in clot formation and with the addition of platelet mapping (TEG-PM) assesses clot strength and platelet response to different agonists[14].

The mechanism behind the coagulation disorders associated with TBI is complex and not fully understood[3,7,9,15,16]. Some authors believe it is related to increased tissue factor (TF) release, disseminated intravascular coagulation (DIC), platelet dysfunction, and activation of protein C pathways[12,15,17,18]. One study proposed that injury to brain tissues leads to

increased release of TF into systemic circulation and overactivation of the coagulation cascade causing excess thrombin formation thus increasing platelet activation[19]. This significant increase in platelet activation does not appear to influence platelet count, but instead produces platelets with decreased hemostatic abilities, contributing to the coagulopathy seen in TBI patients[16].

Previously our institution showed that platelet dysfunction, defined as adenosine diphosphate (ADP) inhibition ≥60% on TEG-PM, is an independent predictor of increased mortality in patients with sTBI[20]. These findings led to a practice change at our institution which included platelet transfusions for patients admitted to the surgical ICU with TBI who exhibited ADP inhibition ≥60%. We subsequently were able to show platelet transfusions to be an effective treatment strategy to reverse platelet inhibition and that treating this platelet dysfunction may reduce mortality in patients with sTBI[21]. During a period of platelet shortage our institution substituted desmopressin acetate (1-deamino-8-D-arginine vasopressin; DDAVP) for platelets as our initial therapy of choice for platelet dysfunction in patients with sTBI. We hypothesized that DDAVP would correct platelet dysfunction similarly to platelet transfusions in patients with sTBI.

METHODS

This was a retrospective study of all adult blunt trauma patients who sustained an intracranial hemorrhage and were admitted to our ACS-verified Level 1 trauma center from July 2015 – October 2016. Per our institutional practice patients with sTBI and platelet dysfunction are transfused one unit of apheresis platelets to reverse inhibition. If platelet inhibition persists

on repeat TEG, after this first round of transfusion, the patient then receives a second round of platelet transfusion. A completion TEG is obtained to evaluate effect of transfusion, but no further transfusions are performed for continued platelet dysfunction identified on TEG. During a platelet shortage, we interchanged DDAVP for the initial treatment in this algorithm (Figure 1). Patients were included if they sustained a sTBI (defined as Head AIS ≥3), displayed platelet dysfunction (defined as ≥60% inhibition on the ADP platelet pathway) as measured by TEG-PM drawn at admission to the ICU, received either DDAVP or platelet transfusion as the initial therapy for platelet dysfunction, and had a repeat TEG after intervention for platelet dysfunction. Patients were excluded if the time to first TEG or between TEGs exceeded 24 hours, if hemostatic agents were given prior to first TEG or if DDAVP was co-administered with the platelet transfusions. Study patients with severe TBI and platelet inhibition who received a platelet transfusion (PLT) or DDAVP infusion were compared.

Data collection included patient demographics, admission physiology, injury severity score (ISS), head abbreviated injury scale (AIS), prothrombin time (PT), INR, PTT, platelet count, admission Na level, lowest Na level within 24 hours of admission, and pre-injury antiplatelet therapy. TEG specific variables included split point (SP), R time (R), K time (K), alpha angle (angle), maximum amplitude (MA), G value (G), estimated percent lysis (EPL), and platelet assay variables including ADP and AA inhibition. The primary outcome was correction of ADP inhibition. Secondary outcomes included mortality as well as hospital and ICU length of stay.

Baseline characteristics and outcomes data were analyzed using chi square with Yates correction for categorical variables and unpaired Student's t-test or Wilcoxan rank-sum test for continuous parametric and non-parametric data, respectively. A GLM procedure was used to compare serial TEG parameters following platelet transfusions. Values are reported as mean ± standard deviation or raw percentages. An a priori alpha value of 0.05 was identified for statistical significance. This study was approved by our local institutional review board.

RESULTS

A total of 57 patients with sTBI and platelet dysfunction who received either DDAVP infusion or platelet transfusion (PLT) during our study period were included (DDAVP, n=23; PLT, n=34). When comparing the DDAVP to the PLT group (Table 1) those in the PLT group were more often Caucasian (65% vs. 94%, p=0.005), but there was no significant difference in age (41 vs. 40, p=0.86) or male gender (74% vs. 82%, p=0.44). Because our groups significantly differed in their racial composition we used a logistic regression to evaluate the effect of being Caucasian between groups on their ability to correct their ADP dysfunction to <60%. This showed that being Caucasian was not significantly associated with correction of ADP inhibition (odds ratio = 1.1, 95% confidence interval: 0.21 – 5.77, p = 0.91)

When comparing the DDAVP group to PLT group there was no difference in admission heart rate (97 ± 24 vs. 105 ± 31, p = 0.30), hypotension (5% vs. 12%, p = 0.64), or GCS (9 ± 5 vs. 9 ± 6, p = 0.77). Patients who received DDAVP were more severely injured (ISS: 29 ± 12 vs. 23 ± 9, p=0.045) but there was no difference in Head AIS (4 ± 0.90 vs. 4 ± 0.77, p = 0.16).

When comparing traditional coagulation parameters, there was no difference in admission platelet count (244 ± 68 $\times 10^3$/uL vs. 265 ± 66 $\times 10^3$/uL, p =0.24), PT (12.4 ± 2.2 seconds vs. 11.8 ± 1.9 seconds, p =0.31), INR (1.07 ± 0.19 vs. 1.03 ± 0.17, p =0.41), PTT (27.5 ± 7.6 seconds vs. 28.8 ± 5.5 seconds, p = 0.46), or rate of preinjury antiplatelet therapy (9% vs 9%, p = 0.65). We compared sodium levels prior to and within 24 hours of therapy and evaluated the change in sodium associated with each intervention. There was no significant difference between groups (-1.9 mmol/L vs -0.94 mmol/L p=0.38).

Following treatment, clot strength improved to a greater degree following platelet transfusion compared to DDAVP, as represented by decreased split point, increased α angle, maximum amplitude, and G-value (Table 2). DDAVP administration appeared to correct ADP inhibition to a similar degree as platelet transfusion (-24.9 ± 25 vs. -18.5±19; p=0.28) (Figure 2). Following one round of DDAVP infusion 57% of patients had correction of their ADP inhibition to <60% as compared to 32% of patients who underwent platelet transfusion. There was no significant difference between in-hospital all-cause mortality between the two groups (22% vs. 9%; p=0.25).

DISCUSSION

To date, no strong evidence exists regarding the treatment of platelet driven coagulopathy in TBI patients. It is still unclear whether the presence of platelet dysfunction in this patient population is a prognostic indicator or a therapeutic target. Generally, treatment options for any coagulopathy should target the underlying cause. There still continues to be a knowledge gap regarding the etiology of the platelet dysfunction that develops in TBI patients which makes

treatment in these patient's more difficult. DDAVP has long been used as an adjunct for treatment in coagulopathy and has been validated in its use for congenitally acquired coagulopathies such as von Willebrand disease and hemophilia type A. In our current study we were able to show that DDAVP corrects platelet dysfunction to a similar extent as platelet transfusions in patients with sTBI. To understand the mechanism of action of DDAVP in bleeding disorders it is important to recognize specific steps of the coagulation cascade. After endothelial disruption platelets adhere to subendothelial collagen through platelet surface glycoprotein receptors (GPIb-V-IX) and von Willebrand factor (vWF). These adherent platelets undergo a process of degranulation releasing ADP, histamine, serotonin, TXA2, PDGF, platelet factors (including platelet factor VIII; FVIII) and other components. Adenosine diphosphate and TXA2 act as stimuli for platelet aggregation and platelet plug formation[22,23]. DDAVP works as a hemostatic agent by increasing the release of FVIII and vWF levels in the body, which are major contributors to intrinsic coagulation cascade and primary hemostasis[24]. Many studies have shown the use of DDAVP increases these factors about 2-6-fold[25,26].

The evidence surrounding the use and efficacy of DDAVP in treating congenital bleeding disorders is strong[27,28] and many studies have further validated its use in acquired bleeding disorders. In 1983 Mannucci et al. conducted a double-blind controlled study examining the effects of DDAVP versus placebo on bleeding time in uremic patients. He showed that after DDAVP infusion all patients had improved bleeding times[29]. He went on to perform another randomized control trial evaluating both acquired and congenital disorders associated with prolonged bleeding times and their response to DDAVP. This study showed that DDAVP was able to significantly shorten the bleeding times in patients with cirrhosis, those taking antiplatelet

drugs and those with an unclassified disorder causing prolonged bleeding times[30]. When focusing on DDAVP effect on patients taking antiplatelet agents, Cattaneo et al. was able to show that after giving healthy patients ticlopidine, an ADP receptor inhibitor, DDAVP was able to significantly improve these patient's bleeding times[31]. Levine et al was able to show similar results using an animal model where rats were given clopidogrel and this study showed that DDAVP was able to partially reverse clopidogrel-induced platelet dysfunction[32]. Koscielny et al. identified 254 patients with either acquired or inherited coagulopathy undergoing elective surgery and prospectively studied the preoperative use of desmopressin to correct this coagulopathy. This study found that preoperative desmopressin therapy led to correction of platelet dysfunction in 90.2% of patients with 66.9% showing correction of the ADP pathway[33]. This collective body of literature supports the efficacy surrounding the use of DDAVP in both congenital and acquired bleeding disorders

When specifically looking at patients with intracranial hemorrhage Kapapa et al. concluded that DDAVP was able to stabilize platelet function in neurosurgical patients with intracranial hemorrhage who had received aspirin[34]. Naidech et al. also found that patients with acute intracerebral hemorrhage with abnormal platelet activity or known aspirin use had improved platelet activity after DDAVP infusion.[35]. There is very little information regarding the use of DDAVP in platelet dysfunction in trauma patients and none, to our knowledge, regarding its use in the platelet dysfunction associated with sTBI. Our current study not only confirms the ability of DDAVP to reverse acquired platelet dysfunction to a similar degree as platelets but shows that DDAVP is effective in reversing platelet dysfunction associated with

sTBI. It is still uncertain whether this reversal is associated with improved clinical outcomes and further research in this field is needed to answer that question.

A lot of debate still exists surrounding the utility of different TEG parameters, such as ADP inhibition, as prognostic indicators or therapeutic targets in trauma patients. Stettler et al. assessed ADP inhibition in severely injured trauma patients. In this study, they analyzed the predictive value of admission ADP inhibition level and found that in all severely injured trauma patients ADP inhibition was not predictive of mortality, need for massive transfusion, or for platelet transfusion [36]. The big difference between this study and our current study is the population. We examined only sTBI patients, while this study analyzed all severely injured trauma patients. As discussed earlier, platelet dysfunction is implicated in the mechanism leading to the acquired coagulopathy seen in TBI patients. We believe that trauma patients in general behave differently than TBI patients, so while this study was unable to show a predictive value in ADP inhibition there has been data to support the use of ADP inhibition in sTBI patients as a prognosticator[20]. Holzmaher et al. looked at all TBI patients on preinjury antiplatelet therapy and evaluated both those who were transfused with platelets and those who were not to see the effect platelet transfusions had on TEG parameters and CT progression. They found that platelet transfusions improved both AA and ADP inhibition, but only AA inhibition improved significantly. They saw no improvement in mortality using platelet transfusions in this population [37]. Again, this supports further need for larger randomized controlled trials to thoroughly evaluate the therapeutic value of platelet transfusions in patients with TBI.

One notable finding from our current study was the difference in improvement of TEG-PM parameters in those receiving DDAVP versus platelets. The PLT group corrected almost every element of the TEG-PM including our primary outcome of correction of ADP while DDAVP only showed significant correction of ADP inhibition. When giving a closer look into the components of apheresis platelets this result is not unexpected. Each unit of platelets contains about 50mL of plasma likely resulting in a more broad improvement in TEG specific variables as compared to DDAVP[38]. We are unsure if this more robust effect on the overall TEG confers any benefit to patients.

With ongoing shortages of blood products and the significant adverse reactions associated with allogeneic transfusions, methods to limit blood product use is important. Over one million units of platelets are transfused in the United States each year and over two million in Europe[39,40]. Platelet transfusions can lead to a spectrum of transfusion reactions[41], the most common and most mild of these including fever, chills, hives, and itching. These reactions normally are self-limiting and resolve with little or no treatment. Severe reactions, some of which have the potential to be life threatening, associated with platelet transfusion include infection, transfusion related acute lung injury (TRALI), transfusion associated circulatory overload (TACO), and anaphylactic reactions[42,43]]. Although rare, a 2016 study involving platelet transfusions in France found that approximately 6 per 1000 transfusions with apheresis platelets were associated with adverse reactions[44]. In addition to risk, utilization of allogeneic blood products, such as platelets, have the potential to delay therapy. These products require compatibility testing and, at most institutions, are not readily accessible. Even in the cases of traumatic bleeding, when blood product availability should be prioritized, the average time to

administration of platelets has been reported to be 2–3 h[45]. All of these factors have led to the investigation of alternative agents to use as adjunctive or substitutive therapy to blood products.

In general, DDAVP appears to be a well-tolerated and relatively safe pharmaceutical agent[46]. DDAVP is a synthetic analogue of vasopressin and because it is not an allogeneic blood component there are fewer significant risks associated with its use. There are a number of mild side effects described with the use of DDAVP and most are very nonspecific symptoms[42]. The most well described and severe adverse effect of this medication is hyponatremia, which corresponds with its well-known antidiuretic property. This electrolyte abnormality becomes important in TBI patients as it relates to intracranial pressure (ICP). Many of therapies directed at lowering ICP ultimately do this by causing hypernatremia, ultimately drawing fluid off the brain leading to decreased edema and thus pressure. In these patients significantly reduction in sodium level would be worrisome as this could lead to increased ICP and ultimately worse outcomes. Most literature related to desmopressin induced hyponatremia exists related to its use in the treatment of nocturnal enuresis.[47,48]. In a systematic review looking at hyponatremia associated with desmopressin in these patients, only 54 cases of severe hyponatremia were identified[49]. Other studies evaluating the efficacy and safety of desmopressin have found only mild decreases in serum sodium levels, especially in those receiving only a single dose[50,51]. The half-life of desmopressin is 2-4 hours making the duration of action about 6-14 hours[42], so effects of a single dose are expected to be seen within the first 24 hours of administration. In our current cohort we were unable to show a statistically significant difference in sodium change prior to and after therapy with either DDAVP or platelet

transfusions. Overall, as compared to platelet transfusions, DDAVP appears to be associated with less side effects and is tolerated more favorably by patients.

Another important factor to consider when comparing two therapeutic options is cost. Desmopressin appears to be a more cost-effective option than platelets. The Lexicomp published price of injectable desmopressin acetate is $12.34-70.55 for 4 mcg/1 mL. During our study we used a dose of 0.3mcg/kg, so using this pricing, the cost of DDAVP in a patient of average weight, ranged from $65 to $370[42]. This is significantly cheaper than a unit of apheresis platelets which costs, on average, about $534[52].

Several limitations of this study can be attributed to the inherent retrospective design. We relied on the accuracy and heterogeneous documentation practices in the medical chart and/or the trauma registry. We would have liked to have more information related to vWF levels and activity, ICP data, osmolarity but our data collection was limited to what was captured by our trauma registry. TEG-PM utilization was not an automated process and ordering of this test was subject to the physician discretion which may have influenced patient selection thus creating a bias. Another limitation was our heterogeneous groups which may have influenced our results. Specific to this, our DDAVP group was more severely injured than our PLT group. The increased severity of non-brain injuries may have resulted in influences on TEG-PM as well as some of our secondary outcomes such as mortality. The racial difference in groups may also have been a confounding factor as some sources have implicated race in differences in platelet biology [53]. We did attempt to address this by performing a logistic regression to better understand the racial influence in the ability of patients to correct their ADP dysfunction.

Although our regression showed that the ability to correct ADP dysfunction was independent of race, a better study design is necessary to more effectively evaluate this. Another significant limitation was our small sample size which may have skewed our overall results and conclusions.

CONCLUSION

In patients with sTBI and platelet dysfunction, DDAVP may be an alternative to platelet transfusions to correct platelet dysfunction. Given the improved safety profile, reduced cost, and comparable correction of platelet dysfunction, DDAVP appears to be an attractive alternative for therapy in patients with sTBI and platelet dysfunction. More research, including randomized controlled trials, is needed to more strongly validate the effectiveness of DDAVP to correct platelet dysfunction in patients with sTBI and establish its ability to influence clinical outcomes such as mortality.

Author contributions:

Literature review: EF, MJD, CVRB

Study design: EF, MJD, PGT, TBC, JDA, CVRB

Data collection: EF, PS, MJD, PGT, TBC, JDA, CVRB

Data analysis: EF, MJD, PGT, TBC, JDA, SA, CVRB

Data interpretation: EF, MJD, PGT, TBC, JDA, CVRB

Writing: EF, MJD, CVRB

Critical revision: EF, CVRB

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Figure Legends:

Figure 1. Algorithm for treatment of platelet dysfunction in TBI patients diagnosed on TEG.

Algorithm for platelet transfusion. In patients with TBI with admission TEG showing ADP inhibition of ≥60% they would be transfused (0.3mcq/kg IV). The TEG would be repeated and if ADP inhibition had corrected to <60% no further transfusions based on TEG would occur. If on the 2nd TEG there was continued ADP inhibition of ≥60% then another round of platelet transfusion would occur. The third TEG was obtained to evaluate response but no further treatment would occur based on the 3rd TEG.

TEG; thromboelastography

ADP; Adenosine diphosphate

DDAVP; desmopressin

Figure 2.

Visual representation of the change in platelet ADP inhibition along the AA (p=0.80) and ADP (p=0.28) pathways after DDAVP and platelet transfusion.

ADP; Adenosine Diphosphate

AA; Arachadonic Acid

DDAVP; desmopressin

Table Legends:

Table 1 Demographic comparison by cohort

Description of each cohort regarding demographics, operative interventions, coagulation parameters, prehospital antiplatelet therapy, and blood products given.

ED; emergency department

AIS; abbreviated injury scale

ISS; injury severity score

ICU; intensive care unit

ICP; intracranial pressure

PT; prothrombin time

INR; international normalized ratio

PTT; partial thromboplastin time

FFP; fresh frozen plasma

PRBC; packed red blood cells

Na; sodium

Table 2. TEG variable. Before (TEG1) and after (TEG2) intervention (mean ± SD)

Baseline TEG (TEG1) was obtained on admission to the ICU. Second TEG (TEG2) was obtained following one round of platelet transfusion (PLT) or DDAVP infusion. The changes between TEG1 and TEG2 for each parameter was then compared and these values (**Δ)** for DDAVP and PLT groups compared.

TEG; thromboelastogram

DDAVP; desmopressin

ADP; Adenosine Diphosphate

AA; Arachadonic Acid

EPL; Estimated percent lysis

MA; Maximal amplitude

Figure 1.

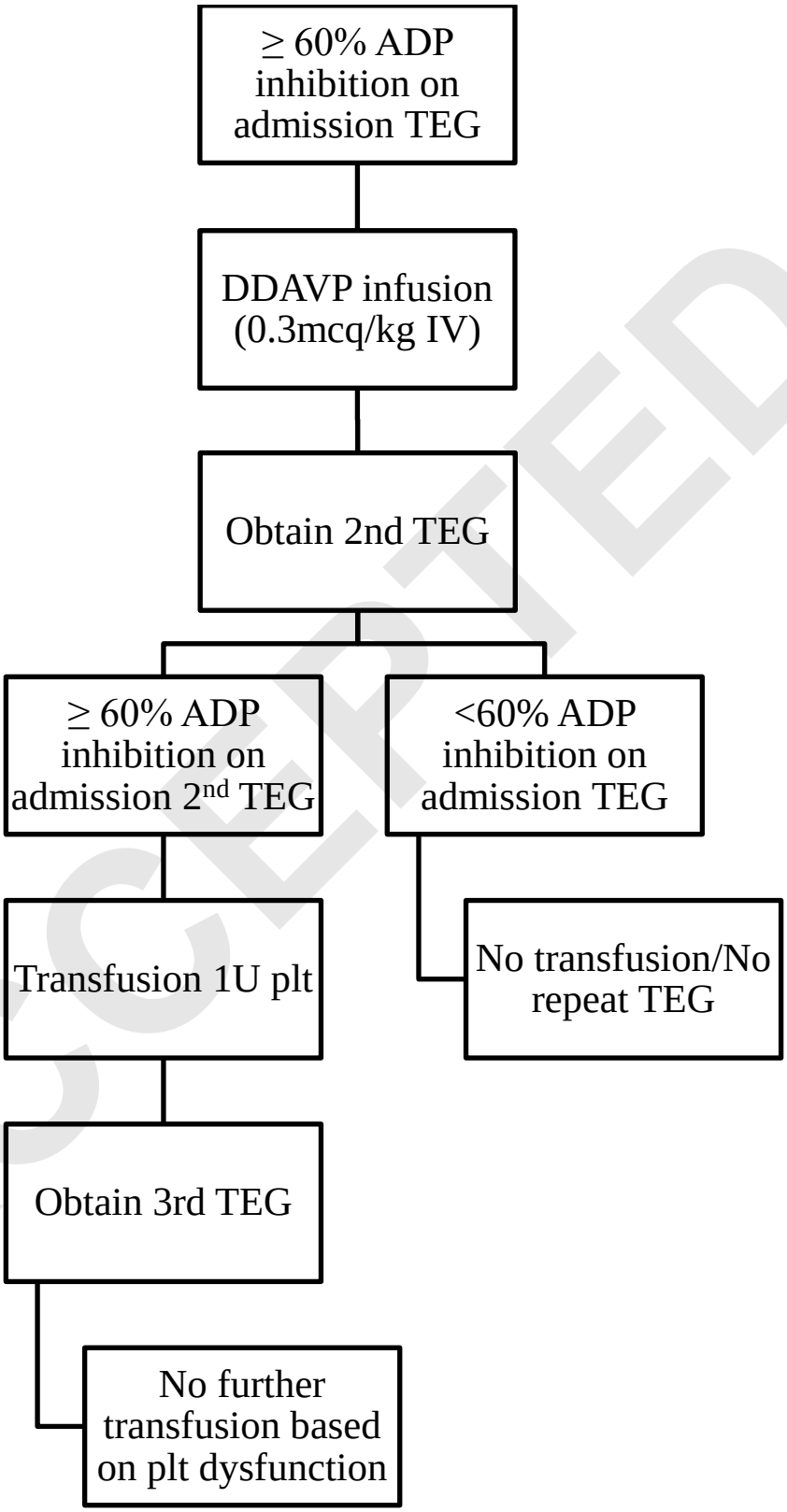

Figure 2.

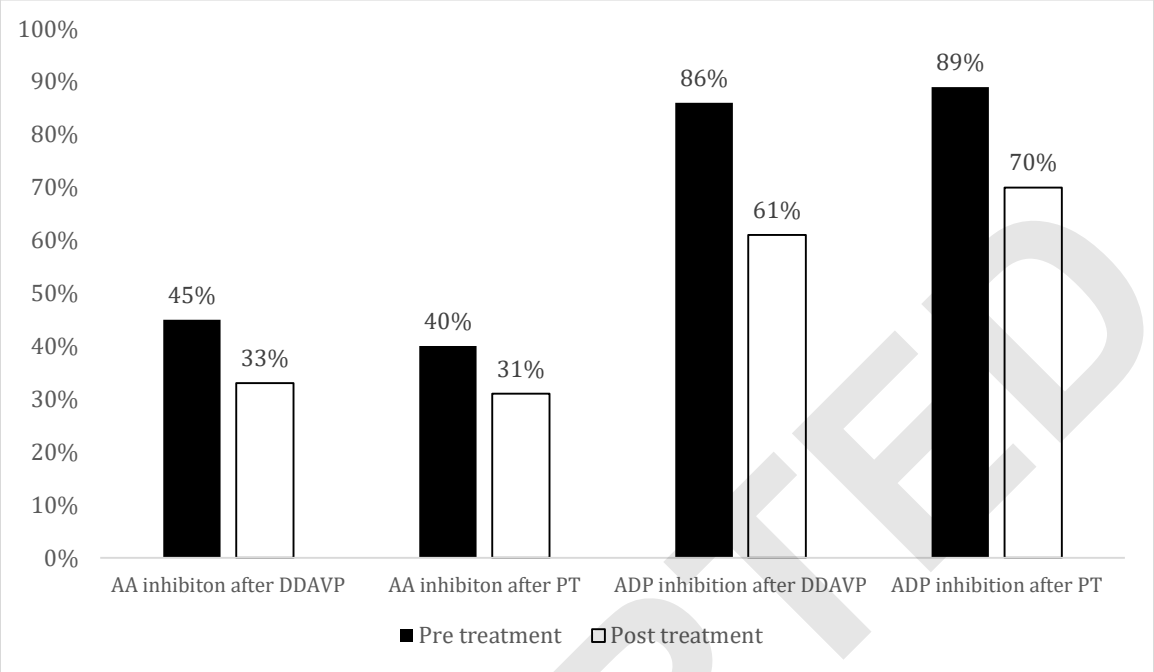

Table 1. Demographic comparison by cohort

	DDAVP group N=23	PLT group N=34	P value
Age	41±22	40±17	.86
Male	17(74)	28(82)	.44
White	15(65)	32(94)	.005
Pre Hospital Systolic (mmHg)	137±34	152±29	.17
Pre Hospital Pulse (bpm)	103±21	103±30	.99
Pre Hospital GCS	9±5	9±5	.58
ED Respiratory Rate	19±8	16±10	.42
Hypotension (SBP <=90 mmHg)	1(5)	4(12)	.64
ED SBP (mmHg)	138±28	142±36	.68
ED Pulse (bpm)	97±24	105±31	.30
ED GCS	9±5	9±6	.77
AIS Head	4±.90	4±.77	.16
AIS Face	.70±.93	.76±1.1	.80
AIS Chest	.87±1.4	.94±1.3	.84
AIS Abdomen	.43±.99	.15±.50	.15
AIS Extremities	.91±1.3	.79±1.1	.72
AIS External	..65±.65	.85±.61	.24
ISS	29±12	23±9	.045
Dead	5(22)	3(9)	.25
Hospital LOS (days)	15±10	15±18	.90
ICU LOS (days)	8±5	9±14	.79
Ventilation days	5±5	3±5	.19
Admission Platelet Count $\times 10^3$/uL	244±68	265±66	.24
Admission PT (seconds)	12.4±2.2	11.8±1.9	.31
Admission INR	1.07±.19	1.03±.17	.41
Admission PTT (seconds)	27.5±7.6	28.8±5.5	.46
Pre Injury Antiplatelet Therapy	2(9)	3(9)	.65
ΔNa (mmol/L)	-1.9±3.9	-.94±4.1	.38

Table 2: TEG variable. Before (TEG1) and after (TEG2) intervention (mean ± SD)

TEG variable	DDAVP group			PLT group			
	TEG1	TEG2	Δ	TEG1	TEG2	Δ	P value*
Split point (SP; min)	3.4±.84	4.1±1.5	.71±1.3	3.9±1.3	3.8±.82	-.09±1.5	.045
Reaction time (r; min)	3.7±.92	4.4±1.7	.69±1.5	4.3±1.4	4.1±.88	-.17±1.7	.06
Clot formation time (K; min)	3.3±8.4	1.8±.72	-1.5±8.4	1.6±.76	1.1±.22	-.50±.71	.49
Angle (α; degree)	69.2±5.4	67.1±7.7	-2.1±6	68.5±7	73.8±2.9	5.4±6.3	< .0001
MA (mm)	62.5±5.5	61.3±5.9	-1.2±3.8	63±6.8	67.8±4.2	4.8±6.1	< .0001
G value (dynes/cm^2)	8.6±2.0	8.3±2	-.34±1.4	8.9±2.4	10.8±2.1	1.8±2.1	< .0001
EPL (%)	.90±1.5	.70±1.1	-.19±1.4	2.5±3.9	2.4±2.7	-.11±3.7	.92
ADP inhibition (%)	85.7±12.0	60.8±26.4	-24.9±25	88.9±12.7	70.3±21.7	-18.5±19	.28
AA inhibition (%)	45.2±32.5	33.4±28.2	-11.8±34.0	40.3±33.1	30.9±28.7	-9.9±22.0	.80

***P value is comparing change in TEG parameters between PT and DDAVP group**