UDK: 616.31-089.16-005.1-085.273.53(497.7)"2019/2024"

DENTOALVEOLAR MANAGEMENT OF PERIOPERATIVE BLEEDING IN PATIENTS WITH PLATELET HYPOAGGREGABILITY

ДЕНТОАЛВЕОЛАРНО МЕНАЏИРАЊЕ НА ПЕРИОПЕРАТИВНОТО КРВАВЕЊЕ КАЈ ПАЦИЕНТИ СО ХИПОАГРЕГАБИЛНОСТ НА ТРОМБОЦИТИТЕ

Gashi S.[1]*, Dvojakovska S.[2], Pepic S.[2]

[1]Istog Dubrava -The health station, correction institute, [2]JZU U Clinic for maxillofacial surgery - Skopje,

[1]*Correspondence Author

Abstract

Introduction: Platelet hypo aggregability, consequence of the reduction of the levels of ADP, collagen and ristocetin, is a life threatening condition, and present prolonged post extraction bleeding (PEB). Usage of Tranexamic acid (TXA) prevents excessive bleeding, accompanied by carefully performed surgical technique and local suturing, leads to a safe postoperative success. **The aim** of this study was to establish the protocol for perioperative management of hypoagreggability patients and to correlate PEB with levels of ADP, collagen and ristocetin and extensiveness of treatment. **Materials and Methods:** We analyzed 64 patients with hypoaggregability, treated at the University Clinic for Maxillofacial Surgery in Skopje, between 2019- 2024. Laboratory tests for ADP, collagen and ristocetin; clinical data of location and extensiveness of dentoalveolar treatment were correlated with bleeding tendency. TXA was applied perioperatively. Surgery was performed with minimal traumatic technique, and local hemostatic methods were evaluated. **Results:** Mean BT before diagnosis was (Me=4 IQR (2.5-9.5) versus PEB (Me=4 IQR (1-7)) (p =.000000). The difference is significant between dentoalveolar versus maxilla and dentoalveolar versus mandible for p=.0453). The difference between bleeding time (BT) and localization of the extraction is significantly longer in dentoalveolar surgery vs. maxilla and mandible (p =.0032). Tranexamic acid demonstrated a significantly lower risk of developing PEB. **Conclusion:** Bleeding control performing dentoalveolar procedures under the proper evaluation of hemostasis usingbenefits of perioperative TXA and local hemostasis is necessary for reducing PEB in thrombocytopathia. **Keywords:** platelet hypo aggregability, Dentoalveolar surgery, post extraction bleeding, Tranexamic acid.

Апстракт

Вовед: Хипоагрегабилноста на тромбоцитите, последица на смалени нивоа на АДП, колаген и ристоцетин, понекогаш може да биде животозагрозувачка, поради опасноста од абудантни постекстракциони крвавења (PEB). Употребата на Транексамична киселина (ТХА) спречува прекумерно крвавење, а придружено со внимателно изведена хируршкиметоди на хемостазаводи до безбеден постоперативен успех. **Целта** на оваа студија е да се воспостави протокол за периоперативно менаџирање на пациентите со хипоагрегабилност на тромбоцитите и да се корелираат нивоата на АДП, колаген и ристоцетин, со времетраењето и инвазивноста на PEB. **Материјал и методи:** Анализиравме 64 пациенти со хипоагрегабилност, третирани на Универзитетската клиника за максилофацијална хирургија во Скопје, во периодот 2019–2024 година. Лабораториски тестови за АДП, колаген и ристоцетин; клиничките податоци за локацијата и обемот на дентоалвеоларниот третман беа корелирани со тенденцијата за крвавење. Покрај интравенски предоперативна доза на ТХА, по потреба, доколку има крвавење, после 8ч. беше аплицирана уште една доза. Операцијата беше изведена со минимална трауматска техника, а беа евалуирании локалните хемостатски методи. **Резултати:** Просечното време на крвавење (ВТ) пред дијагнозата беше (Me=4 IQR (2,5–9,5) наспроти PEB (Me=4 IQR (1–7), (p=,000000). Разликата помеѓу (ВТ) и локализацијата на екстракцијата е значително подолга кај дентоалвеоларната хирургија во споредба со обична екстракција во максила и мандибула за p=.0453) и (p=,0032), соодветно. Транексамична киселина покажа значително помал ризик за развој на PEB (p=0,00). **Заклучок:** Контролата на крвавење при изведување дентоалвеоларни процедури со правилна евалуација на хемостазата, користејќи ги придобивките од периоперативната ТХА и локални техемостатски методи, е неопходна за намалување на PEB кај пациентите со хипоагрегабилност. **Клучни зборови:** хипоагрегабилност на тромбоцити, дентоалвеоларна хирургија, крвавење после екстракција, Транексамична киселина.

Introduction

Decreases of platelet aggregation deserve special attention due toserious postextractionbleeding (PEB) tendency. This condition includes deficiencies of receptors for adenosine diphosphate- ADP, collagen, and ristocetin, with episodes of spontaneous or induced mucocutaneous bleeding, epistaxis[1], hematomas, menorrhagia, and severe bleeding episodes after surgery, sometimes requiring-bloodtransfusion[2,3]. When the bleeding history is suspicious, it is a common practice to proceed to a staged series of investigations to confirm an abnormality of primary hemostasis or coagulation and to determine a precise diagnosis, in order toreduce the need of blood transfusion requirements and reoperations caused by bleedings[4].

Understanding the appropriate diagnostic and therapeutic approaches can only enhance thepatients' safety: (1) adiagnostic approach to the management of a patient's hypoaggregability is in close collaboration with transfusionspecialist. There is a consensusfor carrying out a few tests: platelet counts, prothrombin time (PT), and activated partial thromboplastin time (aPTT). To exclude congenital or acquired defects of plasmatic coagulation factors that influence primary hemostasis, in the first instance, the von Willebrand factor vWF and the aggregation levels of ADP, collagen, and ristocetin[5]; (2) protocol for perioperative management of patients with prophylactic usage of Tranexamic acid. The majority of guidelines recommend using intravenous/i.v. application of a Tranexamic acid as a gold standard for preventing excessive bleeding in platelet hypoaggregability, which works by slowing the breakdown of blood clots and helps to prevent prolonged bleeding[3,6].Tranexamic acid was the only agent that demonstrated a significantly lower risk of developing postoperative bleeding events (OR 0.27, P= 0.007)7; and (3) proposing an updated clinical practice guideline for local and systemic hemostatic methods. Although tooth extraction has been shown to be safe in patients with higher bleeding risk, PEB events have still been reported[8].

Therefore, finding the best supplementary measures for achieving more effective hemostasis has become vital[9,10]. In literature, correctmanagement and perioperative treatment with aadequate hemostasis consist of systemic intravenous tranexamic acid-an antifibrinolytic agent and local hemostatic measurements is crucial for the success of invasive dental treatment in platelet hypo aggregability patients[11]. Many authors found that this success rate decreased from 88.9%-98%, depending on the comorbidities of patient, when TXA and appropriate local methods were usedinpatients undergoing minor dental procedures. Some of them applied at least 2 repeated doses of TXA every 2–6 hours[12].

Acknowledgement for these circumstances, we evaluated the difference between PEB incidences beforeachieving diagnosis (not treatedand correlate them with PEB in prepared patients). Guidelines for hypoaggregability in patients requiring dental extraction was also investigated due to the risk factors for the incidence of postextraction bleeding[13].

Local hemostatic agents and techniques, such as pressure, surgical packs, sutures of the edges of the postextraction wound may be used individually or in combination in the local hemostatic agents, such as topical socket with solution of TXA[14]. Topical TXA is an effective agent used in conjunction with other hemostatic measures when applied directly on the bleeding wound as it converts fibrinogen to fibrin and allows rapid hemostasis in a wound. There is a wide array of techniques suggested for the treatment of PEB, which include interventions aimed at both local and systemic hemostatic methods.

Aim

We aimed to identify the significant predictors of PEB and to assess the efficacy of TXA for preventing bleeding complications in patients with hypoaggregabilityundergoing minor oral surgery or dental extractions. We will determine and incidence of PEB in correlation with extensiveness of treatment in order to assess guideline for managing PEB in these patients.

Material and method

Retrospective study was conducted on 64 patients diagnosed with platelethypoaggregability, treated at the University Clinic for Maxillofacial Surgery in Skopje (2019- 2024 year).

Preoperative diagnostic management:1) clinical symptoms and screening hemostasis and coagulation-laboratory tests: complete blood count (CBC); partial thromboplastin time (pTT); activated PTT (aPTT); prothrombin time (pT); optical aggregometry tests for levels of ADP, collagen and ristocetin were made to determine significant predictors for diagnosing platelet hypoaggregability (completed, within one week before the surgery), were evaluate in collaboration with the Institute for Transfusion Medicine; 2) Rtg orthopantomogram or CBCT were performed in order to confirm the indication for extraction (location and extensiveness of treatment: single tooth extraction or minor dentoalveolar surgery, all dates were noted and analyzed).

Operative procedures: 1) the usage of preoperative TXA for one-day elective surgery procedures is substantial (singleprophylactic dose of i.v. TXA (1-1,5 gr.) was administrated 45 min. before surgery; 2) single tooth

extraction or dentoalveolar surgery (cystectomy or impacted toothextraction with osteotomy and raising a mucoperiosteal flap) were conducted under a local anesthesia. Minimally invasive extraction techniques were used by experienced maxillofacial surgeons. 3) Local hemostatic methods such as washing the socket with topic tranexamic acid, gauze pressure for 30 min.and suturing the wound, were used to control bleeding. Extra measures were applied provided the socket was still bleeding (moderate or heavy);for ensuring successful hemostasis: repeating the dose of i.v. TXA, every 8 hours, revision of wound or electro cauterization were applied. Postoperative cautions were given to all patients, especially to avoid NSAID drugs.

Postoperative evaluation and follow-up of bleeding events were monitored and recorded for the next 7 days. PEB, which cannot be controlled with basic hemostatic procedures (bleeding that cannot be stopped by gauze packing and requires medical treatment between 30 minutes and 7 days), is considered clinically significant bleeding time (BT). According toAmeer's model, depending on the intensity and types of PEB, we defined bleeding event as: oozing/ light, moderate and heavy bleeding. Referent ranges for bleeding timeis 9-20 minutes.

The variables and the examined parameters of all 64 patients were analyzing and correlated: clinical data; levels of ADP, ristocetin and collagen (as significantpredictors for hypoaggregability), localization and extensiveness of treatment were correlated with PEB before achieving the diagnosis and after prophylactic use of TXA and local hemostatic methods. Statistical analyses were performed using IBM SPSS Statistics 20.0 (IBM, Somers, NY) and Statistic 10, using the following statistical methods: coefficients on relationships and proportions, chi-square test was performed to compare bleeding events, and T-test for dependent samples was applied to compare the relative volume of bleeding. Correlative relationships between variables are determined by the Pearson coefficient of correlation (r). For univariate analyses, a chi-square test was performed, and the significance of the difference was tested with the non-parametric Kruskal-Wallis ANOVA test, and the individual difference with Multiple Comparisons p-values. Shapiro-Wilk`s test examined the normal distribution of the variables and for CI (confidence interval $^{238}_{93}$ 95% CI) statistical significances were considered significant for $p< 0.05$.

Results

In 64 patients, diagnosed with platelet hypoaggregability,according to the demographic characteristics, 68.75% of the patients are female and 31.25% are male, the registered difference is significant for p<.05 (p=.0000) between female and male. The average age is 42.9±18.4 years (females 42.89±18.4, ranging 12-82; males (42.95±18.9, ranging 10-82), no difference in terms of age is registered.

Analyzesscreening laboratory diagnostic tests and risk factors for PEB, showed that: CBC, BT, pTT, (aPTT) and PT demonstrate a normal, reference ranges and insignificant correlation with bleeding time (r=0978, p=.446). In all patients, the values of ADP (69-88), Ristocetin (87-102), Collagen (70-94) and PT (9.8-14.2) are below the reference values. Analyzingthe average value of ADP in our patients is 36.6±13.3, ranging from 7.0 to 60.0. In 50.0% of patients, the value is under 39.5 (Me=39.5 IQR (24.5-47), for Ristocetin is 61.4±14.0, ranging from 23 to 86.0 and in 50.0% the value is under 65.0 (Me=65.0 IQR (51-71). The average value of collagen in patients is 49.1±15.5, ranging from 19.0 to 90.0. In 50.0% of patients, the value is under 50.0 (Me=50.0 IQR (39-58). (Table 1)

The average value of ADP in moderate intensity of bleeding is 43.8±10.4, range from 7 to 60. The average value of ADP in severe intensity of bleeding is lower and is 27.9 ±10.5, in range from 7 to 49. The value of ADP in light bleeding intensity is 58.0 (one patient). The average value of Ristocetin in moderate intensity of bleeding is 66.2±9.3, ranging from 47 to 83. The average value of Ristocetin in severe intensity of bleeding is lower and is 55.6 ±16.6, in range from 23 to 86. The value of Ristocetin in light bleeding intensity is 68.0 (one patient). The average value of

Table 1. Average value of ADP, Ristocetin, Collagen and PT in patient with platelet hypoaggregability

	No.	average	Me	Min.	Max.	/IQR	IQR	Stand. Dev.
ADP	64	36.9	39.5	7.0	60.0	24.5	47.0	13.27471
Ristocetin	64	61.4	65.0	23.0	86.0	51.0	71.0	14.03044
Collagen	64	49.1	50.0	19.0	90.0	39.0	58.0	15.49615
PT	63	11.5	11.0	9.7	26.0	10.0	12.0	2.39639

Table 2. Presentation of the mean value of ADP, Ristocetin, Collagen in correlation with bleeding intensity before achieving diagnosis

Bleeding intensity/ ADP	%	No	St.dev.	Min.	Min.
Light	58.0	1	0.00000	58.0	58.0
Moderate	43.8	34	10.41890	7.0	60.0
Heavy	27.9	29	10.51846	7.0	49.0
Ristocetin					
Light	68.0	1	0.00000	68.0	68.0
Moderate	66.2	34	9.34127	47.0	83.0
Heavy	55.6	29	16.60984	23.0	86.0
Collagen					
Light	59.0	1	0.00000	59.0	59.0
Moderate	52.4	34	11.34050	27.0	86.0
Heavy	44.9	29	18.81855	19.0	90.0

Table 3. Presentation of the average value of ADP, Ristocetin, Collagen in relation to the intensity of post-extraction bleeding in treated patient with TXA

Bleeding intensity/ ADP	average	No.	St.dev.	Min.	Min.
oozing	43.5	8	3.46410	38.0	49.0
light	35.6	54	14.01563	7.0	60.0
moderate	45.0	2	5.65685	41.0	49.0
Ristocetin					
oozing	69.4	8	9.10161	58.0	83.0
light	60.2	54	14.55164	23.0	86.0
moderate	63.0	2	2.82843	61.0	65.0
Collagen					
oozing	59.0	8	12.08305	49.0	86.0
light	47.6	54	15.63670	19.0	90.0
moderate	50.0	2	15.55635	39.0	61.0

Collagen in moderate intensity of bleeding is 52.4 ± 11.3, in range from 27 to 86, of Collagen in severe intensity of bleeding is lower 44.9 ± 18.8, in range from 19 to 90. And for Collagen in light bleeding intensity, the average value is 59.0 (Table 2.).

Local hemostatic procedures are performed in 98.4% of the patients (topic TXA applied locally with gauze and suturing the edges of the wound) data is missing for one patient.After i.v. application of TXA, performing dentoalveolar surgery and implementation of local hemostasis measurement: Heavy bleedings were not registered postextraction compared to preoperatively (before diagnosis), were registered in almost half (45.3%) of the patients and the absence of bleeding after extraction was registered in 8

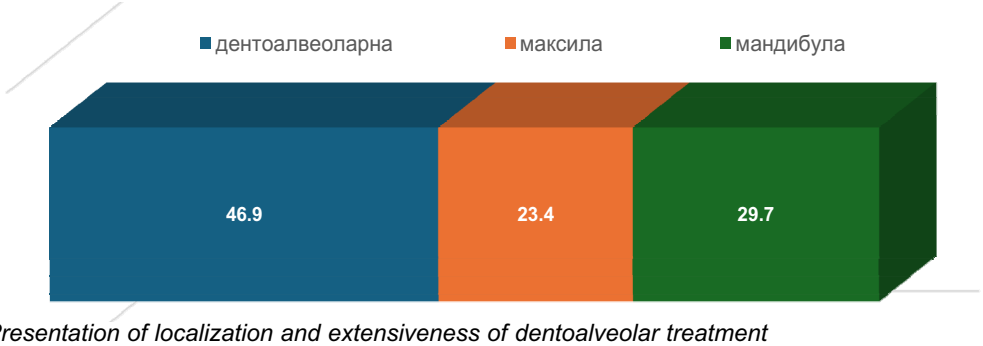
Table 4. Presentation of average bleeding time before diagnosis/days after TXA application and local hemostasis methods/ hours

	No.	average	Med	Min.	Max.	Std.Dev.	IQR/ rank	IQR rank
(BT) before diagnosis/days	64	5.9	4.0	1.0	14.0	3.995502	2.5	9.5
(BT) after TXA application/ hours	62	5.1	4.0	0	30.0	5.741133	1.0	7.0

*(BT) Bleeding time

Table 5. Analyzing the effectiveness of i.v. application of TXA and local hemostasis methods following tooth extraction correlation with bleeding time. Presentation of T-test for Dependent Samples between preoperative versus post-extraction bleeding time

Bleeding time	Mean	Std.Dv.	N	Diff	Std.Dv. - Diff.	t	df	p	Confiden. - 95.000%	Confiden. +95.000%
Before diagnosis	138.97	94.52677								
After i.vapplication of TXA	5.1	5.74113	62	133.8871	93.00293	11.33543	61	0.000000	110.2688	157.5054



Graph 1. *Presentation of localization and extensiveness of dentoalveolar treatment*

(12.5%) patients; Light intensity was registered in 54 (84.4%) versus (1.6%) only in one patient before achieving diagnosis (p<.05; Diff. test, p = ,0000); Moderate bleeding intensity was registered in two (3.1%) patients vs. pre-diagnosis in 34 (53.1%) patients (p<.05; Diff. test, p=.0000) (Table 3.).

The average bleeding time before dentoalveolar procedure in patients is 6 ± 4 days, ranging from one to 14 days. In 50% of patients, the bleeding is over 4 days (Me=4 IQR (2.5-9.5) (Table13.). The average post-extraction bleeding time in patients after establishing the diagnosiswas 5.1±5.7 hours, ranging from 0 to 30 hours, but only light bleeding. A high standard deviation is registered, which indirectly speaks of large variations of the statistical units around the average value. In 50% of patients, the bleeding is under 4 hours (Me=4 IQR (1-7) (Table 4.).

The difference between prediagnostic bleeding (expressed in hours) versus postextraction bleeding is statistically significant for p<.05 (p=.000000) (Table 5.).

Out of a total of 64 patients who underwent surgery, in 30 (46.9%) dentoalveolar surgery (cystectomies, impacted tooth extraction) was performed; and maxillary single tooth extractions in 15 (23.4%) and in mandibulae, 19 (29.7%).

The difference between dentoalveolar surgery versus maxilla and dentoalveolar versus mandible is significant for p<.05 (Difference test, p=.0054, p=.0453), the other differences are not significant (Graph 1.).

A significant association was registered between the registration of postextraction bleeding time and the localization and extensiveness of the treatment before proper diagnostic protocol (Chi Square, =9.39950, df=2, p=.009098) (Table 6.)

Post-extraction bleeding in the dentoalveolar procedure, after performing complete protocol (systemic and local hemostatic methods), lasts 5.0±5.9 hours, in the maxilla 6.7±2.7 and in the mandible 3.9±7.1, withoozing and light intensity.The difference in the duration of bleeding in relation to the localization of the extraction and extensiveness

Table 6. Contingency table for bleeding event in relation with localization and extensiveness of treatment

BT	Dentoalveolar procedures	maxillae	Mandibulae	total
No bleeding	2	0	6	8
Prolongated bleeding	28	15	13	56
total	30	15	19	64

Table 7. Presentation of bleeding time in relation to localization of extraction and extensiveness of treatment, after performing complete protocol (systemic and local hemostasis methods)

Dentoalveolar procedures	average	No	St.dev	Min.	Max.
Dentoalveolar surgery	5.0	29	5.916080	0	30.0
maxilla	6.7	15	2.716791	2.0	12.0
mandibula	3.9	18	7.128145	0	30.0

of treatment: significantly longer in the maxilla in relation to the mandible and dentoalveolar (Kruskal-Wallis test: H (2, N= 62) =11.48415 p =.0032) (Table 7.).

According to the dynamics index, a 530% increase in oozing and light intensity PEB,was registered compared to the PEB before achieving diagnosis.

According to the dynamism index, the rate of decrease in the light intensity of PEB is registered by 94.1% in relation to the pre-diagnosing moment.Tranexamic acid demonstrated a significantly lower risk of developing postoperative bleeding events (OR 0.27, P=0.007). Based on the comparative statistical analysis of the diseases of the most frequently used dose of TXA (1-1,5gr)/one dose before intervention in 92% of the patients, the need for second dose was registered only in 2 patient (3%) and it was due to comorbidities (1 patient with cirrhosis and the second one with diabetes mellitus).

Discussion

In daily practice, dental practitioners frequently meet patients with platelet hypoaggregability, suffering from excessive bleedings after dentoalveolar procedures. Currently, guidelines regarding the diagnosis or treatment of patientsare a great challenge in order to achieve a systemic and local hemostatic measures[15]. We performed a review of all relevant literature from 2013-2023 for managing platelet hypoaggregability and comparingto our results[16].Alamelu J. et al.[16], reported that most often, 88.8% of the cases were diagnosed due to gingival bleeding and his high percentage is due to dentoalveolar surgery. Further in the study, she confirmed that 80 - 90% of the patients have a normal number of platelets, but have reduced values of ADP, collagen and ristocetin, as a high-risk factor of bleeding. In agreement with all other authors, we confirm that reduced levels of ADP, Collagen and Ristocetin as a significant predictors for diagnosis in all patients: ADP/36.6±13.3, range: (7.0-60.0); <39.5 (Me=39.5 IQR(24.5-47), Ristocetin / 61.4±14.0, range: (23- 86.0); <65.0 (Me=65.0 IQR(51-71) and Collagen/ 49.1±15.5, range: (19.0 - 90.0); <50.0 (Me=50.0 IQR(39-58), as a risk factors for diagnosing hypoaggregability and prolongated bleeding.

In addition, our results are consistent with the findings of allother authors, meaning that the decrease in levels of ADP, Collagen and ristocetin is directly proportional to prolonged and excessive bleeding (Table 2.). Moenen F. et al.[17], confirmed that in 86% of patients the difference was significantly lower in those with excessive bleeding than in controls for ADP (118±27 s vs 94±13 s, p=0.007); for ristocetin (mean±1 SD (range): 81±31 U dL−1 (36–163) vs. 92±32 (26–199) p=0.039 and for collagen, 97 (162; 51–191) p<0.001[18]. OnlyFrontroth JP et al[19], describe the results of the study, prove that the mean values for platelet aggregation responses to collagen, ADP, ristocetin within much

smaller reductions: (p=0,5; p=0,51 and p=0,6, respectively.

Evaluating the available literature for the usage of TXA as a hemostatic agent, and based on our experience for minimizing bleeding risk of periprocedural dentoalveolar surgeries, we confirmed 530% increase in the light intensity bleeding after TXA application compared to the pre-diagnosing extractions, and decrease in the moderate intensity of postextraction bleeding in 94.1% versus pre-diagnosing extractions bleeding, according to the dynamics index. After i.v. application of TXA, performing dentoalveolar surgery and implementation of local hemostasis measurement, heavy bleedings were not registered postextraction compared to bleeding time and intensity before diagnosis. Oozing bleeding was significantly dominant in 84.4%versus 1.6% before achieving the diagnosis (p<.05; Diff. test, p=.0000); moderate intensity ofbleeding was registered in 3.1% patients vs. pre-diagnosis in 53.1% (p<.05; Diff. test, p=.0000)[20]. Several randomized studies in many different fields of surgery have confirmed its efficiency innoteworthy reduction in post-operative bleeding following dental extraction when TXA was used, in addition to topic TXA and suturing the postextraction wound. Patients receiving TXA showed a decrease in postoperative bleeding (SMD= -0.26, 95% CI -0.51 to -0.01, p=0.04) and following the grade rating system, the quality of evidence of bleeding wasobserved as oozing and low, respectively[21]. Contrary to our findings only Lam et al.[7], following the grade of quality of evidence of bleeding, she observed thatthe intensity is moderate 13% and low in 78%, respectively,contrary toour results, oozing in 84.4% and moderate in 3.1% patients, perhaps this is due to the inconsistency of the group of patients.

The average bleeding time before establishing the diagnosis in our study was 6 ± 4 days, (Me=4 IQR (2.5-9.5) and after usage of TXA is 5.1±5.7 hours, range: 0 - 30 hours (Me=4 IQR (1-7) (Table 3.). The percentage difference is significant between heavy bleeding vs. light and moderate vs. light bleeding for p<.05 (Difference test, p=.0000). (Table 1.). These findings are in accordance with previously reported figures, which proved significant difference (p<0.001- 0,003) and established the usage of TXA as a most important in achieving postextraction hemostasis in thrombocyte patients with hypoaggregability[22].

Exploring the extensiveness and type of the surgery (single-tooth extraction or extraction of impacted tooth, and cystectomies) and prevalence of post-operative bleeding event, in our study: out of total of 64 patients/30 (46.9%) underwent dentoalveolar surgery (cystectomies, impacted tooth extraction); maxillarysimple tooth extractions 15 (23.4%) and mandibular single tooth extraction, 19(29.7%). Our results confirm significant difference in incidenceof PEB in dentoalveolar surgery versus maxilla and mandible p<.05 (Dif. test, p=.0054, p=.0453), duration of BT after dentoalveolar surgeries was two times more than single tooth extractions. In our study, we confirm the significant association between PEB and the localization and extensiveness of the treatment after proper diagnostic protocol (systemic and local hemostatic methods), TXA (Chi Square, = 9.39950, df=2, p=.009098).PEB in dentoalveolar procedure lasts 5.0±5.9 hours, in the maxilla 6.7±2.7 and in the mandible 3.9±7.1, with oozing and light intensity and doesn't require additional hemostatic measures[23,24]. The difference in BT, in relation to the localization of the extraction and extensiveness of the treatment was significantly longer in the maxilla,related to the mandible (Kruskal-Walli's test: H (2, N= 62) =11.48415 p=.0032). Our finding is result of not consistent group of dental extraction like in other studies where the prevalence of bleeding is much more frequent in the mandibula than in the maxilla 62-83% vs 38-17%, respectively. Ockerman A. et al.[25], confirmed the reduction in delayed bleeding after multiple extractions (rate ratio, 0.40; 95% CI, 0.20 to 0.78) to be lower in the TXA group[26]. The analysis of all processed dates present in study data shows that in total of 64 dentoalveolar procedures, theprimary bleeding was stopped. There was no difference related to the location or extensiveness (whether it is a single-tooth extraction or dentoalveolar surgery), implementation ofthe correct diagnosis, preoperative preparation with TXA and the use of local hemostatic methods, lead to reliable, safe and secure dealing with PEB[27].

Conclusions

Determination of reduced levels of ADP, ristocetin and collagen as a significant predictor for bleeding, and systemic and local usage of TXA is effective and safe in minimizing the risk of bleeding event after performing dentoalveolar surgery. The close collaboration with the Transfusion Medicine Institute is the only successful pathway for managing patients with thrombocyte hypo aggregability. Management of perioperative bleeding is complex and involves multiple assessment tools and strategies to ensure optimal patient care with the goal of reducing morbidity and mortality. Future studies should focus on genetical investigation to assess the precise diagnosis forthe condition platelethypoaggregability and targeted therapy to impair the long-term impact on reducing the PEB complications.

Reference

1. Tunkel DE, Anne S, Payne SC, Ishman SL, Rosenfeld RM, Abramson PJ, et all. Clinical Practice Guideline: Nosebleed (Epistaxis). Otolaryngol Head Neck Surg. 2020 Jan;162(1_suppl):S1-S38. doi: 10.1177/0194599819890327. PMID: 31910111

2. Kirchmaier CM, Pillitteri D. Diagnosis and Management of Inherited Platelet Disorders. Transfus Med Hemother. 2020;37(5):237-246.
3. 3.Hong P, Liu R, Rai S, Liu J, Ding Y, Li J. Does Tranexamic Acid Reduce the Blood Loss in Various Surgeries? An Umbrella Review of State-of-the-Art Meta-Analysis. Front Pharmacol. 19 (13):887386, 2022.
4. 5. Danilatou V, Zubair M. Laboratory Evaluation of Coagulopathies. [Updated 2024 Jul 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. [53,54].
5. Colomina MJ, Contreras L, Guilabert P, Koo M, Ndez E, Sabate A. Clinical use of tranexamic acid: evidence and controversies. Braz J Anesthesi. 2022 Nov-Dec; 72 (6):795-812
6. Lam T, Medcalf RL, Cloud GC, Myles PS, Keragala CB. Tranexamic acid for haemostasis and beyond: does dose matter? Thromb J. 2023 Sep 12;21(1):94.
7. Franco R, Miranda M, Di Renzo L, De Lorenzo A, Barlattani A, Bollero P. Glanzmann's Thrombastenia: The Role of Tranexamic Acid in Oral Surgery. Case Rep Dent. 2018 Sep
8. Mahardawi, B., Jiaranuchart, S., Arunjaroensuk, S. et al. The effect of different hemostatic agents following dental extraction in patients under oral antithrombotic therapy: a network meta-analysis. Sci Rep 13, 12519 (2023)
9. Kietaibl S, Ahmed A, Afshari A, Albaladejo P, Aldecoa C, Barauskas G, De Robertis E, Faraoni D, Filipescu DC, Fries D, Godier A, Haas T, Jacob M, Lancé MD, Llau JV, Meier J, Molnar Z, Mora L, Rahe-Meyer N, Samama CM, Scarlatescu E, Schlimp C, Wikkelsø AJ, Zacharowski K. Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care: Second update 2022. Eur J Anaesthesiol. 2023 Apr 1;40(4):226-304.
10. Mathews N, Rivard GE, Bonnefoy A. Glanzmann Thrombasthenia: Perspectives from Clinical Practice on Accurate Diagnosis and Optimal Treatment Strategies. J Blood Med. 2021; 12:449-463.
11. Neuenfeldt FS, Weigand MA, Fischer D. Coagulopathies in Intensive Care Medicine: Balancing Act between Thrombosis and Bleeding. J Clin Med. 2021 Nov 18;10(22):5369
12. Poon MC, d'Oiron R, Zotz RB, et al. The international, prospective Glanzmann thrombasthenia registry: treatment and outcomes in surgical intervention. Haematologica. 2015;100(8):1038–1044. doi: 10.3324/haematol.2014.121384.
13. Kumbargere Nagraj S, Prashanti E, Aggarwal H, Lingappa A, Muthu MS, Kiran Kumar Krishanappa S, Hassan H. Interventions for treating post-extraction bleeding. Cochrane Database Syst Rev. 2018 Mar 4;3(3):CD011930
14. Gupta A, Epstein JB, Cabay RJ. Bleeding disorders of importance in dental care and related patient management. J Can Dent Assoc. 2007 Feb;73(1):77-83.
15. DuangratO,Patompong U, Weerapat O . Efficacy of local tranexamic acid treatment for prevention of bleeding after dental procedures: A systematic review and meta-analysis, Journal of Dental Sciences, Volume 14, Issue 1, March 2019, Pages 21-26.
16. Alamelu J, Liesner R. Modern management of severe platelet function disorders. Br J Haematol2019; 149:813–23. 10.1111/j.1365-2141.11
17. Moenen FC, Vries MJ, Nelemans PJ, van Rooy KJ, Vranken JR, et all. Screening for platelet function disorders with Multiplate and platelet function analyzer. Platelets. 2019; 30(1):81-87.
18. Heidbüchel H, Thijs V, Verhamme P, Hermans C, Peeters A, Scavée C. Practical guide dabigatran: guidance for use in particular situations.
19. Frontroth JP, Favaloro EJ. Ristocetin-Induced Platelet Aggregation (RIPA) and RIPA Mixing Studies. Methods Mol Biol. 2017; 1646:473-49420. Engelen ET, Schutgens RE, Mauser-Bunschoten EP, van Es RJ, van Galen KP. Antifibrinolytic therapy for preventing oral bleeding in people on anticoagulants undergoing minor oral surgery or dental extractions. Cochrane Database Syst Rev. 2018 Jul 2;7(7):CD012293.
20. Lewandowski, B., Myszka, A., Migut, M. et al. Analysing the effectiveness of topical bleeding care following tooth extraction in patients receiving dual antiplatelet therapy-retrospective observational study. BMC Oral Health 21, 31 (2021
21. Abdullah WA, Khalil H. Dental extraction in patients on warfarin treatment. Journal of Clinical, Cosmetic and Investigational Dentistry, 2014;6:65-9.
22. Kumbargere NS, Prashanti E, Aggarwal H, Lingappa A, Muthu MS, Kiran Kumar Krishanappa S, Hassan H. Interventions for treating post-extraction bleeding. Cochrane Database Syst Rev. 2018 Mar 4;3(3):CD011930.
23. van Galen KP, Engelen ET, Mauser-Bunschoten EP, van Es RJ, Schutgens RE. Antifibrinolytic therapy for preventing oral bleeding in patients with haemophilia or Von Willebrand disease undergoing minor oral surgery or dental extractions. Cochrane Database Syst Rev. 2015 Dec 24;(12):CD011385
24. Ockerman lA., M. Vanhaverbeke, I. Miclotte, A. Belmans, et all. Tranexamic acid to reduce bleeding after dental extraction in patients treated with non-vitamin K oral anticoagulants: design and rationale of the EXTRACT-NOAC trial. British Journal of Oral and Maxillofacial Surgery. 2019 Dec; 57(10): 1107-1112
25. Dignam P, Elshafey M, Jeganathan A, Foo M, Park JS, Ratnaweera M. Prevalence and Factors Influencing Post-Operative Complications following Tooth Extraction: A Narrative Review. Int J Dent. 2024 May 9; 2024:7712829
26. Heyns M, Knight P, Steve AK, Yeung JK. A Single Preoperative Dose of Tranexamic Acid Reduces Perioperative Blood Loss: A Meta-analysis. Ann Surg. 2021 Jan 1;273(1):75-81.
27. Engelen ET, Schutgens RE, Mauser-Bunschoten EP, van Es RJ, van Galen KP. Antifibrinolytic therapy for preventing oral bleeding in people on anticoagulants undergoing minor oral surgery or dental extractions. Cochrane Database Syst Rev. 2018 Jul 2;7(7):CD012293