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Discontinuation of Oral Antiplatelet Agents before Dental Extraction - Necessity or Myth?

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Background: The risk of excessive bleeding often prompts physicians to interrupt the antiplatelet agents as acetylsalicilyc acid and clopidogrel before dental extractions which puts patients at risk of adverse thrombotic events.

Aim: To assess the bleeding risk during dental extractions in patients with continued antiplatelet therapy.

Materials and methods: The study included 130 patients (64 men and 66 women) aged between 18 and 99 years old. Sixty-eight of the patients received 100 mg acetilsalicilic acid (ASA); these were divided into two groups: 34 patients continued taking ASA and 34 patients stopped it 72 hours before extraction. Sixty-two of the patients were treated with 75 mg clopidogrel; these were also divided into two groups: 31 continued taking clopidogrel and 31 patients stopped it 72 hours before extractions. Extraction was performed under local anaesthesia as no more than 3 teeth per visit were extracted. Local haemostasis with gelatine sponge and/or suturing was used to control bleeding.

Results: Mild bleeding was observed most frequently in the first 30 minutes, successfully managed by local haemostasis. Only 1 patient in the control and 1 in the experimental group receiving ASA reported mild bleeding in the first 24 hours, controlled by compression with gauze. No major haemorrhage requiring emergency or more than local haemostasis occurred. No statistically significant difference in bleeding between two groups was found.

Conclusion: Single and multiple dental extractions in patients receiving acetylsalicylic acid or clopidogrel can be safely performed without discontinuation of the therapy with provided appropriate local haemostasis.

BACKGROUND

Cardiovascular and cerebrovascular diseases are the leading cause of mortality and disability worldwide, causing annually about one-third of all deaths on Earth. They cause over 47% of deaths in Europe and over 60% of all deaths in Bulgaria.[1,2]

Antiplatelet therapy is essential in the treatment and prevention of these diseases - it reduces blood clotting and prevents serious thromboembolic complications.

Many patients in dental practice receive antiplatelet medications and the need of teeth extraction is very common, while treatment protocol is still controversial and dental care is often delayed due to fear of complications.[3]

Clinical trials involving tooth extractions in patients on antiplatelet therapy have been conducted for many years, the standard practice in the past being the interruption of antiplatelet agents for 3 to 7 days before tooth extraction to reduce the bleeding risk.[4] Current guidelines advice against interruption of antiplatelet agents prior to dental extraction.[5-7] However, there is still no clear evidence of the safest approach for these patients.

AIM

The aim of the present study was to evaluate bleeding after single or multiple tooth extraction in patients on monotherapy with acetylsalicylic acid (100 mg.) or clopidogrel (75 mg) once daily and to determine the need of discontinuation the therapy prior to dental extraction.

MATERIALS AND METHODS

Material

The study recruited 130 patients on monotherapy with acetylsalicylic acid (100 mg) or clopidogrel (75 mg) once daily for at least the past six weeks, referred to the Department of Oral Surgery at the Faculty of Dental Medicine for single or multiple tooth extraction between 2012 and 2015.

Exclusion criteria included patients with: concomitant treatment with other hemostasis altering drugs, acute inflammation in the area of the tooth extraction, hypertension > 160/100 mm Hg, heart rate > 100, kidney disease, diabetes, liver disease, stroke/heart attack less than six months before surgery, prior major bleeding, thrombocytopenia, hemophilia or other disorders of hemostasis, and with concomitant therapy with cytotoxic drugs.

Patients

Patients were divided into:

- *Group A:* 68 patients receiving ASA 100 mg, divided into group A1 - 34 patients who continued ASA intake and group A2 - 34 patients in which ASA was discontinued 72 hours before the extraction.
- *Group B:* 62 patients receiving clopidogrel 75 mg daily, divided into group B1 - 31 patients who did not stop clopidogrel and group B2 - 31 patients in which clopidogrel was discontinued 72 hours before dental extraction.

Methods

All the patients had given their written informed consents before treatment.

For safety reasons, without changing or interrupting antiplatelet therapy it was accepted to extract no more than 3 single rooted teeth, 2 multi-rooted teeth; or a surgical extraction of one tooth per visit. In case of need of extraction of more teeth, several visits were planned.

Degree of surgical trauma was determined as follows: 1 - extraction of tooth with 1 root; 2 - extraction of tooth with 2 roots; 3 - extraction of tooth with 3 roots; 4 - surgical extraction; as in case of numerous extractions degree of trauma is computed.

Patients requiring prophylaxis of infective endocarditis had received amoxicillin 2.0 g one hour preoperatively in accordance with recommendations of the American Heart Association.[8,9]

Hemostasis evaluation

Bleeding time is only in vivo method for assessing platelet function and antiplatelet therapy. Multiple literature data and many current studies indicate that increased bleeding time is not necessarily associated with increased bleeding during and after tooth extraction.

There is enough evidence to advise against using it as a screening method for determining the bleeding risk in patients receiving antiplatelet agents.[10-14] At present, there is no suitable assay for routine evaluation of the haemostasis in these patients.[11,15]

For this reason, evaluation of antiplatelet therapy by laboratory tests is not included in the present study.

All patients underwent treatment under local anesthesia with articaine hydrochloride - 40 mg/ml (4%) combined with adrenaline hydrochloride (equivalent to 0.005 mg adrenaline) - 0.006 mg. For each patient a maximum of 2 cartridges of 1.7 ml anesthetic solution was used. Because of the risk of hematoma formation during injection, mandibular block was avoided and periodontal ligament injection was used when possible **(Fig. 1)**.[16,17]

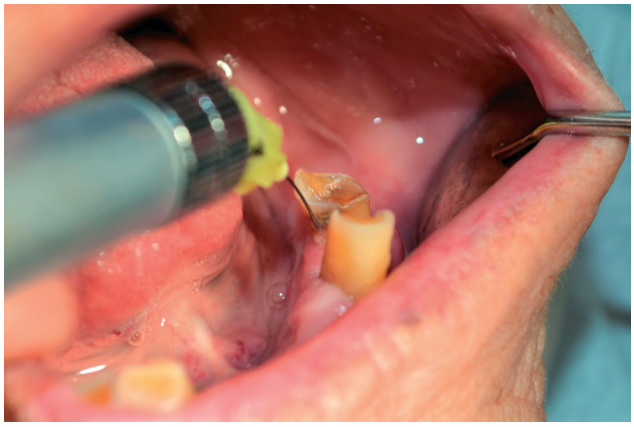

Figure 1. Periodontal ligament injection.

Initial control of postextraction bleeding was achieved by compression with sterile gauze for 6-10 minutes followed by replacement with new one in case of persisting bleeding. Patients were asked to keep it for at least 30 minutes. Gelatin sponge and suturing of the extraction wound with non-absorbable sutures (polyamide 3/0) were used in case of persistent bleeding **(Figs 2, 3).**

Patients were monitored for an hour for control and detection of immediate bleeding. In the postoperative period, they were instructed, if bleeding continues or resumes, to apply pressure by biting gauze for 20 minutes. In case of uncontrolled bleeding they were to contact a doctor immediately.

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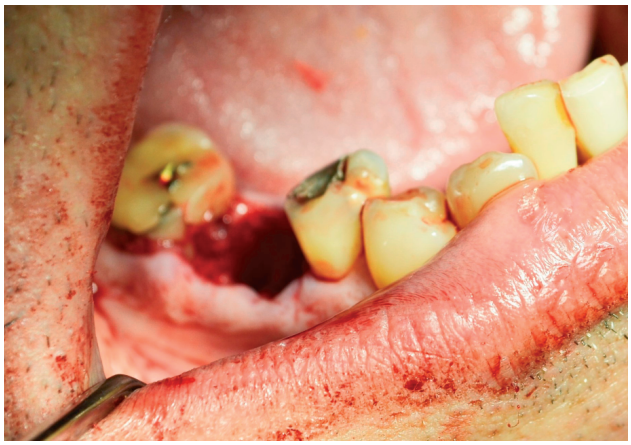

Figure 2. Postextraction socket.

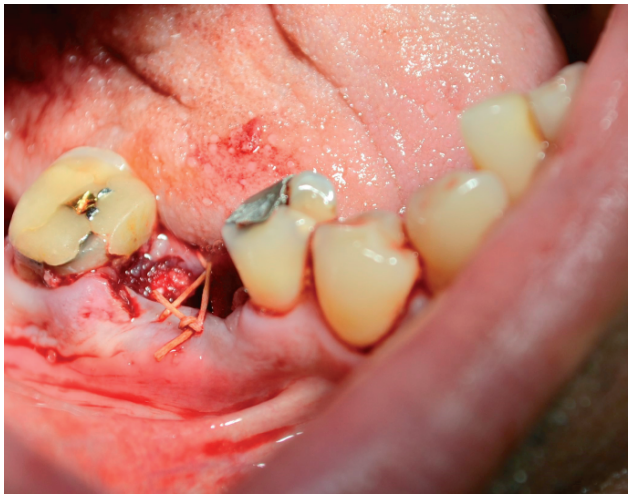

Figure 3. Local hemostasis with gelatin sponge and suture.

Paracetamol (500 mg in doses of 1-2 tablets 3-4 times daily) was prescribed for pain control.

The presence of bleeding was assessed at 1, 24, and 48 hours, and day 7.

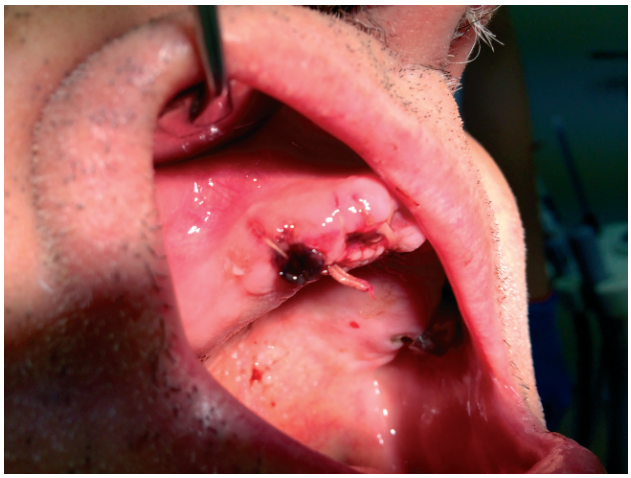

Figure 4. Liver clot.

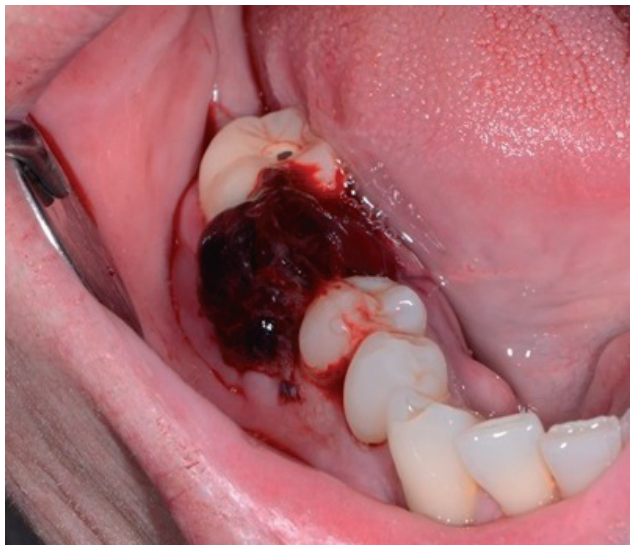

Figure 5. Liver clot.

Oozing from extraction site or presence of liver clot was considered bleeding **(Figs 4, 5).**

If local hemostasis with gelatin sponge and suture proved insufficient, tamponade of the extraction wound, electrocoagulation, and if needed - intravenous platelet transfusion was performed.[18]

Bleeding was considered clinically significant if it lasted more than 12 hours, had made the patient seek emergency care, had led to the formation of a large hematoma in the soft tissues or necessitated platelet transfusion.[18]

Statistical Analysis

Statistical software SPSS v.22.0 was used for statistical analysis.

Parametric methods for evaluation of the statistical relationships: Student's t-test; paired simple t-test; analysis of variance (one-way ANOVA); correlation analysis; coefficient of linear correlation r (coefficient of Pearson)

Non-parametric methods for assessing the statistical significance: Fisher's exact test; chi-square (χ^2) criterion; Mann-Whitney test; Kruskal-Wallis test.

RESULTS

Group A

Characteristics of the patients in Group A are presented in **Table 1**.

Most often indication for therapy with ASA (35.5% in A1, 20.6% in A2) was ischemic heart disease (acute coronary syndrome, myocardial infarction, angina pectoris), followed by heart rhythm disorders (23.5% in A1, 26.5 % A2); cerebrovascular

Table 1. Characteristics of group A patients

Characteristics		Group A1 number	Group A1 %	Group A2 number	Group A2 %
Included patients	68 (100%)	34	50 %	34	50 %
Sex	Male	16	47.1%	15	44.1%
	Female	18	52.9%	19	55.9%
Age	to 60 years	6	17.6%	6	17.6%
	61-70 years	15	44.1%	14	41.2%
	71-80 years	10	29.4%	9	26.5%
	Over 80 years	3	8.8%	5	14.7%

accident A1 11.8%; A2 14.7%; peripheral vascular disease A1 8.8 percent; A2 11.8%; heart failure A1 11.8%; A2 5.9%; Valvular diseases/prosthetics A1 8.8 percent; A2 2.9%; Ischemic cerebrovascular disease A1, 0%; A2 17.6%; Percutaneous angioplasty and vascular stenting A1 5.9%; A2 5.9%; ischemic cardiomyopathy A1, 0%; A2 8.8%; joint replacement A1 5.9%; A2, 0%.

A leading diagnosis requiring dental extraction was radix gangraenosae (55.9% in both groups), followed by teeth with third degree mobility (29.4% A1; 35.3% A2) and teeth with periapical lesions

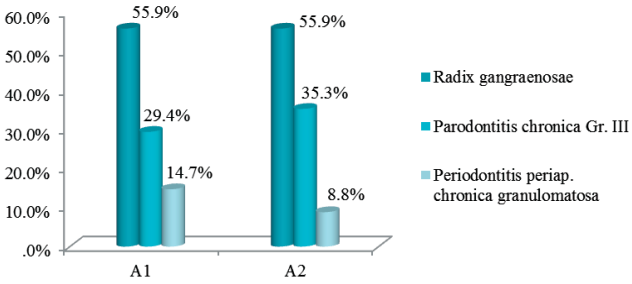

Figure 6. Distribution by surgical diagnosis requiring teeth extraction in groups A1 & A2.

(14.7% A1; 8.8% A2) **(Fig. 6)**.

80% of the patients in group A1 and 68% in the group A2 had 1 tooth extracted per visit. The degree of trauma in 44% of patients in group A1 was 1, 32.4% had degree of trauma 2 and 20.6% - 3. Only 1 patient in group A1 had highest degree of trauma 5. One-third of patients in group A2 had trauma defined as 1, 25% as 2 and 41.2% patients were with trauma 3. Only 1 patient in group A2 suffered the highest degree of trauma – 4. **(Fig. 7)**.

In both groups most of the extractions were accomplished within 5 min. (A1 67.6%, A2 67.6%)

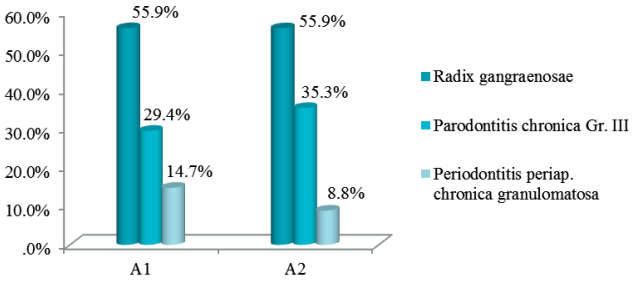

Figure 7. Number of extracted teeth and level of surgical trauma inflicted in groups A1 & A2.

In more than two-thirds of the patients in both groups (67.6% in A1 and 73.5% in A2) no additional

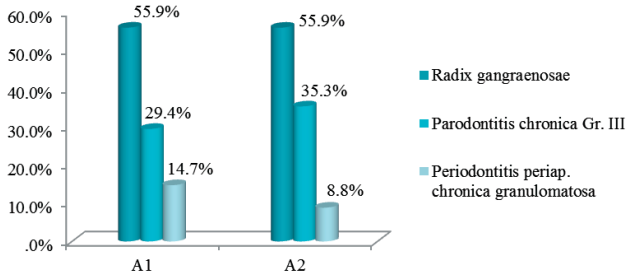

Figure 8. Local haemostatic measures in groups A1 & A2.

local haemostatic measures were needed **(Fig. 8)**.

Most frequently, bleeding stopped within the first 10 min. after the extraction (A1 23.5%, A2 26.5%). Bleeding for more than 10 min. but less than 30 min. was observed in only 5.9% in the two groups. Only two patients, one in group A1 and on in group A2, had clinically significant bleeding (more than 12 hours after extraction). None of the patients reported bleeding 24 hours after surgery

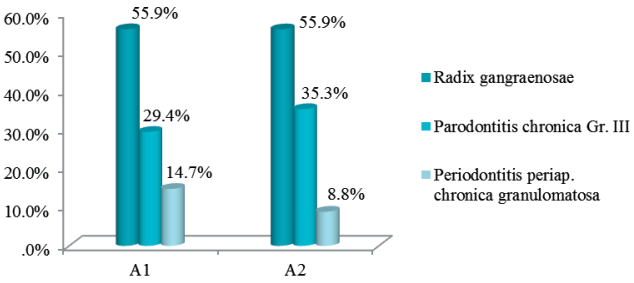

Figure 9. Postextraction bleeding in Group A1 & A2.

and did not seek additional help **(Fig. 9)**.

No statistically significant difference in the postoperative bleeding was found between the two groups (P<0.05). Postextraction bleeding in all cases was managed by gelatin sponge and/or suture placement.

Group B

The characteristics of group B patients are shown in **Table 2**.

Table 2. Characteristics of group B patients

Characteristics		Group B1 number	Group B1 %	Group B2 number	Group B2 %
Included patients	62 (100%)	31	50.0%	31	50.0%
Sex	Male	19	61.3%	14	45.2%
	Female	12	38.7%	17	54.8%
Age	to 60 years	4	12.9%	5	16.1%
	61-70 years	13	41.9%	14	45.2%
	71-80 years	9	29.0%	8	25.8%
	Over 80 years	5	16.1%	4	12.9%

The mean age of the patients in Group B was 69.52 ± 8 yrs. The distribution by sex in group B1 was 61.3% male and 38.7% female compared to 45.2% male and 54.8% female in group B2.

Most often, indication for antiplatelet therapy with clopidogrel were: ischemic heart disease (acute coronary syndrome, myocardial infarction, angina pectoris), 45.2% in B1 and 38.7% in B2; deep vein thrombosis in 12.9% in B2; percutaneous angioplasty and vascular stenting, 3.2% in B1 and 12.9% in B2; coronary artery bypass surgery: 3.2% in B1 and 6.5% in B2; valvular diseases/ prosthetics at 3.2% in B1 and 3.2% in B2; heart rhythm disorders in 12.9% of B1 and 16.1% in B2; ischemic cerebrovascular disease in 3.2% in both subgroups; cerebrovascular accident occurred in 35.5% in B1 and 6.5% in B2; peripheral vascular disease in 6.5% in B1 and 12.9% in B2; heart failure in 3.2% in both subgroups.

Leading diagnosis for extraction was radix gangraenosae (71%), followed by teeth with third degree mobility (25.8%) and teeth with periapical lesions (3.2%) in both groups **(Fig. 10)**.

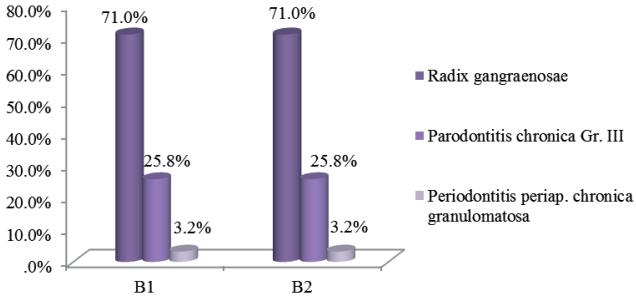

Figure 10. Distribution by diagnosis requiring teeth extraction in groups B1 & B2.

In group B1 67% of the patients had single tooth extraction. In group B1, 12.9% of the patients had extraction of 3 teeth, while in B2 most frequently (54.8%) 2 teeth were extracted, followed by 45% of patients with single tooth extraction per visit .

Surgical trauma in more than one-third of patients in subgroup B1 was 3 (32.3%), followed by 2 (29%) and 1 (29%). More than half of patients in B2 had trauma 2 (51.6%). Highest degree of trauma 6 was inflicted on one patient in each group **(Fig. 11).**

In both groups most extractions were performed within 5 min. (B1 58.1%, B2 61.3%)

Half of the patients in both groups (A1 48.4%, A2 58.1%) did not need suture or gelatin sponge

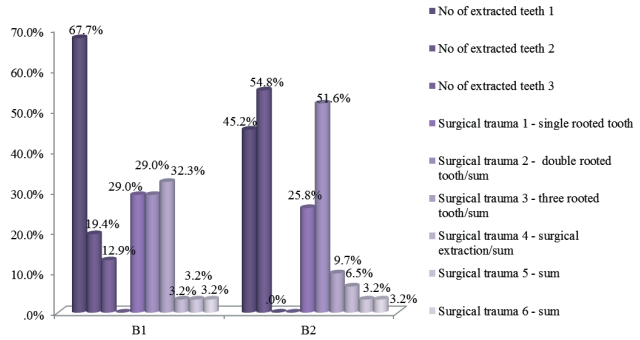

Figure 11. Number of extracted teeth and level of surgical trauma inflicted in groups B1 & B2.

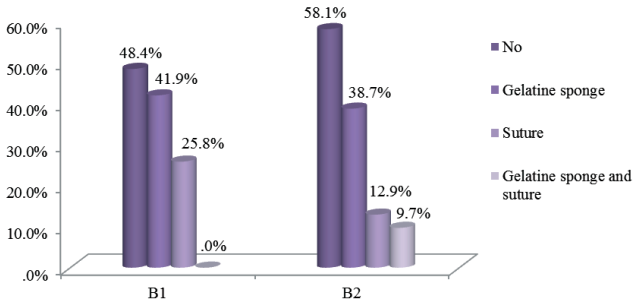

Figure 12. Local haemostatic measures in groups B1 & B2.

for control of bleeding **(Fig. 12)**.

In patients on monotherapy with clopidogrel bleeding occurred mainly in the first 10 min. after extraction (26% B1; 20% in B2). Only one patient from group B1 had bleeding for 30 minutes. None of the patients reported late bleeding **(Fig. 13)**.

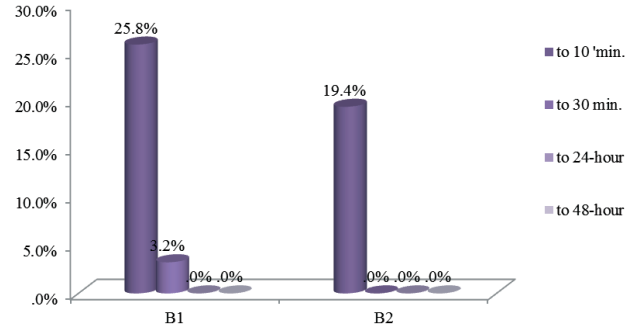

Figure 13. Postextraction bleeding in Group B1 & B2.

No statistically significant difference in the postoperative bleeding was found between the two groups ($P<0.05$).

DISCUSSION

The majority of the patients in both groups had blood pressure above normal range which can cause bleeding. In case of blood pressure above 160/100 mm Hg RR extraction of teeth was postponed due to the increased risk of bleeding.[19,20]

Using periodontal injection was based on several recommendations for avoiding block anaesthesia in patients receiving antiplatelet drugs due to the risk of soft tissue haematoma formation.[16,17,21]

Patients most commonly underwent single tooth extraction, and from here the level of inflicted trauma was often low, which was in accordance with the recommendations of many authors for limitation the risk of bleeding by decreasing the surgical trauma.[22]

Extraction in most patients was rapid, which could also influence postextraction bleeding.[23]

Local haemostasis with gelatin sponge and/or suture placement in the group treated with ASA was used rarely, and in the group receiving clopidogrel in nearly half of the patients. It was sufficient to control bleeding.

In both groups, bleeding most commonly was observed in the first 10 minutes; lasted 30 min. in 5 patients, as all cases were easily controlled by gelatin sponge and/or suturing. Only 2 patients in group A reported mild bleeding in the first 24 hours, but did not require additional haemostasis and had stopped spontaneously. None of the patients receiving clopidogrel had late bleeding.

No statistically significant difference in postoperative bleeding was found between group A1 and A2 and B1 and B2 **(Table 3)**.

CONCLUSIONS

1. In patients on monotherapy with ASA 100 mg. or clopidogrel 75 mg a day single or multiple teeth extraction can be performed without risk of uncontrolled bleeding, provided that additional bleeding causing factors are excluded.
2. No statistically significant difference in postextraction bleeding between patients taking ASA or clopidogrel and those who discontinued the therapy before the extraction was found.
3. Local haemostasis with gelatin sponge and/or sutures was sufficient in 100% of cases for control of postextraction bleeding in patients on monotherapy with ASA or clopidogrel.

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Table 3. Postoperative bleeding in both groups

	ASA 0.1			Clopidogrel 0.75		
	Group A1 (n=34)	**Group A2 (n=34)**	**p**	**Group B1 (n=31)**	**Group B2 (n=31)**	**p**
Postoperative bleeding in the first 10 min.	8 (24%)	9 (27%)	0.783	8 (26%)	6 (19%)	0.551
Postoperative bleeding in the first 30 min.	2 (6%)	2 (6%)	1.000	1 (3%)	0 (0%)	0.325
Postoperative bleeding in the first 24h	1 (3%)	1 (3%)	1.000	0 (0%)	0 (0%)	-
Postoperative bleeding in the first 48h	0 (0%)	0 (0%)	-	0 (0%)	0 (0%)	-

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Прекращение приёма пероральных антитромбоцитарных препаратов перед экстракцией зубов – необходимость или миф?

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Введение: Возможность обильного кровотечения часто заставляет врачей прекращать приём таких антитромбоцитарных препаратов, как ацетилсалициловая кислота и Клопидрогель перед экстракцией зубов и тем самым подвергают пациента риску нежелательных тромбоцитных явлений.

Цель: Целью настоящего исследования является оценка риска кровотечения во время экстракции зубов у пациентов с продолжающейся антитромбоцитарной терапией.

Материал и методы: В исследовании приняли участие 130 пациентов в возрасте от 18 до 99 лет, 64 мужчины и 66 женщин. 68 пациентам, распределённым в две групы, был назначен приём ацетилсалициловой кислоты в дозе 100 мг.: 34 пациента продолжили приём АСК, а остальным 34 пациентам прекратили приём за 72 часа до экстракции. 62 пациентам, распределённым в две группы, был назначен приём Клопидрогеля в дозе 75 мг.: 31 продолжили приём Клопидрогеля, а 31 прекратили приём за 72 часа до экстракции. Экстракция была осуществлена под местным наркозом с удалением не более трёх зубов в рамках одного посещения. Был использован локальный гемостаз желатиновой губкой и/ или наложением швов для контроля кровотечения.

Результаты: Лёгкое кровотечение наблюдалось чаще всего в течение первых 30 минут и было успешно приостановлено с помощью локального гемостаза. Только один пациент в контрольной группе и один в экспериментальной, которые принимали АСК, сообщили о лёгком кровотечении в рамках первых 24 часов после экстракциии, которое было приостановлено прижатием марлевым тампоном. Не наблюдалось случаев обильного кровотечения, требующих неотложной помощи или применения более серьёзных средств, чем локальный гемостаз. Не установлено статистически значимой разницы в кровотечении в обеих группах.

Заключение: Одиночные и множественные экстракции зубов у пациентов, принимающих АСК или Клопидрогель, могут осуществляться без опасности для пациента с обеспечением локального гемостаза без прекращения терапии.

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