ASSESSMENT OF EFFECTS OF ANTIPLATELET DRUGS ON BLEEDING RISK AFTER TEETH EXTRACTIONS

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ABSTRACT
The aim of this study was to determine the bleeding risk after teeth extractions among patients on daily doses of Aspirin® (ASA) in the range of 75 mg to 300 mg. Forty-four patients, under antiplatelet treatment, referred to our clinic for teeth extractions. ASA interrupted 7 days before dental extractions served as control group (19 patients), while study group had their ASA regimen regularly administered (25 patients). Investigation of bleeding time (BT) was performed on the day of extractions. Managing postoperative bleeding differs from local pressure by gauze to locally applied tranexamic acid.

The mean BT was within normal limits in both groups. When compared in terms of BT, a statistical significance was found (p=0.001) between the groups. When compared in terms of bleeding control the difference between the groups was significant (p=0.008).

We may conclude that most minor oral surgery procedures can be carried out safely without interruption of long-term ASA regimen.


Keywords: antiplatelet drugs, bleeding complications, minor oral surgery

Introduction
The surgical management of the patient receiving oral antiplatelet drugs is an area of great interest to oral and maxillofacial surgeons. A significant percentage of the population receives antiplatelet therapy for prevention and treatment of thromboembolic diseases such as myocardial infarction, ischaemic stroke, peripheral arterial insufficiency (14, 16). Although antiplatelet medication include Aspirin® (ASA), clopidogrel, dipyridamole, non-steroidal anti-inflammatory drugs and cyclooxygenase-2 (COX-2) inhibitors, low dose ASA (75-300 mg, daily) is the most common medication, which is used for prophylaxis against arterial thrombosis (20, 23). ASA inhibits irreversibly platelet aggregation within one hour of ingestion and this lasts for the life of platelets (7-10 days). When platelets are inhibited it takes longer time for free blood flow from a cut to stop and for primary haemostasis to occur i.e the bleeding time (BT) is prolonged (8, 17, 20).

In the literature, most of the studies have suggested to stop ASA therapy because of the risk of prolonged bleeding after surgery (9, 12, 22). However, interruption of the drugs may increase the risk of serious thromboembolism, myocardial infarction or cerebrovascular accident (12, 13, 22). It has been a dilemma of whether antiplatelet therapy should be altered or not before minor oral surgery. Recently several authors suggested that ASA therapy can be maintained and subsequent postextraction haemorrhage are treated by local measures (3, 7, 15).

Although low dose ASA are used widely in patients with cardiovascular disease, the range is different and depend on the patients’ systemic conditions such as gastric intolerance. Most of the authors have reported the effect of lower doses of ASA without interruption of the treatment with ASA. However, there is no study on the effect of different daily doses of ASA after dental extractions without stopping the drug.

Few trials examined the bleeding that was secondary to dental procedures after therapy with daily doses of ASA in the range of 75 mg to 100 mg. However, there was only one study in the literature with ASA doses greater than 100 mg per day (3). The present study assessed the bleeding risk after dental extractions among patients on different daily doses of ASA in the range of 75mg to 300mg.

Materials and Methods
This study involved ninety-eight extractions in 44 patients who received ASA therapy with different indications, and who were referred to our clinic for dental extractions. All patients were randomly divided into two groups: patients with interrupted ASA therapy 7 days before dental extractions served as control group; while the study group consisted of patients taking ASA regimen regularly. Decision for interruption of the ASA therapy, were made by the patient’s cardiologist. Each group was divided into two subgroups according to the used daily dose of ASA (75-150mg and 150-300mg). The exclusion criteria were as follows: oral contraceptives, hormone replacement therapy, other anticoagulation, any other drug such as NSAIDs that could interact with the ASA, patients with a known liver disease, and those taking drugs likely to affect liver function or to produce any effect either directly or indirectly on haemostasis. Procedures were performed with local measures.
the understanding and written consent of each subject and according to ethical principles, including the World Medical Association Declaration of Helsinki.

At the initial consultation a past medical history, clinical and radiological examinations were recorded. Bleeding time was measured with the Ivy method in all patients one hour before the extraction procedure. Dental extractions were done under local anaesthesia using Mepivacaine HCL 3% (Isocaine, Novocol, NY, USA). Local infiltration and regional blocks were used in the mandible and maxilla as appropriate. The protocol for controlling postoperative bleeding consisted of (a) local pressure by soaked gauze applied for 15 minutes; (b) resorbable gelatin sponge for 15 minutes; (c) sutures for 30 minutes; (d) locally applied tranexamic acid. Control of the bleeding was followed up at 15, 30, 60 minutes, 24, 48 hours and 1 week, after the procedure. The paired student’s test and Spearman’s rank correlation were used in the statistical analyses of the data and comparisons were considered significant at p<0.05.

Results and Discussion

Patient characteristics are shown in Table 1. The control group consisted of 19 patients (6 female and 13 male) with a mean age of 64.32±10.74 years (range 44 to 86) while 25 patients (15 female and 10 male) with a mean age of 62.84±11.01 years (range 44 to 83) served as a study group.

<p>| TABLE 1 |</p>
<table>
<thead>
<tr>
<th>Control group</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64.32±10.74</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6 (13.6%)</td>
</tr>
<tr>
<td>Male</td>
<td>13 (29.5%)</td>
</tr>
<tr>
<td>ASA dose</td>
<td></td>
</tr>
<tr>
<td>75-100 mg</td>
<td>11 (25%)</td>
</tr>
<tr>
<td>150-300 mg</td>
<td>8 (18.3%)</td>
</tr>
<tr>
<td>BT</td>
<td>2.80±0.83</td>
</tr>
</tbody>
</table>

The most commonly used dose of ASA was 75-100 mg in both groups. There were significant differences in the bleeding time between the control and study groups (p<0.01). Significant positive correlation was found between the bleeding time and daily ASA dose (Fig. 1). In one patient bleeding time was 12.3 min within the normal limits and bleeding was controlled with gauze soaked with resorbable gelatin sponge application for 15 min.

Marketplace- 25 (56.8%) was the most common indication for ASA therapy in control and study groups: 14 (31.8%) and 11 (25%) patients, respectively (Table 2).

In the control group the most common localization of extractions was in the mandible (30 extractions, 30.6%) whereas in the study group it was observed in the maxilla (31 extractions, 30.6%). Significant correlation between bleeding time and localization of the teeth was not found in both groups.

TABLE 2

<table>
<thead>
<tr>
<th>Indications for ASA</th>
<th>Control group</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marketplace</td>
<td>11 (25%)</td>
<td>14 (31.8%)</td>
</tr>
<tr>
<td>Coronar Angioplasty</td>
<td>1 (2.2%)</td>
<td>2 (4.5%)</td>
</tr>
<tr>
<td>Coronar By-Pass</td>
<td>5 (11.3%)</td>
<td>6 (13.6%)</td>
</tr>
<tr>
<td>MI</td>
<td>1 (2.2%)</td>
<td>3 (6.8%)</td>
</tr>
<tr>
<td>Mitral Insufficiency</td>
<td>1 (2.2%)</td>
<td>---</td>
</tr>
</tbody>
</table>

Overall ninety-eight extractions were performed with the indications of caries, periodontal problems and prosthetic reasons. The most common cause of extraction was periodontal problems (32 extractions, 32.6%) in control group and caries in the study group (31 extractions, 31.6%) (Table 3). In both groups, there was no correlation between bleeding time and indications for extractions.

TABLE 3

<table>
<thead>
<tr>
<th>Localization</th>
<th>Control group</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxilla</td>
<td>18 (18.5%)</td>
<td>31 (31.6%)</td>
</tr>
<tr>
<td>Mandibula</td>
<td>30 (30.6%)</td>
<td>19 (19.3%)</td>
</tr>
<tr>
<td>Indications for extraction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caries</td>
<td>16 (16.3%)</td>
<td>31 (31.6%)</td>
</tr>
<tr>
<td>Periodontal diseases</td>
<td>32 (32.6%)</td>
<td>17 (17.3%)</td>
</tr>
<tr>
<td>Prosthetic indication</td>
<td>---</td>
<td>2 (2.2%)</td>
</tr>
</tbody>
</table>

The distributions of the extracted teeth in both groups in terms of bleeding control are shown in Fig. 2a and Fig. 2b. In local haemostatic measurements gauze-soaked (46%) and gauze soaked with resorbable gelatin (44%) were equivalent in study groups. The gauzed-soaked was involved in a higher percentage of cases (87%) in the control group. A statistically significant differences were found in terms of bleeding control between control and study group (p=0.008).

Table 4 shows bleeding in patients subdivided by the daily ASA doses. The BT was prolonged when the dose of ASA increased. The correlation between the dose of ASA and BT was significant (p=0.001).
ASA is still the most common antiplatelet drug used for treatment and prevention of thromboembolic diseases by irreversibly inactivating (for the life of the platelet) the enzyme cyclooxygenase (COX). This enzyme is responsible for the formation of prostaglandins and thromboxane A₂, which are involved in platelet activation and aggregation mechanisms (2, 3, 7, 11, 15).

Platelet adhesion, activation, and aggregation are important steps in the formation of a thrombus, thus explaining in a simplified way the antiplatelet effect of ASA (15, 20). The antiplatelet properties of ASA are effective up to 320 mg daily (19). Accordingly, ASA is maximally effective as an antiplatelet agent at doses much lower than those required for anti-inflammatory and analgesic functions. Doses of ASA higher than 320 mg daily may be less effective as an antiplatelet because of inhibition of prostacyclin production (2). Evidence based studies have suggested that daily doses of ASA in the range of 75 to 100 mg were optimal for the long-term prevention of serious vascular events in high risk patients (2, 19). However, recent data from randomized clinical trials indicate that the optimal dose of ASA to prevent myocardial infarction and stroke is 160 mg per day (10).

In the present study, most of the patients used ASA for prophylaxis against cardiovascular disease without a prescription from a physician. The doses of taken daily ASA differed individually from 75 mg to 300 mg and this dose differences did not affect the BT results.

The oral and maxillofacial surgeon is frequently required to treat patients who are receiving ASA therapy for prophylaxis against myocardial infarction, ischaemic stroke, peripheral arterial insufficiency. Although, low doses of ASA can prevent cardiovascular disease outcomes, also the risk for bleeding after dental extraction may be increased. Original recommendations had been made for the discontinuation of ASA use for 7 to 10 days prior to surgical procedures (4, 9, 18, 22, 24). More recently, it was discussed that ASA can be discontinued for 3 days, which would ensure that a sufficient number of new platelets are released into the circulation. Nevertheless, interruption of the ASA therapy may expose these patients at risk of developing thromboembolism, myocardial infarction, or cerebrovascular accident (25). Therefore, there has been some debate as to whether, prior to minor oral surgery, antiplatelet treatment should be altered or not; the risk of serious postoperative haemorrhage has to be balanced against the potential for life-threatening thromboembolism. The literature does not support the routine withdrawal of antiplatelet therapy before dental treatment for patients who are taking such medications (1, 3, 6, 7, 15). Recently, several authors suggested that levels of antiplatelet drugs are to be maintained and that any subsequent post-extraction haemorrhage is to be treated with local measures (12, 14, 22). In this study, of the local haemostatic measurements, the gauze-soaked was involved in a higher percentage of cases (87%) in the control group whereas gauze-soaked (46%) and gauze soaked with resorbable gelatin (44%) were equivalent in the study group and only one patient experienced increased intra-operative bleeding that was adequately controlled with local measures.
ASA per day before a wide range of invasive dental procedures including single tooth and multiple extractions (15).

In a placebo-controlled randomized clinical trial, 36 patients were randomized to 325 mg of ASA or placebo for 2 days before and 2 days after a single tooth extraction (6). An association between the use of ASA and bleeding outcome measures was not identified. Moreover, Sonksen et al. showed that the increase in BT caused by daily ASA in doses of up to 300 mg did not exceed normal limits in most patients (21). Thus, patients need not to stop taking ASA before dental surgery, as the hemorrhagic risk is not greater than the thromboembolic risk associated with interruption of the drug regimen. When intra-operative or postoperative bleeding does occur, local haemostatic methods are generally very effective.

The best screening test for the effect of ASA on coagulation is the platelet function analyzer (PFA-100). If this is not available, then the BT can be used to determine platelet function. Because of the wide variability and lack of specificity of this test, its use in the detection of blood dyscrasia is limited. Nevertheless, BT test remains useful in the preoperative assessment of patients with haemostatic disorders (21). In the present study, BT was examined preoperatively. The correlation between the dose of ASA and BT was statistically significant (P=0.001). The BT was prolonged when the dose of ASA increased.

Primary haemostasis was easily maintained with local haemostatic measures and intra-operative and/or postoperative bleeding was recorded. There was no intraoperative and postoperative secondary bleeding in any case including the patient with prolonged BT of 12.3 minutes. There was no statistically significant postoperative bleeding between the two groups.

Since ASA is a marketplace drug a large portion of the adult population takes daily ASA to prevent the risk of heart attack and stroke without the intervention of a physician. Apart from recommended usage, ASA was also used for its antiplatelet, anti-inflammatory, and analgesic properties (7).

Blinder et al. evaluated the postoperative bleeding in patients treated with oral anticoagulant drugs who underwent dental extractions without interruption of the treatment. It was reported that the most common cause for extractions are periodontitis (27%) and deep caries (5.5%) and the site of postoperative bleeding was more common in the maxilla in 4 patients in comparison to the mandible in 2 patients. In the present study the correlation between postoperative bleeding and cause for extractions and the site of postoperative bleeding was not statistically significant (5).

**Conclusions**

While the number of patients included in our study is small, we can conclude that the BT was prolonged when the dose of ASA increased. It is supposed that dental extractions can be carried out safely without stopping long-term ASA regimen. Further studies including higher number of patients and daily ASA doses greater than 100 mg are needed.

**REFERENCES**