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Review Article

Effectiveness of local hemostatic agents following dental extraction: A systematic review

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ABSTRACT

If the local hemostatic agent is effective in controlling postextraction bleeding in patients undergoing dental extraction patients. To evaluate the effectiveness of local hemostatic agents in the management of bleeding in dental extraction sockets. To evaluate the difference between various local hemostatic agents in causing hemostasis in patients undergoing dental extraction. An electronic search was initiated for scholarly articles on local hemostatic agents, oral anticoagulant therapy (OAT), and dental extraction. The search was PubMed based. The search methodology applied was a combination of MESH terms and suitable keywords based on PICO formulated for the review. The database search yielded 356 articles out, of which 201 articles were discarded after reading the abstract and 151 articles were excluded based on exclusion criteria. Finally, 4 articles were selected and subjected to data extraction and statistical analysis. The obtained articles exhibited a significant amount of heterogeneity with respect to the method of assessment and outcome parameters. Hence, a meta-analysis cannot be performed. The commonly used hemostatic agents in patients undergoing OAT, gelatin sponge, histoacryl glue, tranexamic acid, fibrin glue, and collagen sponge and this review observed no statistically significant difference among local hemostatic agents. This systematic review concluded that local hemostatic agents are additionally effective than the conventional suturing technique used to control post-operative bleeding following dental extraction.

Keywords: Anticoagulants, bleeding, extraction, hemostatic agents

Introduction

Anticoagulant drugs are involved in the prevention and management of cardiac valve disease, cardiac arrhythmia, prosthetic heart valve, pulmonary embolus, and cerebrovascular accident.[1] Patients who receive oral anticoagulant therapy (OAT), dental extractions is a common procedure. In the past, it was controversial that dental extractions in patients under anticoagulant therapy pose the problem between stopping or carrying on treatment as there is serious risk of post-operative hemorrhage and thromboembolism.[2] The post-operative bleeding time and hemostasis using local hemostatic agents in patients who were undergoing or stopped anticoagulant intake during dental extraction were calculated by means of the international normalized ratio (INR).[3] Various hemostatic agents have been found successful in controlling post-operative bleeding in patients undergoing anticoagulant therapy which includes histoacryl glue,[2] gelatin sponge,[4] collagen sponge[5] tranexamic acid, and autologous fibrin glue.[6] Cyanoacrylate glues are biocompatible, bactericidal and quick healing.[7] Tranexamic acid has antifibrinolytic activity and effective mouthwash in patients taking oral anticoagulants.[8] Gelatin sponge has excellent hemostatic properties and biocompatibility.[9] Fibrin glue is effective tissue adhesive, biodegradable, produces hemostasis, and reduced complications.[10] Hence, this systematic review is composed with the following aims and objectives.

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Aim

To evaluate the effectiveness of local hemostatic agents in the management of bleeding in dental extraction sockets. To evaluate the difference between various local hemostatic agents in causing hemostasis in patients undergoing dental extraction.

Materials and Methods

Sources used

An electronic search was initiated for scholarly articles on local hemostatic agents, OAT, and dental extraction. The search was PubMed based. The search methodology applied was a combination of MESH terms and suitable keywords based on PICO formulated for the review.

Search methodology

The search methodology applied was a combination of MESH terms and suitable keywords (Chart 2a).

PICO analysis

Population: Patients are undergoing extraction, patients under OAT, antithrombotic therapy, antiplatelet therapy, thrombocytopenia, hemophilia, scurvy, purpura, von willebrand disease, and vitamin K deficiency.

Intervention: Local hemostatic agents, hemostatic collagen, bone wax, cellulose, tranexamic acid, fibrin glue, gelatin sponge, histoacryl glue, collagen flees, and local antifibrinolytic solutions.

Comparison: Dental suture.

Outcome: Hemostasis, coagulation of blood, cessation of bleeding.

Selection of studies**:** The review process comprises two phases. In the first phase, the title and abstracts of the articles obtained through PubMed search were examined for relevance. The full text of relevant articles was obtained and accessed. In the second phase, relevant articles were isolated based on inclusion and exclusion criteria, for further data extraction and statistical analysis.

Inclusion criteria

- Clinical trials
- Patients undergoing anticoagulant therapy
- Patients undergoing dental extraction
- Use of local hemostatic agents.

Exclusion criteria

- Genetic disorders
- Animal study
- Reviews.

Results

The database search yielded 356 articles out, of which 151 articles were excluded based on exclusion criteria, and 201 articles were discarded after reading the abstract. Finally, 4 articles were selected, and the data from the finally included studies (Figures 1-3). Data were extracted and tabulated (Table 1).

- Study design
- Study groups
- Treatment
- Method of assessment
- Post-operative bleeding
- Statistics
- Inference.

All the included studies were randomized control trial and mean INR was used to compare the post-operative bleeding. Danielle Blinder

Table 1: Variables of interest and general information on selected articles

Journal	Authors	Study design	Study group	Treatment	Method of assessment	Post-operative bleeding	Statistics	Inference
OOOO JNL, 1999	Danielle Blinder *et al.*	Randomized control trial	Group 1, 2, 3 - (n=150) Oral anticoagulant therapy	Group 1 - Gelatin sponge and sutures Group 3 - Gelatin sponge, sutures, tranexamic mouthwash Group 2 - Fibrin glue, gelatin sponge, and sutures	INR	Group I - 2.89 Group II - 2.6 Group III - 2.3	Chi-square test (χ^2=1.22, P=0.54)	No statistically significant difference. But gelatin sponge and sutures are sufficient
JOMS, 2003	Carter *et al.*	Randomized control trial	Group A and Group B (n=49) - Oral anticoagulant treatment	A - 4.8% tranexamic acid B - Autologous fibrin glue	INR	A - 3.0 B - 3.1	Chi-square test and independent sample t-test (P=0.12)	No statistically significant difference between both the groups observed both the techniques are equally effective
JOMS, 2003	Al-Belasy *et al.*	Randomized control trial	Control (n=15), study group (n=15) and negative control (n=10)	gelatin sponge and multiple interrupted resorbable sutures (control and negative control) Histoacryl glue and resorbable sutures (Study group)	INR	Study group - 2.51 Control - 2.42 Negative control - 1.0	Mantel-Haenszel test analysis of variance (P=0.046)	A statistically significant difference in study group and negative control (P=0.001)
JOMS, 2009	Bajkin *et al.*	Randomized controlled trial	Group A n=109 (continued oral anticoagulant) and Group B n=105 (LMWH replacement)	A - Resorbable collagen sponges B - No hemostatic agents	INR	A - 2.45 B - 2.49	Chi-square test with yates correction (χ^2, Yates=0.253, P>0.05)	No statistical significance difference between two group

INR: International normalized ratio, LMWH: Low molecular weight heparin

et al. evaluated post-operative bleeding in patients treated with oral anticoagulant drugs and compared the effect of three different hemostatic modalities. Carter *et al*. compared the effectiveness of a 4.8% tranexamic acid mouthwash versus an autologous fibrin glue preparation for controlling bleeding. Al-Belasy *et al*. evaluated the local hemostatic effect of n-butyl-2-cyanoacrylate (histoacryl glue) in warfarin-treated patients undergoing dental extraction. Bajkin *et al*. evaluated the post-operative bleeding and thromboembolic complications during dental extractions in anticoagulated patients who continued OAT and switched to low molecular weight heparin (LMWH) before extraction. The obtained articles exhibited a significant amount of heterogeneity with respect to the method of assessment and outcome parameters. Hence, a meta-analysis cannot be performed. Hence, there was no statistical significance among local hemostatic agents used following dental extraction.

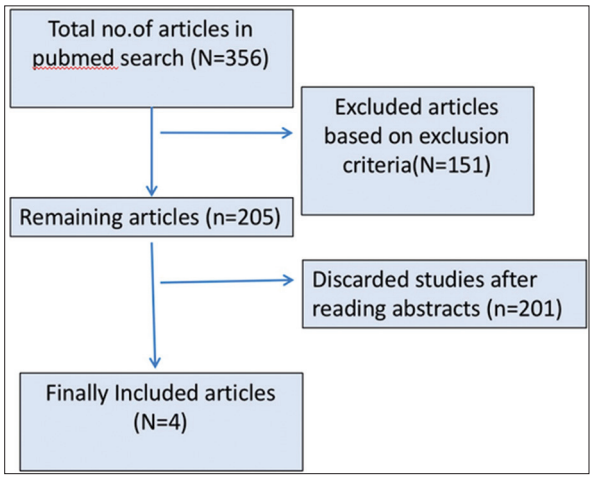
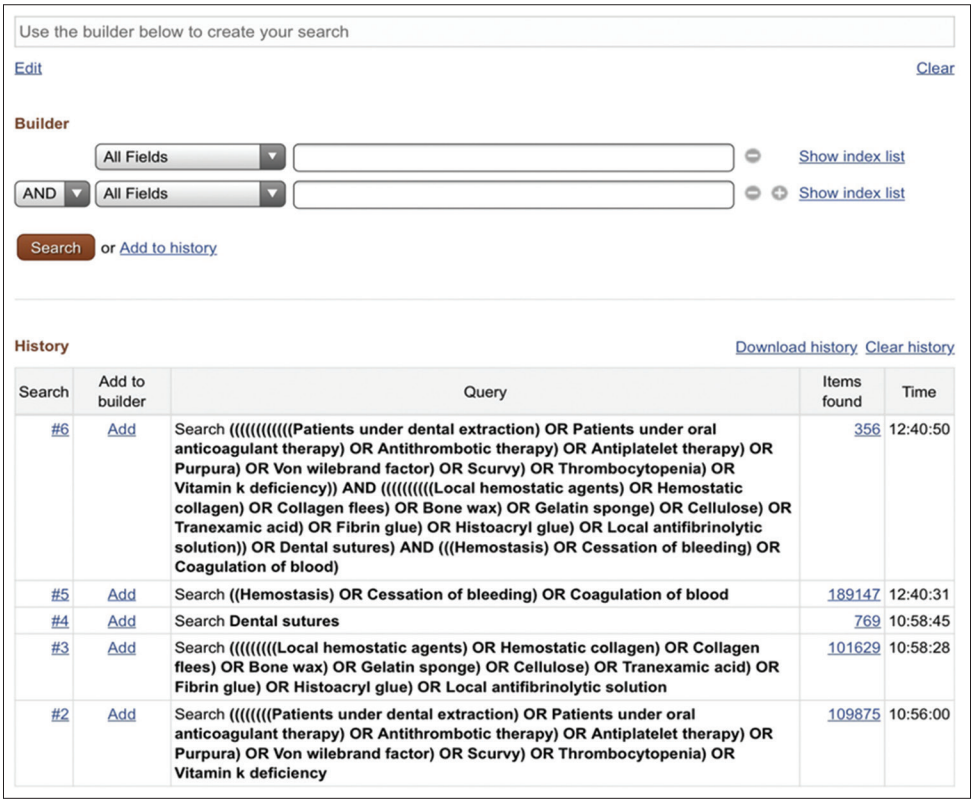


Figure 1: Flow chart for search strategy

Discussion

The literature consists of more number of randomized control trial with respect to patients under anticoagulant therapy undergoing extraction and effectiveness of local hemostatic agents. All the 4 studies selected for review process were randomized control trials and the method of assessment was predominantly by INR (Blinder *et al.*, Carter *et al*.). The study group varied with each study designed with different study and test groups. Danielle Blinder *et al*. 1999 (Table 1), evaluated post-operative bleeding in patients treated with oral anticoagulant drugs who underwent dental extractions without interruption of the treatment and to compare the effect of three different hemostatic modalities. The mode of hemostatic agents for treatment was: Group 1 (119 extractions) with gelatin sponge and sutures; Group 2 (117 extractions) with gelatin sponge, sutures, and mouthwash with tranexamic acid; Group 3 (123 extractions) with fibrin glue, gelatin sponge, and sutures. The mean INR values were measured postoperatively Group 1 - 2.89, Group 2 - 2.6, and Group 3 - 2.3. Hence, dental extractions can be performed without interruption in patients treated with an oral anticoagulant. There was no statistical significance ($\chi^2 = 1.22$, $P = 0.54$), hemostasis with gelatin sponge and sutures is sufficient.

Carter *et al.* 2003 (Table 1), compared the effectiveness of Group A - 4.8% tranexamic acid mouthwash ($n = 26$) and Group B - autologous fibrin



Search	Add to builder	Query	Items found	Time
#6	Add	Search ((((((((((Patients under dental extraction) OR Patients under oral anticoagulant therapy) OR Antithrombotic therapy) OR Antiplatelet therapy) OR Purpura) OR Von wilebrand factor) OR Scurvy) OR Thrombocytopenia) OR Vitamin k deficiency)) AND ((((((((Local hemostatic agents) OR Hemostatic collagen) OR Collagen flees) OR Bone wax) OR Gelatin sponge) OR Cellulose) OR Tranexamic acid) OR Fibrin glue) OR Histoacryl glue) OR Local antifibrinolytic solution)) OR Dental sutures) AND (((Hemostasis) OR Cessation of bleeding) OR Coagulation of blood)	356	12:40:50
#5	Add	Search ((Hemostasis) OR Cessation of bleeding) OR Coagulation of blood	189147	12:40:31
#4	Add	Search Dental sutures	769	10:58:45
#3	Add	Search ((((((((Local hemostatic agents) OR Hemostatic collagen) OR Collagen flees) OR Bone wax) OR Gelatin sponge) OR Cellulose) OR Tranexamic acid) OR Fibrin glue) OR Histoacryl glue) OR Local antifibrinolytic solution	101629	10:58:28
#2	Add	Search ((((((((Patients under dental extraction) OR Patients under oral anticoagulant therapy) OR Antithrombotic therapy) OR Antiplatelet therapy) OR Purpura) OR Von wilebrand factor) OR Scurvy) OR Thrombocytopenia) OR Vitamin k deficiency	109875	10:56:00

Figure 2: PubMed search using MESH terms and keywords

Figure 3: PubMed Search

glue ($n = 23$) in controlling bleeding after dental extraction in patients taking warfarin as an anticoagulant. The post-operative bleeding was measured by INR; the mean INR values were Group A - 3.0 and Group B - 3.1. Statistically, there was no significant difference between both the groups ($P = 0.12$) Al-Belasy *et al*. 2003 (Table 1) evaluated the local hemostatic effect of n-butyl-2-cyanoacrylate (Histoacryl glue) in warfarin-treated patients undergoing dental extraction. Patients were assigned into control ($n = 15$), study ($n = 15$) and negative control ($n = 10$). The INR was determined preoperatively. Hemostasis and primary closure were achieved by gelatin sponge, and multiple interrupted resorbable sutures were used in the control and negative control groups, and histoacryl glue and interrupted resorbable sutures were used in the study group. Local hemostasis was obtained immediately in study patients with mean INR (2.51) and only after 10-20 min in the control (2.42) and negative control patients (1.0). The level of anticoagulant need not be altered preoperatively, and histoacryl glue is an effective and easily applicable local hemostatic agent. Bajkin *et al.* 2009 (Table 1) evaluated the post-operative bleeding and thromboembolic complications during dental extractions in anticoagulated patients using two protocols. Group A ($n = 109$) included patients who received continual OAT before and after their intervention. A resorptive collagen sponge was used as a local hemostatic agent, without primary suture and INR was calculated to be 2.45. Group B ($n = 105$) consisted of patients who were switched to LMWH from OAT before their dental intervention, No hemostatic agents were used, and the mean INR value was found to 2.49. Although patients who had continued OAT had a higher incidence of postextraction bleeding, no statistically significant difference was found between these 2 groups of patients, and there were no signs of thromboembolic complication (χ^2, Yates' = 0.253, $P > 0.05$). All the hemostatic agents have a similar effect in controlling post-operative bleeding. The authors used a different method of assessment, i.e., different hemostatic agents and study groups in each study. Hence, the data could not be categorized into homogenous strata, and a meta-analysis could not be initiated.

Conclusion

Hence, local hemostatic agents are additionally effective than the conventional suturing technique in post-operative bleeding. There is no statistically significant difference among different local hemostatic agents used to control bleeding in dental extraction sockets.

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