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Efficacy of Local Haemostatic Agent Following Minor Surgery (An Experimental and Clinical Study)

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الخلاصة

الأهداف: يهدف البحث إلى تقييم استخدام الاوستين كمادة موقفة للنزف في العظام. **المواد وطرائق العمل**: الجزء التجريبي يضم ١٥ أرنبا تم تقسيمهم إلى ثلاث مجموعات حسب وقت قياس وقف النزف خمسة ارانب لكل مجموعة التي بدورها قسمت إلى ثلاث مجموعات حسب مواد البحث (الاوستين، الجيل فوم، السيطرة)، ثلاث ثقوب تم إحداثها في عظم الفخذ ومع بدء النزف يتم وضع المواد أعلاه ويستخدم قطنه مناسبة لقياس زمن توقف النزف، الطريقة نفسها يتم استخدامها بالجزء ألسريري بعد حقن التخدير الموضعي وقلع الضرس ويحتسب الوقت بطريقة جرافيمترك. **النتائج**: في الجزء التجريبي بعد المقارنة بين استخدام الاوستين والجيل فوم كموقف للنزف اتضح ان الاوستين الأفضل في كل الأوقات حيث كان هناك فرقا معنويا إحصائيا. في الجزء السريري كان الاوستين أيضا الأفضل حيث كان هنالك فرق معنوي على الجيل فوم عند الأوقات (الدقيقة الأولى و٣٠ دقيقة) ولم يكن هناك فرقا معنويا عند (الدقيقة ٥ و١٠) ،ايضا اظهر الاوستين فرقا معنويا في التقليل من الانزعاج الذي يحدث للمريض بعد عملية القلع الناتج من طعم الدم في اللعاب وبالتالي تكون عملية القلع أكثر سهولة من وجهة نظر المريض مقارنة بالجيل فوم. **الاستنتاجات**: الاوستين أفضل في إيقاف نزف الدم الناتج من إصابات العظام كما تم إثباته بالجزء التجريبي وكذلك في الاستخدام السريري بعد قلع الاسنان.

ABSTRACT

AIMS: This study aims to estimate the efficacy of Ostene as bone hemostatic agent clinically and experimentally and their effect on the ease of operation in clinical dental practice. **MATRIALS AND METHODS**: For experimental part: Fifteen males rabbits were divided into three groups according to the time interval for hemostasis measurement, five rabbits in each group. Each group subdivides into other three groups according to study material "ostene, gelfoam, control". On femoral bone, three holes were made. After bleeding started, study material was placed inside holes, then a uniform piece of cotton was applied with gentle pressure, then hemostasis measured using the gravimetric method. For the clinical part: after complete extraction, a piece of study material was implanted inside the tooth socket and covered with uniform cotton for hemostasis, then hemostasis measured using the gravimetric method. **RESULTS**: For experimental part: study result revealed that the comparison between two local hemostatic agents (ostene and gelfoam) groups for hemostatic effect show Ostene has superiority effect over gelfoam in control bleeding at all interval times. Friedman test revealed a significant difference between study materials P =0.00 ($P \leq 0.05$). For the clinical part: clinical measurement, ostene showed significant over gelfoam at 1min, 30 min While there were no significances between ostene and gelfoam at 5min,10min. Regarding visual analog scales for assessing bleeding and ease of operation, ostene, when comparing it with gelfoam, appeared better than gelfoam. **CONCLUSIONS**: Hemostatic effect of ostene is superior to gelfoam experimentally and after tooth extraction.

Key words: local hemostatic measure; ostene; gelfoam; bone hemostatic agents, bleeding.

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INTRODUCTION

Blood loss from socket after tooth extraction is a predictable obstacle facing dentist [1]. The incidence of post-extraction bleeding varies from 0% to 26% [2]. Regarding the high vascularization of the oral cavity and disclosure of the open socket to the patient's exploring tongue and fingers, it is difficult to achieve complete hemostasis [3]. Post-extraction hemorrhage categorized in relation to timing in to (primary, reactionary and secondary hemorrhage [4]. Hemostasis at the site of dental extraction is considered to be a necessity before the patient leaves the clinic and a number of different medical local agents and medications may interfere with hemostasis [4]. Ideal hemostatic agents must achieve instant closure of blood vessels without damage to surrounding tissues, be immunologically inert and must maintain the tissue seal until vascular obliteration and tissue healing occurs [5,6]. One of the most common bone hemostatic effect is Gelfoam®. It is a physical hemostatic agent derived from non-human source product (pigs or cows), yet non-antigenic [7]. It can distend to more than two times its initial dimensions creating a template in which a clot can figure while absorbing adjacent fluids [8].

It is a porous, pliable, absorbable gelatin sponge manufactured as films, gelatin sponges (Gelfoam), or fine particles that is mixed to form a paste [9]. Gelfoam has exceedingly small tissue response and liquefies in the oral cavity within seven days being fully absorbed within 1-1.5 month and can be used dry or after moistening it with saline or thrombin [10]. Ostene® a new water-soluble polymer wax that newly been commenced as a biocompatible resorbable osseous haemostatic agent [11].

It is a super alternative material to other bone hemostatic agents with an advantage of not impairing osteogenesis or promoting infection. It is used for immediate and effective hemostasis by attaching to the bone shell thus producing a mechanical and physical obstacle [12]. It is a biocompatible polymer and is removed from the body unchanged via renal clearance [13,14].

Lower rate of osteomeylitis and positive bone cultures are approved significantly on rabbit tibial cortical defects treated with ostene [15]. "Ostene" is a biocompatible and absorbable hemostatic mediator as many studies show ostene achieve instantaneous hemostasis by making a mechanical, physical obstacle but not biochemically, the only disadvantage of this agent is that of more expensive than any other. [16]

Aims of the study: This study aims to estimate and evaluate the efficacy of using Ostene as a bone haemostatic agent and their effects on the ease of operation in clinical dental practice.

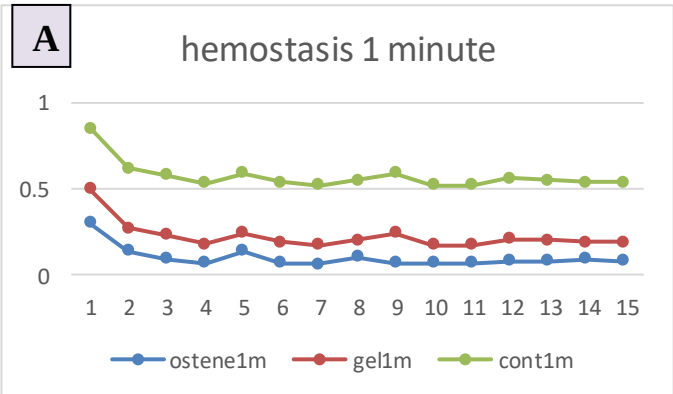
MATERIALS AND METHODS

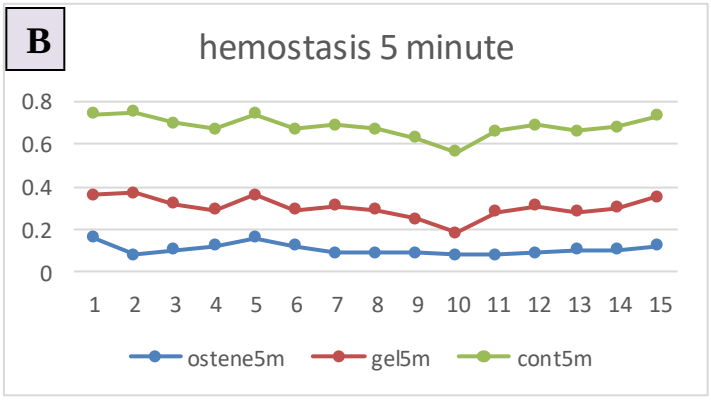
The study was approved by the scientific ethics and research committee of the College of Dentistry, the University of Mosul for experimental and clinical studies. Regarding Food and Drug Administration-approved water-soluble implant substance "Ostene" which suitable for use in manage of hemorrhage from osteal shell [17]. The current study was divided into two parts: First achieving hemostasis using two hemostatic agents, gelfoam and ostene in surgically created deformities in the femoral bone in rabbits. Second following extraction of posterior teeth in human."Ostene®" (Alkylene oxide copolymer) substance was offered by "Ceremed Inc., and Gelfoam® was purchased from SEPTODONT"

1) **Trial Study**: Adult fifteen males' local rabbits, 6-8 months' age were used with a weight of each 2.3 ± 0.5 kg. The animals were housed in an animal house throughout the study fed on normal food and water via veterinarian. For anesthesia, each rabbit was given an intramuscular dose of ketamine hydrochloride anesthetic and analgesic 4mg/kg in 50mg/ml and xylazine base sedative and muscle relaxant 5mg/kg in 20mg/ml[18], injected into rabbit's thigh muscle. After 10-15 minutes, the anesthetic integrity was checked by testing loss of ear pinch reflex [19].

Surgical procedure for animal study: Fifteen rabbits were alienated into three groups according to the instance period for hemostasis measurement one minute, five minutes and ten minutes, five rabbits in each group. Each group subdivides into three groups according to study material "ostene, gelfoam, control which left without treatment". After checking anesthesia, an incision (5cm in length) was done to expose the right femoral bone for the rabbit. Three holes were made using surgical bur 5mm±3mm mounted on straight surgical handpiece with normal saline as a cooling agent. After bleeding started from holes, the study material was implanted inside holes, then a uniform piece of cotton was applied.

The pieces of cotton to be used in this study were weighed for standardization (0.05gm). After that, the cotton with absorbed blood was weighed again during interval times of one minute, five minutes and ten minutes using the gravimetric method [20] as shown in Figure (1).





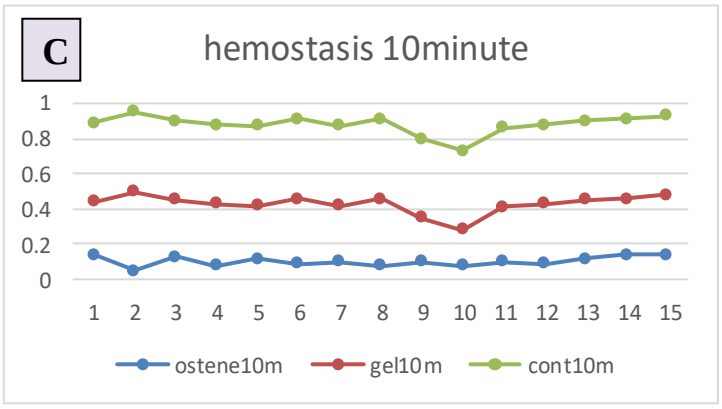


Figure (1): Differences between study groups at different times interval (A= at one minute, B= at five minutes, C= at ten minute) for experimental study.

2) **Clinical study**: Fifteen males were enrolled as volunteers to conduct this study after signing a consent form but six of them were complete follow-up. For standardization, an inclusions criterion was included (target teeth were posterior teeth of maxilla for both side, technique of anesthesia, technique of tooth extraction, age of patients ranged between (25y-45y), no smoking, no drinking, medically fit, having multiple extractions of their posterior teeth, not take any medications). **Surgical procedure for clinical study**: Infiltration technique was given (one dental cartridge contains Lidocaine 2% with epinephrine 1:80,000). After securing anesthesia and gingival separation, extraction was done using atraumatic forceps extraction. Piece of study material was placed inside the tooth socket and covered with uniform cotton for hemostasis which was weighed for standardization. The time interval for weighting ranged from one minute, 5 minutes,10 and 30 minutes using the gravimetric method [20,21].

Data collected included time to hemostasis and hemorrhage. Visual analog scales (VAS) were used to document prejudiced data by the surgeon to evaluate bleeding next to cotton taking away (0= none, 1= minimize/restricted, 2= moderate/diffuse, 3 = severe/brisk) and ease of operation (1= extremely easy, 2= difficult 3= some effort, 4= usual 5=easy , 6 = extremely difficult) for both study materials. [22]

Data analysis: Information were progress statistically by the **SPSS version 21** for Windows 10. The association between study materials within the same period of hemostasis was studied using Friedman Npar test.

The Wilcoxon Signed Ranks Test was used to explain differences between study materials at different periods of hemostasis for both experimental and clinical study.

RESULTS

1- **Experimental study**: Study of difference among three trial groups with the Friedman test revealed a highly significant difference between them as revealed in Table (1) ($P \leq 0.01$). Wilcoxon signed rank test was used to assess the significant difference among study materials in each experimental group as shown in Table (2).

Table (1): Mean rank and *P*-Values of Friedman Npar test explained the effect of study materials in different periods of hemostasis in experimental animals.

Materials	1 min	5min	10min
Ost	1.20	1.00	1.00
Gel	1.80	2.00	2.00
Cont.	3.00	3.00	3.00
P-value	0.000**	0.000**	0.000**

**highly significant at $P \leq 0.01$

Table (2): Wilcoxon Signed Rank test explained the differences between study materials at different periods of hemostasis in experimental animals

P-values	Ost-gel	Ost-cont	Gel-cont
1min	0.009**	0.001**	0.001**
5min	0.001**	0.001**	0.001**
10min	0.001**	0.001**	0.001**

**highly significant at $P \leq 0.01$

Overall, study result revealed that the comparison between two local hemostatic agents (ostene and gelfoam) groups for hemostatic effect show Ostene has superiority effect over gelfoam in control bleeding at all interval times as shown in Figure (2 A, B, C).

2- **Clinical study**: clinical measurement, ostene showed significant over gelfoam at 1minute, 30 minutes (*P*=0.043, *P*=0.043 respectively). While there were no significances between ostene and gelfoam at 5m,10m (P=0.183, P=0.080 respectively), when *P* is significant at 0.05 as shown in Table (3). Regarding visual analog scales for assessing bleeding and ease of operation, ostene, when comparing it with gelfoam, appeared better than gelfoam as showed in Table (4).

Table (3): Wilcoxon Signed Rank test explained the differences between study materials at different periods of hemostasis after tooth extraction.

	gel1m - ost1m	gel5m - ost5m	gel10m - ost10m	gel30m - ost30m
P-value	0.043*	0.138	0.080	0.043*

*significant at $P \leq 0.05$

Table (4): Wilcoxon Signed Rank test explained the differences between study materials using VAS for bleeding and ease of operation after tooth extraction.

	VAS for bleeding Ostene-Gelfoam	VAS for ease of operation Ostene-Gelfoam
P-value	0.024*	0.023*

*significant at $P \leq 0.05$

DISCUSSION

Cotton is considered one of the earliest topical hemostatic agents that is available in many forms like gauzes, sponges, rolls, and others. In some cases, patient's compliance following proper post-operative instructions is difficult to achieve hemostasis, hence dislodgment of a fragile clot that has formed is possible. As such, further bleeding is to be expected. In this regard and to achieve fast and proper hemostasis, biotechnology made an explosive growth in introducing topical hemostatic agents in the last decade [7,23]. According to our knowledge the introduction of Ostene® as a hemostatic agent after tooth extraction in human is recent and no clinical studies have been published to study the efficacy and adverse reactions of this material although it has been approved by FDA as a water-soluble implant material indicated for use in the control of hemorrhage from bone surfaces[19].

In this study, the material was assessed clinically and experimentally. According to the findings of an experimental study on rabbits, ostene appeared to be the most effective compared to other hemostatic agents used (gelfoam, control) to control bleeding. This came in agreement with the study of Vestergaard et al as they found Ostene to stick well to the bone and acts as a mechanical obstacle which precludes blood emerge from bare spongy osseous tissue thus inducing hemostasis [24]. Further study showed that ostene is suitable to arrest bleeding as it is an inert hydrophilic material that does not interfere with coagulation properties, absorbed within 48hours and eliminated from the body unchanged [25]. When comparing ostene with gelfoam both clinically and experimentally, ostene appeared better than gelfoam in controlling bleeding with the latter inducing infection when left inside the socket. This agreed with many studies in which they found that gelfoam acts as a foreign body in which bacteria can become enmeshed in the sponge leading to eventually formation of an abscess causing delayed bone healing in comparison to ostene that did not effect on osteogenesis[26_30], while in other hand disagreed with study of Spotnitz et al which said gelfoam had a little tissue reaction[10]. Clinically, the hemostatic effect of ostene appeared superior to gelfoam according to a gravimetric method that was used in this study. The amount of oozing blood decreased after the first five minutes after tooth extraction although the weight of cotton was continuing to increase within a time interval of measurement because of salivary secretion. When handling ostene, it appeared easy on handling and shaping as it`s a wax material and can be softened to adapt to the shape and size of the socket by hand, hence more preferable than gelfoam in use. Regarding visual analog scales for control bleeding and assessing the difficulty of extraction, ostene appeared better than gelfoam in controlling bleeding as such, patients felt more comfortable after extraction because the oozing from the socket and bloody taste of saliva were decreased.

CONCLUSIONS

Bone hemostatic effect of ostene is superior to gelfoam experimentally and after tooth extraction.

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