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The Role of Topical Gel Containing Chitosan, 0.2% Chlorhexidine, Allantoin and Dexpanthenol on the Wound Healing After Surgical Extraction of Impacted Mandibular Third Molar

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Abstract--Odontostomologic procedures like extractions especially surgical removal of impacted 3rd molars, implants, biopsies etc are often associated with post-operative pain and inflammation. Traditionally chlorhexidine was used in this regard. Recently, topical gel, Bexident Post (ISDIN, SPAIN) has been in use to control post-operative discomfort. The aim of this study is to clinically evaluate the efficacy of Bexident Post (ISDIN, SPAIN) that contains chitosan, dexpanthenol, allantoin and 0.2% chlorhexidine on wound healing after surgical extraction of mandibular impacted 3rd molars. A study sample of 10 patients with similar type of bilateral impacted mandibular 3rd molar was included in the study. Total of 10 extractions were assigned in one of the two groups. Only difference

between the two sides in terms of surgical protocol will be the Experimental side applied 10 mL thrice daily for 10 days while Control side did not. All patients were aware of the purpose of present study and written consent was taken requiring their participation. Results showed that facial swelling, mouth opening and pain were all significant between the two groups. The groups were homogenous only in terms of infection as neither of the groups showed post-operative signs of infection. Bexident Post (ISDIN, SPAIN) has shown promising results in controlling post-operative discomfort after surgical removal of impacted 3rd molars along with improving the overall aesthetic appearance of the wound post-operatively.

Keywords---3rd molar impactions, chitosan, allantoin, dexpenthanol, 0.2% chlorhexidine.

Introduction

Wound healing is a natural restorative response to tissue injury. Although healing reach its crescendo uneventfully in most instances, however various factors intrinsic or extrinsic can either facilitate or hamper the process of healing. Once the tissue is injured, body sets into motion an automatic series of events known as “Cascade of healing” that begins with hemostasis and culminates through three inter-connected stages namely inflammatory, proliferative and remodelling. Thus, surgeons always strive to optimize wound healing by using various biological approaches at their disposition.⁽¹⁾

In this direction, one such product that has shown promising results is Bexident post. Bexident post is a topical gel commercialized by ISDIN, Spain that contains Chitosan, 0.2% chlorhexidine, Allantoin and Dexpenthanol^(2,3). Thus, a hypothesis was proposed that Bexident Post do not improve the healing after surgical removal of mandibular 3rd molars.

Study subjects / sample

A prospective study was conducted to determine the effect of topical gel containing chitosan, 0.2% chlorhexidine, allantoin, and dexpenthanol on 10 subjects requiring similar type of bilateral extraction of impacted mandibular 3rd molars.

Eligibility Criteria

Cases

Inclusion criteria:

- Adult patients with similar type of bilateral impacted mandibular 3rd molars.

Exclusion criteria:

- Those who did not want to participate in the study or not willing for follow up visits.

- Individuals allergic or intolerant to substances used in the study.
Medically compromised patients
- Smokers

Sampling method

A study sample of 10 patients with similar type of bilateral impacted mandibular 3rd molar was included in the study.

Methodology

Patients with similar type of impacted mandibular 3rd molar according to Winter's and Pell & Gregory classification were selected and two sides were designated as control side (CS) and experimental side (ES). Total of 10 extractions were assigned in one of the two groups. Only difference between the two sides in terms of surgical protocol was that the experimental side applied 10 mL thrice daily for 10 days while Control side did not. All patients were aware of the purpose of present study and written consent was taken requiring their participation. Patient's complete medical history was reviewed, identifying their age, sex, hygiene practice and toxic habits. Anaesthesia used was 2% lidocaine with 1:80,000 adrenaline. In all patients an envelope incision was made with vertical extension mesial to lower 2nd molar, a mucoperiosteal flap was raised and ostectomy was performed. All surgeries were performed by single surgeon. Wound was irrigated with normal saline and povidone iodine solution. Wound edges were carefully sutured with simple interrupted sutures using 3-0 silk non absorbable sutures. Patients were prescribed antibiotics and analgesics to be taken 8 hourly for 5 days. Only difference between the two will be experimental side applied 10ml topical gel containing chitosan, 0.12% chlorhexidine, allantoin, and dexpenthenol, Bexident Post (ISDIN, SPAIN) while control side will not. All the clinical parameters were evaluated on 1st(T1), 3rd(T2), 8th(T3) and 14th(T4) day.

Following clinical parameters were evaluated-

1) Wound Healing-

A) Edges of the wound will be evaluated for presence or absence of bleeding and categorized as **good, acceptable** or **bad**.

	GOOD	ACCEPTABLE	BAD
Wound edges	Aesthetic, clean, good opposing edges	Slightly irregular, light bleeding or erythema	Irregular, moderate or heavy bleeding, exudate, pus, foul odor. Signs of infection.

B) Colour of the oral mucosa will be evaluated and categorized as **good, acceptable** or **bad**.

	GOOD	ACCEPTABLE	BAD
Colour of the oral mucosa	Identical to the surrounding area	Mild erythema present	Severe Erythematous

- C) Wound closure will be evaluated for wound dehiscence or keloid formation or other complication associated with closure of the wound and categorized as **good, acceptable** or **bad**

	GOOD	ACCEPTABLE	BAD
Wound closure	Complete / no dehiscence	Dehiscence 1 - 2 mm dehiscence	Dehiscence > 2 mm, open wound. Keloid formation or unaesthetic closure

		ES	CS
Wound closure	Day 1		
	Day 3		
	Day 8		
	Day 14		

- D) Exudate, pus, foul odor or other signs suggestive of infection depending on cultu will also be recorded and will be termed **present** if will be **positive** or will be **absent** if culture sensitivity will be **negative**.

	PRESENT	ABSENT
Infection		

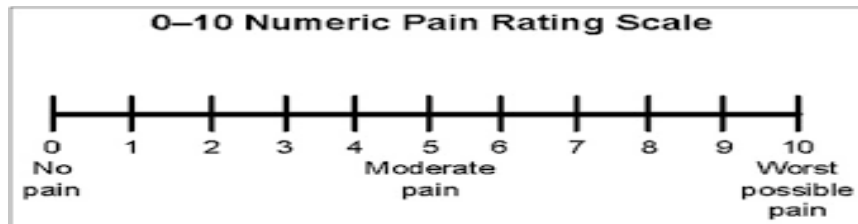
2) Inflammation:

- A) Level of inflammation in terms of facial swelling will be recorded on 1st, 3rd, 8th and 14th day following surgery by measuring in millimetres using 2-0 nylon thread and scaled ruler. To evaluate markings will be made on following facial points:

- Overall size of patient's face
- Mandibular angle
- Tragus
- Lateral canthus of eye
- Base of nasal ala
- Oral commissures
- Pogonion

- B) Level of trismus was determined by measuring interincisal distance between maxillary and mandibular central incisors on 1st, 3rd, 8th and 14th day using scaled ruler and divider.

- C) Pre and post operative pain levels will be recorded on 1st, 3rd, 8th and 14th day following surgery (beginning 6 hours from surgery) using VAS from 1 to 10 (with 0 being no pain to 10 being extreme pain)



Results

In total, 10 patients with bilateral mandibular impacted 3rd molars were recruited in Department of oral and maxillofacial surgery.

Distribution of subjects according to age

The observation was made that in distribution of subjects according to age maximum subjects were found to be in the age group of 20-30 years with mean age of 24.9 years.

(Table 1 and Graph 1)

Table 1
Mean (SD) age of study population according to gender

	Mean	SD
MALES	24	3.60
FEMALES	25.28	4.23
MEAN AGE (TOTAL)	24.9	3.90

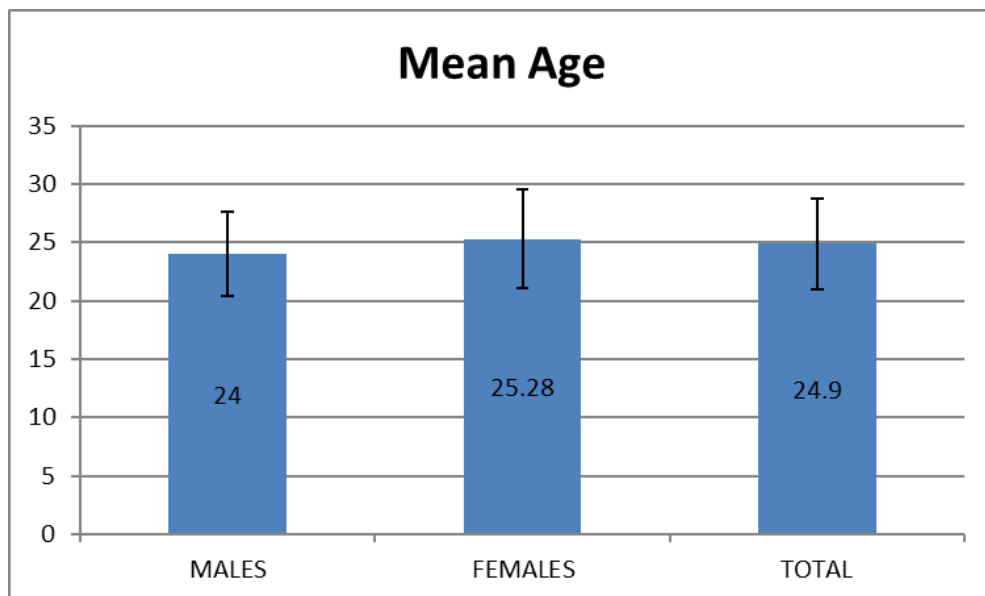


Figure 1. Mean (SD) age of study population according to gender

Distribution of subjects according to gender

It was noticed that distribution of study subjects according to gender in different age groups, the number of males involved were 3(30%) whereas number of females involved were 7(70%).

Table 2
Gender wise distribution of study population

GENDER	MALES		FEMALES		Total	
	n	%	n	%	N	%
	3	30	7	70	10	100

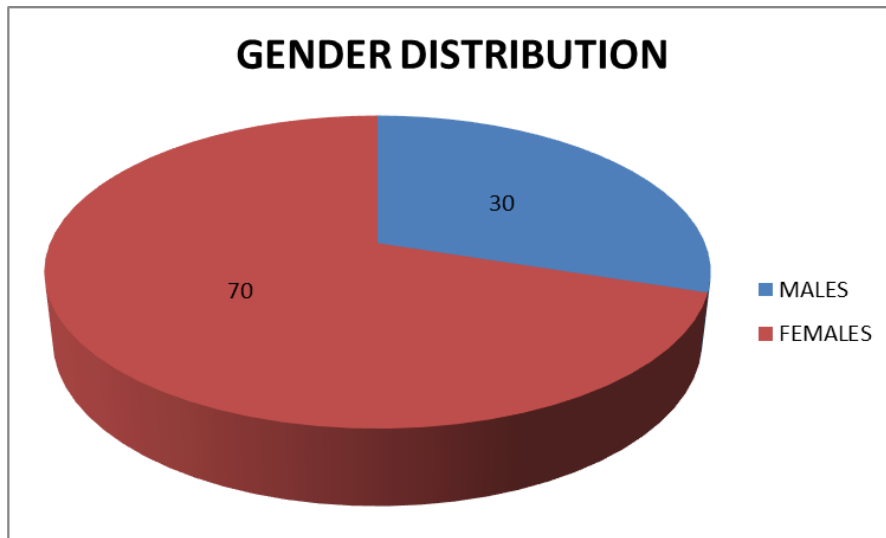


Figure 2. Gender wise distribution of study population

Facial swelling

Results predicted that the Mean for facial swelling statistically significant among the two groups at time interval T1, T2 & T3. The facial swelling was significantly lower among experimental groups.

Table 3
Comparison of Mean and standard deviation of facial swelling in study population at different time intervals (INTER GROUP)

Abbreviation	Time intervals	EXPERIMENTAL		CONTROL		P VALUE
		Mean	SD	Mean	SD	
T1	POST OP DAY 1	34.00	17.81	45.60	13.88	0.002*
T2	POST OP DAY 3	16.8	11.0	25.80	11.72	0.035*
T3	POST OP DAY 8	6.40	7.53	10.00	6.32	0.105
T4	POST OP DAY 14	1.00	2.16	1.42	0.45	0.370

^aPAIRED T TEST , * Significance of relationship at $p < 0.05$

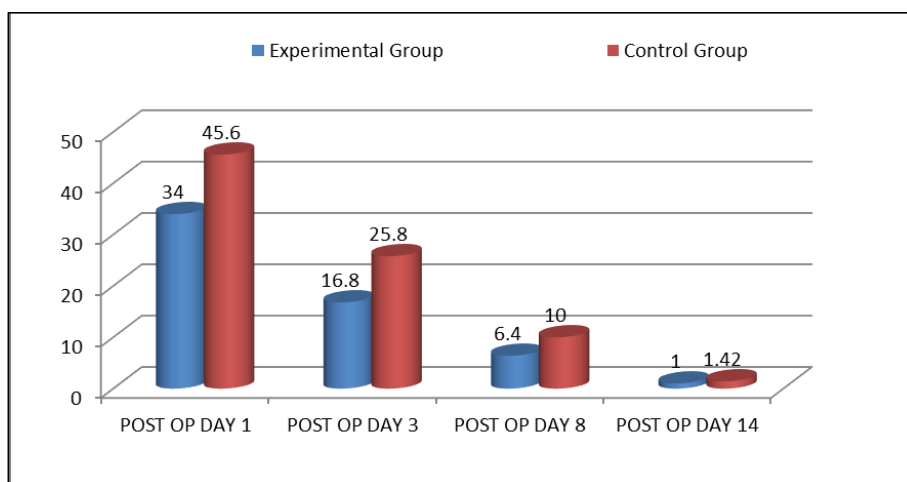


Figure 3. Facial Swelling: Inter Group

Clinical assessment of mouth opening

The Mean for Mouth Opening was found to be statistically significant among both the groups at all time interval. The mouth opening was significantly higher among experimental groups.

(Table 4 and Graph 4)

Table 4
Comparison of mean and standard deviation of mouth opening in study population at different time intervals (INTER GROUP)

Abbreviation	Time intervals	Experimental		Control		P value
		Mean	SD	Mean	SD	
T1	POST OP DAY 1	19.60	3.89	17.30	3.40	0.005*
T2	POST OP DAY 3	23.00	4.88	20.80	4.10	0.002*
T3	POST OP DAY 8	30.70	4.52	26.60	5.21	0.003*
T4	POST OP DAY 14	37.60	3.24	34.10	3.67	0.001*

^aPAIRED T TEST, * Significance of relationship at $p < 0.05$

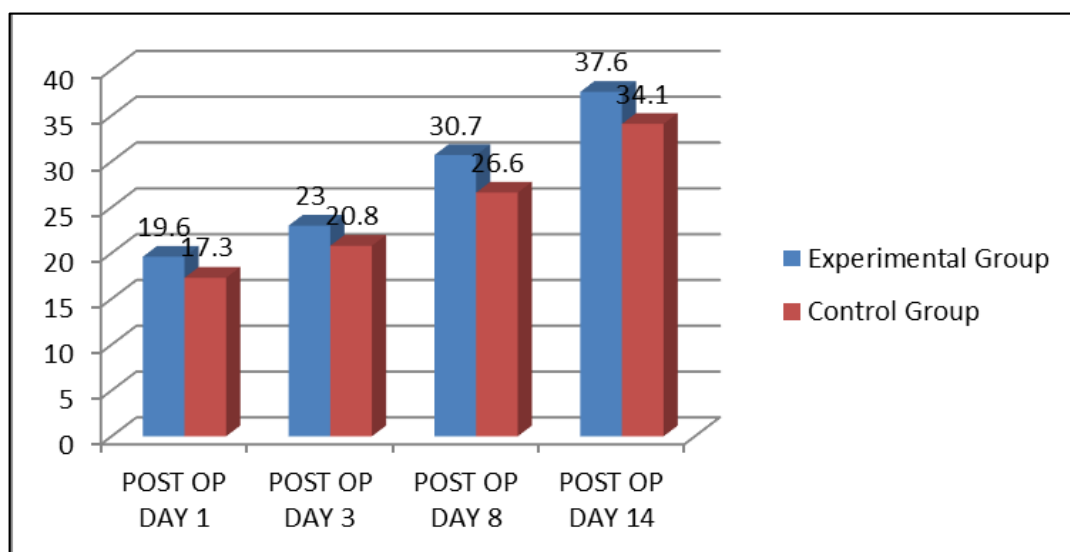


Figure 4. Mouth opening: inter group

Comparison of vas scores

The Mean for VAS SCORES was compared and this difference was found to be statistically significant among both the groups at all-time interval. The VAS SCORES was significantly lower among experimental groups.

Table 5
Comparison of Mean and standard deviation of VAS SCORES in study population at different time intervals (INTER GROUP)

Abbreviation	Time intervals	EXPERIMENTAL		CONTROL		P VALUE
		Mean	SD	Mean	SD	
T1	POST OP DAY 1	6.20	1.40	8.20	0.92	0.001*
T2	POST OP DAY 3	4.50	1.78	6.50	0.71	0.003*
T3	POST OP DAY 8	1.70	1.42	4.30	0.95	0.001*
T4	POST OP DAY 14	0.10	0.32	2.00	0.94	0.001*

^aPAIRED T TEST , * Significance of relationship at $p < 0.05$

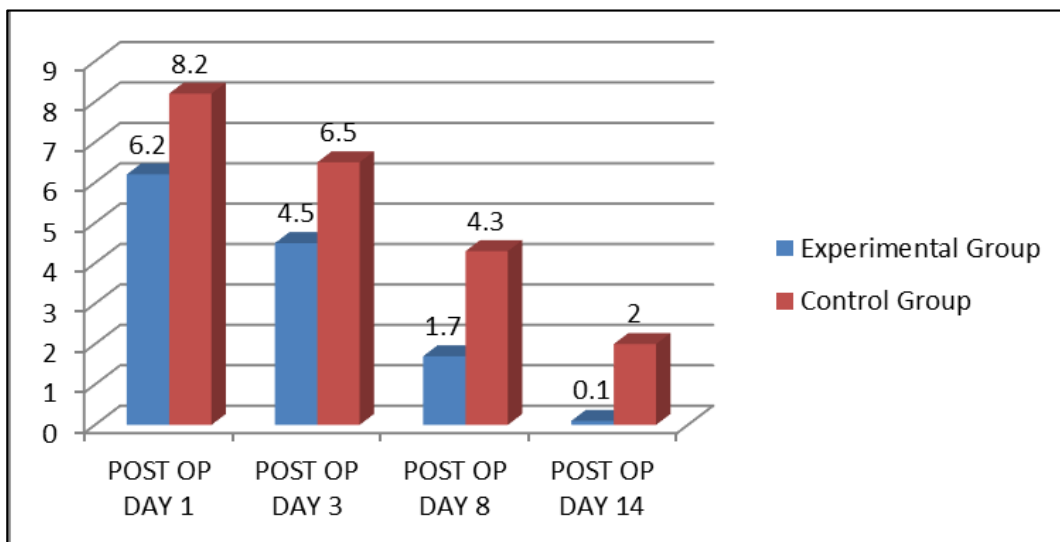


Figure 5. Inter group comparison of vas scores

Discussion

A total of 10 patients with bilateral mandibular impacted 3rd molar were recruited in Department of Oral and Maxillofacial surgery at Kothiwal Dental College and Research Centre, Moradabad. A split mouth study was conducted wherein 10 teeth were included in experimental group (EG) and 10 in control group (CG). The EG applied 10 ml of Bexident Post (ISDIN, SPAIN) containing 0.2% chlorhexidine, Allantoin, Chitosan and Dexpenthanol for 10 days while CG did not applied any topical gel. The same surgeon carried out all the surgeries and also carried the post-operative evaluation. No allergic reactions or infectious complications were noted. All the patients were put on antibiotics and analgesics post-operatively for 5 days. Patients were evaluated on Day 1, Day 3, Day 8 and Day 14.

Wound healing was evaluated as being good or acceptable. However, significant statistical difference was observed in mouth opening, facial swelling, colour of mucosa and post-operative pain as evaluated by VAS scores. A similar study was conducted by Jimenez et al. (2016), where they studied the effects of Bexident Post (ISDIN, SPAIN) on wound healing after surgical removal of impacted 3rd molars and found that overall wound's aesthetic appearance improved after topical application of Bexident Post (ISDIN, SPAIN) similar to the present study but there was no significant finding regarding post-operative swelling and pain. ⁽³⁾

In another study conducted by Lopez Lope et al. (2015), compared the efficacy of BexidentPost (ISDIN, SPAIN) with bicarbonate oral rinse in controlling post-operative inflammation and promoting cicatrisation after extraction of molar teeth and concluded that Bexident Post (ISDIN, SPAIN) shows better results as compared to bicarbonate oral rinses in reducing post-operative pain and inflammation. The results of this were homogenous to the present study. ⁽²⁾

Chlorhexidine is a well known antiseptic agent that is widely used in odntostomatology. Torres-Lagares et al. (2010), studied the effectiveness of bioadhesive

0.2% Chlorhexidine (CHX) gel in reducing the incidence of impacted 3rd molars post-extraction alveolar osteitis(AO) in patients with bleeding disorder. They concluded that single intra-alveolar application of bioadhesive 0.2% CHX gel reduces the incidence of AO after removal of impacted 3rd molars in patients with bleeding disorders.⁽¹⁵⁾

Similarly, Sridhar et al. (2011), studied the peri-operative use of 0.2% CHX gluconate for prevention of AO after removal of impacted 3rd molars and found that incidence of AO was reduced significantly after oral rinses with 0.2% CHX gluconate peri-operatively.⁽¹⁷⁾ In another study, conducted by Calla R S et al. (2016), where they studied the effectiveness of intra-alveolar chlorhexidine gel in reducing dry socket following surgical extraction of lower third molars and for this their sample involved the treatment of 40 patients who required extraction of third molars impacted, which were randomly assigned to research groups: experimental group (chlorhexidine gel 0.12%) and control group (placebo gel). Performed the extraction was administered 1 mL of chlorhexidine gel or 1 mL of placebo gel within the socket. The removal of suture was on the fifth postoperative day in which the presence or absence of dry socket was evaluated. The results predicted that however there was no relation between placement of intra-alveolar 0.12% Chlorhexidine gel or placebo gel and incidence of dry socket but there was statistical difference presented in post-operative pain on 5th day. These results were similar to the present study where application of Bexident post in experimental group significant differences in post-operative pain was observed.⁽⁷⁾

Allantoin has been thought to possess numerous pharmacological properties. Most prominent among them are wound healing, anti-irritant, keratolytic actions, hydrating agents and remover of necrotic tissue to name a few.⁽⁶⁾ That's why Allantoin has been in use for over 7 decades in skin creams. However, the action of Allantoin on nerve regeneration was shown in the classic study conducted by Loots et al. (1979), where the nerves were crushed and re-exposed 7, 14, 21, 35 and 90 days after the injury, and removed for histological examination. The results obtained in a group of rats treated with allantoin were compared with those obtained in a control group of rats. The results showed that allantoin had a statistically significant effect on the cellular multiplication seen in the nerve 7 and 14 days after the injury. Myelin degeneration was also found to be more advanced in the allantoin-treated nerve preparations examined 14 and 21 days postoperatively than in the control nerve preparations.⁽⁸⁾

In another study conducted by Araujo et al. (2010), assessed the profile of wound healing process induced by allantoin. For this they selected 60 gemalewistar rats and randomly assigned them to 3 experimental groups: Control group(C)- without treatment;(E) group treated with soft lotion oil water emulsion excipients; (EA) group treated with soft lotion oil water emulsion containing 5% allantoin. The results suggested that profile of healing process was induced by allantoin. Wound healing mechanism induced by allantoin occurs via inhibiting the chemotaxis of inflammatory cells in the site of the wound, thus preventing the release of reactive species responsible for the oxidative stress and tissue damage.⁽⁶⁾In light with the results of this study we can probably state that possible reason for better wound healing in experimental group in the present study is due to the presence in Bexident Post (ISDIN,SPAIN).

In 2012 Stagger et al studied the medicinal properties of Comfrey plant that has been in use since ages in folk medicine across Europe and Asia. It was concluded that therapeutic properties of Comfrey plant are based on its anti-inflammatory and analgesic effects. Allantoin and rosmarinic acid are probably of central importance to its pharmacodynamic effects.⁽¹⁹⁾ This also explains the wound healing properties of allantoin as observed in our study.

Chitosan is a naturally non-toxic, bioactive polysaccharide that lends itself to a wide range of biomedical applications due to its high compatibility, biodegradation and cationic nature, as opposed to other polysaccharides with a neutral or negative charge.⁽²⁷⁾ Chitosan is known for its antibacterial, antifungal, antioxidant, anti-diabetic and anti-inflammatory uses, in addition to its cholesterol-lowering properties. In a study done by Kmiec et al. (2017), revealed the various uses of chitosan in dentistry. Of particular importance were anti-inflammatory, wound healing and hemostasis. For this purpose was used HemCon Dental Dressing (HDD). In US, military is manufactured HemCon Bandage (HB) forms of freeze-dried chitosan. HDD is an oral hemostatic wound dressing delivered from HB. Dressing reduces pain and recovery time by creating a physical barrier to protect the wound surface. This observation was similar to our study that showed improved wound healing in the experimental group. There are several phases of wound healing (Homeostasis & Coagulation, Inflammation, proliferative & Migration, Remodeling) and a number of *in vitro* studies revealed that properties of chitosan are working advantageously in each of them. Before and after surgery it is important to the efficient operation of the immune system. Immunomodulators act as regulators of the body's resistance to various kinds of infections. Chitosan has immunomodulatory properties and stimulates macrophages to release IL-1 which in turn stimulates fibroblast proliferation and collagen synthesis, influencing the structure. Chitosan is also very effective in bone repair. Regarding the properties of chitosan as a biomaterial for bone repair, research was carried out to see the effects of chitosan on dental socket repair after tooth extraction. After 10 weeks, found very interesting results. The bone density in middle and apical sections of the sockets treated was significantly more. Regenerated bone reached up to 98.2% of normal mandibular bone density. In each patient, the bone density in apical and middle sections was increased 29.3% and 10.8% of normal bone density. The results confirm that in chitosan-filled socket bone tissue regeneration will be faster than untreated dental socket.⁽²⁹⁾ Thus, these studies emphasize on the results of the present study relating to good wound healing in the experimental group compared to the control group.

Dexpanthenol, the stable alcohol form of pantothenic acid (vitamin B5), is well absorbed through the skin where it is rapidly converted enzymatically to pantothenic acid, a component of coenzyme A (CoA), which is important in cellular skin metabolism.⁽¹⁴⁾ In a study conducted by Proksch et al. (2002), effects of Dexpanthenol-containing cream on skin barrier repair, stratum corneum hydration, skin roughness and inflammation after sodium lauryl sulphate (SLS) induced irritation were observed. The results were significantly accelerated skin barrier repair was found in treatments with the dexpanthenol-containing cream (verum) compared with vehicle-treated (placebo) or untreated skin. The dexpanthenol-containing cream significantly reduced skin redness as a sign of inflammation in contrast to the vehicle, which produced no effect. This result was

similar to our result in respect to decreased erythema, good colour of mucosa and good wound edges in experimental group. ⁽¹¹⁾

Ebner et al. (2002), also studied the topical use of dexpanthanol in skin disorders, which is the stable alcoholic analog of pantothenic acid. Pantothenic acid is essential to normal epithelial function. Topical use of dexpanthanol is based on good skin penetration, stratum corneum hydration, reducing transepidermal water loss and maintaining skin softness and elasticity. Activation of fibroblasts proliferation which is of relevance in wound healing has been observed both in vivo and in vitro with dexpanthanol thus explaining the results observed in our study.⁽⁵⁾ In the present study almost all vital clinical parameters of wound healing and inflammation were taken into consideration and observations revealed that Bexident Post (ISDIN, SPAIN) contains chitosan, dexpanthanol, allantoin and 0.2% chlorhexidine have proved to be very effective in the cicatrization process after surgical removal of the impacted mandibular 3rd molars.

Conclusion

Bexident Post (ISDIN, SPAIN) seems to be a viable option for promoting wound healing and can be a good answer to question of wound healing in medically-compromised patients. All patients included in the study responded well to the topical application of Bexident Post (ISDIN, SPAIN). However, no medically-compromised patients were included in the present study. This can be considered as the drawback of the study alongwith short sample size and limited follow-up. Thus, we are of the view that more studies should be conducted with inclusion of medically compromised individuals and larger sample size to validate the results observed in the present study.

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