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Research Article

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Comparative Evaluation of the Efficacy of Surgical Suture Coated with Analgesic versus Conventional Suture for Sustained Local Pain Relief- Pilot Study

S Mahantesha, S Ashwini, MV Manjusha*, Ramya Ganesh, Shivani Saxena and R Deveswaran

Department of Periodontics, Faculty of Dental Sciences, Ramaiah University of Applied Sciences, Bengaluru, Karnataka ,India

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ABSTRACT

Aim of the study was to assess the efficacy of analgesic coated suture material for post-operative pain relief.A total of 20 patients who reported to the Department of Periodontology in whom flap surgery was recommended after clinical evaluation and phase I therapy were included in the study. The subjects were divided into 2 groups by simple randomization using lottery method, with 10 patients in each group i.e., Group A (Test-analgesic coated sutures and placebo tablets), Group B (Control-conventional sutures and oral analgesics). Following surgery pain parameters were assessed after 30 minutes, after 1 day and after 1 week using VAS scale and a respondent sheet.On intergroup comparison, statistically significant difference was noted in VAS score wherein Group A demonstrated better results when compared to Group B.Analgesic coated suture material was found to be better in improving pain parameters after periodontal flap surgery.

Keywords: Analgesic coated suture; Post-operative pain; Diclofenac

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INTRODUCTION

Suture plays an important part in surgeries and trauma management [1]. Following an injury or surgical procedure, sutures help in holding apposing tissues together to fasten the healing process [2]. Various factors affecting choice of suture material in management of surgical wound includes number of tissue layers involved in closure of wound, amount of tension present across sutured wound, depth of suture placement, presence of edema, approximate time for which suture has to be kept, inflammatory reactions exhibited by suture material [3]. Surgical sutures should also have significant flexibility for adequate handling during suturing. Other important characteristics includes of suture should include, effortlessness in placement of knot, high knot security and should be free from irritating, or infectious substances [4,5]. The suture materials available commercially generally fulfill most of the primary requirements, but not all. Hence, our present efforts are centered on evolving suture material that has all the required features along with the presence of supplementary abilities such as the potential to deliver analgesic drugs in cells to assist and/or enhance wound healing [6].

To treat local, post-surgical pain, patients are often prescribed drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs), to be administered systemically [7]. As pain usually persists post- surgery, long-term, repetitive drug administrations are required until the surgical wounds have almost completed healing. However, such long-term systemic drug exposure can lead to adverse side effects, including Reye's syndrome, platelet dysfunction and renal impairment [8,9]. Moreover, for oral administration, drug bioavailability, especially at the local level in the wounded site of interest, could be low due to the first-pass metabolism of the liver [10,11]. Therefore, to be

effective, frequent oral administrations of high drug doses are often needed, which may lead to various gastric problems as hemorrhage, ulcer perforation or gastrointestinal tract obstruction [12,13].
Usually, local drug delivery has been considered beneficial for relieving pain at surgical wound sites. Sutures can serve as agent that can approximate the wounds while concomitantly relieving pain via local drug release. Commercially there are various surgical sutures available for clinical use that are made of various biocompatible polymers, such as polycaprolactone, polydioxanone, poly(lactic acid), poly(glycolic acid) and poly(lactic-co-glycolic acid) (PLGA) [14-16]. Sutures eluting the anti-infective drug, triclosan, have already been commercialized [17]. For drug elution, sutures have mostly been dip-coated in a drug solution [18-22].
Post-operative pain originating from the wound is an unavoidable inconvenience for patients and surgical suture is a strand of biocompatible material that is designed for such wound closure. Therefore, analgesic-coated suture can be used as a medical device potentially suitable for local drug delivery to treat post-surgical pain. Hence, purpose of this study is to assess the efficacy of surgical suture coated with analgesic in pain relief after periodontal flap surgery.

SUBJECTS AND METHODS

The present pilot study examined 20 subjects aged between 25 and 60 years. Subjects were selected from the patients who reported to the Department of Periodontology, Faculty of dental sciences, Ramaiah University of applied sciences, Bangalore The subjects were divided into 2 groups by simple randomization using lottery method, with 10 patients in each group as follows: Group A (Test-analgesic coated sutures), Group B (control-conventional sutures). Study was approved by the ethical committee of Ramaiah University of applied sciences. Patients were informed about the procedure and written informed consent was taken from them.

Inclusion Criteria-

- Age between 18 and 60 years;
- Patients with periodontal pocket depth of 5-8 mm and with radiographic evidence of bone loss requiring flap surgery.

Following patients were excluded-

- Patients who had known or suspected allergy to diclofenac.
- Pregnant and lactating women.
- History of using analgesics or other agents that may interfere with the analgesic response with meloxicam films.
- Those who refuse to provide written informed consent.
- Patients who were not able to understand the purposes of the study or who were not willing to return for the control visits.
- Patients who reported with major psychological disorders that could compromise study participation .

The required analgesic coated suture was prepared at the Faculty of Pharmacy, RUAS, Bangalore. The subjects for the study were from the outpatient Department of Faculty of dental sciences, RUAS, Bangalore.

Fabrication of Diclofenac Coated Suture

Analgesic coated sutures were prepared using solution dipping method. Vicryl suture 3-0 and diclofenac sodium were purchased as per the requirements of the study (Figure 1). Initially 4% of eudragit polymer was dissolved in 30 ml of ethanol with the help of a sonicator. Simultaneously 0.9 g of diclofenac sodium was dissolved in 3ml of water

and was added to initially prepared ethanol solution in a beaker. Solution was then transferred to a petridish and suture was immersed completely in it. It was kept overnight and after 12 hours the suture was taken and completely dried in an oven at 400 C. The prepared sutures were used to treat the patients after their evaluation in Faculty of Pharmacy, RUAS, Bangalore (Figures 2 and 3). Tensile strength of the sutures were assessed by performing straight pull and knot pull test using universal testing machine. Characterisation of the sutures were done using differential scanning calorimetry. In all the subjects, periodontal flap surgeries were performed under local anesthesia. In Group A analgesic coated sutures were used and no further oral analgesics were given as a part of research protocol (Figures 4 and 5) .In group B conventional sutures were used and oral analgesics were given. Then routine postoperative instructions were given. The primary outcome measure was postsurgical pain level which was measured using a 100 mm visual analogue scale (VAS) 30 minutes after surgery and 7 days after surgery .During the 7 days following surgery, patients were asked to fill out a questionnaire every day to evaluate the experience of postoperative complaints. The patients were instructed to report back immediately in case of any side effects such as hypersensitivity or anaphylactic reactions.

Statistical Analysis

For comparing the mean VAS scores between two groups at different time intervals, Mann Whitney U test was used. For assessing inter-group pain characteristics at different time intervals Chi-square test was used. Comparison of mean VAS scores between different time intervals in each study group was done using Friedman's test followed by Wilcoxon signed rank test as post hoc analysis.

RESULTS AND DISCUSSION

Results

When a comparison of mean VAS scores between 02 groups at different time intervals using Mann Whitney Test was done at time interval of 30 mins,1 day and 3 day it was found that VAS score was minimum at day 1 and it was found to be statistically significant wherein Group A patients showed better results as compared to Group B patients (Table 1).

Table 1. Comparison of mean VAS scores between 02 groups at different time intervals using Mann Whitney test

Comparison of mean VAS scores between 02 groups at different time intervals using Mann Whitney Test							
Time	Groups	N	Mean	SD	Mean Rank	Z	P-Value
30 Min	Group A	10	0.5	0.53	6.25	-3.365	0.001
	Group B	10	2	0.82	14.75		
Day 1	Group A	10	0.1	0.32	5.95	-3.88	<0.001
	Group B	10	1.1	0.32	15.05		
Day 3	Group A	10	0.3	0.48	7.85	-2.26	0.02
	Group B	10	1	0.82	13.15		

On Comparison of mean VAS scores between different time intervals in each study group using Friedman's test followed by Wilcoxon Signed Rank test as post hoc Analysis was done, it was found that pain reduced significantly in Group B after 30 mins, 1 days and 3 days whereas in Group A it was seen that pain reduced immediately after

analgesic coated sutures were given and thus no statistically significant results were seen after 30mins, 1 day and 3 days (Table 2).

Table 2. Comparison of mean VAS scores between different time intervals in each study group using Friedman's test followed by Wilcoxon Signed Rank test as post hoc Analysis

Comparison of mean VAS scores between different time intervals in each study group using Friedman's test followed by Wilcoxon Signed Rank test as post hoc Analysis									
Suture	Time	N	Mean	SD	Mean Rank	c^2 Value	P-Value	Sig. Diff	P-Value
Group A	30 Min	10	0.5	0.53	2.3	3.429	0.18	..	..
	Day 1	10	0.1	0.32	1.7				
	Day 3	10	0.3	0.48	2				
Group B	30 Min	10	2	0.82	2.7	11.84	0.003*	30M Vs D1	0.01
	Day 1	10	1.1	0.32	1.7			30M Vs D3	0.02
	Day 3	10	1	0.82	1.6			D1 Vs D3	0.56

When an intra-group comparison was done to assess Pain during Eating between different time intervals in each study group using Cochran's Q test it was found that Group B patients reported with symptoms of pain while eating and the results were found to be statistically significant. Similarly when an intra-group comparison was done to assess frequency of pain no significant difference was found between the two groups (Table 3).

Table 3. Comparison of pain during eating between different time intervals in each study group using Cochran's Q test & Comparison of frequency of Pain between different time intervals in each study group using Cochran's Q test

Comparison of Pain during Eating between different time intervals in each study group using Cochran's Q test							
Group	Time	Intermittent		No		Cochran's Q Value	P-Value
		N	%	n	%		
Group A	30 Min	5	50%	5	50%	3.429	0.18
	Day 1	1	10%	9	90%		
	Day 3	3	30%	7	70%		
Group B	30 Min	10	100%	0	0%	6	0.05#
	Day 1	10	100%	0	0%		
	Day 3	7	70%	3	30%		
Comparison of frequency of Pain between different time intervals in each study group using Cochran's Q test							
Group	Time	Intermittent		No		Cochran's Q Value	P-Value
		N	%	n	%		
Group A	30 Min	5	50%	5	50%	3.429	0.18
	Day 1	1	10%	9	90%		
	Day 3	3	30%	7	70%		
Group B	30 Min	10	100%	0	0%	2	0.37
	Day 1	10	100%	0	0%		
	Day 3	9	90%	1	10%		

When an intergroup comparison of Pain characteristics at different time intervals was done using Chi Square test it was seen that frequency of pain reduced in both the group A and B 30min and 1 day post operatively and the results were found to be statistically significant. It was also seen that even after 3 days Group B patients reported with pain but Group A patients reported no pain at all (Table 4).

Table 4. Comparison of Pain characteristics between 02 groups at different time intervals using

Comparison of Pain characteristics between 02 groups at different time intervals using Chi Square test						
Variable	Categories	Group A	Group B		c^2 Value	P-Value
		%	n	%		
Frequency of Pain	Intermittent	50%	10	100%	6.667	0.01
	No	50%	0	0%		
	Intermittent	10%	10	100%	16.364	<0.001
	No	90%	0	0%		
	Intermittent	30%	9	90%	7.5	0.006
	No	70%	1	10%		
Pain During Eating	Yes	50%	10	100%	6.667	0.01
	No	50%	0	0%		
	Yes	10%	10	100%	16.364	<0.001
	No	90%	0	0%		
	Yes	30%	7	70%	3.2	0.07
	No	70%	3	30%		

Chi Square test

Figure 1. Raw materials-ethanol, diclophenac sodium and vicryl suture

Figure 2. Preperation of diclophenac coated suture material

Figure 3. Sealed packaging of coated suture mateial after sterlization

Figure 4. Packaging of placebo tablets

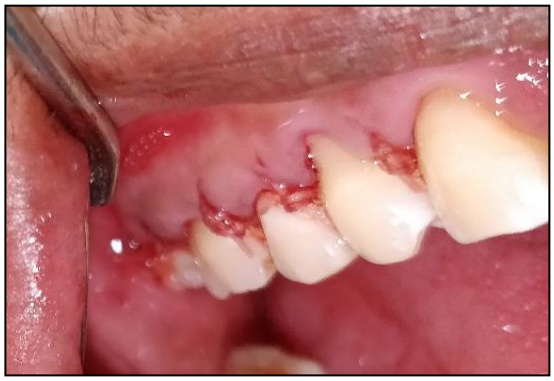

Figure 5. Placement of suture material in patient after periodontal flap surgery

Discussion

Sutures are very widely used in periodontology after surgical procedures to control postoperative complications. Sustained release of drug at a specific site can allow therapeutically relevant concentration locally for prolonged duration without causing systemic toxicity. Various types of new generation sutures include antimicrobial suture, drug eluting sutures, stem seeded sutures and smart sutures.

Generally, chronic conditions are associated with dull pain or no pain at all but it is highly unpredictable what an individual will present with. The level of pain will depend on whether at the time of presentation there is an acute exacerbation of the chronic condition or not. It will also depend on the individual's pain threshold. This individual variation may have been the reason for the pattern observed in this study.

Health professionals tend to under or overestimate their patients' level of pain or assume that some conditions should be painful while some should be painless. The result of the study by George et al reveals that individuals with same diagnosis have varying level of pain and that no dental condition is painless in all cases. This supports the previous report that the extent and quality of the damage, the individual's previous experience of pain and his emotional state at the time all determine the individual's level of pain [23,24]. There is therefore a need to assess each case.

According to Dionne et al. [25] pain assessment tools should be understandable, clinically relevant, closely related to the response of the patient, responsive to change, valid in a variety of pain conditions and its clinical utility should be demonstrable. Casalini et al. [26] investigated a theoretical model of a bioresorbable (poly - e - caprolactone) suture with an active lidocaine and their release kinetics in tissues. The study reported that increasing the diffusion coefficient and half-life of the drug improved the potency of the drug eluting from the suture material. An in vivo

study reported the inhibition of neointimal hyperplasia, inflammatory response and granulation tissue formation with a drug-eluting suture coated with tacrolimus in porcine model [27]. Zurita et al investigated drug (Ibuprofen—a Non-Steroidal Antiinflammatory Drug) loading and their release profile in poly (p-dioxaonone) monofilament surgical sutures [28]. With release period of longer than 120 hrs, the drug coated monofilament poly (p-dioxaonone) suture material reported to affect mechanical property of suture slightly due to swelling and diffusion process28.

Results of our study showed that analgesic coated suture material is better than oral diclofenac tablets which is in accordance with the results done by Hemant Bhaskar et al. [29] and Raja Rajeswari S et al. [30] where transdermal patch was compared to oral diclofenac tablets. The results of our study showed that patients compliance was better for analgesic coated suture material than systemically administered analgesic- in accordance with study by Rohan Hasmukh Vithlani et al. [31] where it was concluded that transdermal analgesics reduce the need for frequent dosing, hence increasing treatment compliance. Results of our study showed that the drug-delivery sutures can effectively relieve the pain at the surgical site in a sustained manner during the period of wound healing, while showing biocompatibility and mechanical properties comparable to those of the original surgical suture in clinical use which were in accordance with the in-vivo study results done by Ji Eun Lee et al. [32]. Study done by Beom Kang Huh et al. [33] showed that when analgesic coated suture was tested in-vivo,its mechanical properties were not degraded compared with the original surgical suture in clinical use which were similar to the results obtained in our study.

CONCLUSION

To relieve local, surgical pain in clinical settings, patients are often prescribed with a load of long-term, repeated drugs, to be administered systemically via the oral route or injection until the surgical wounds have completed healing. Such long-term systemic drug exposure can cause adverse side effects, including gastric irritation, Reye's syndrome, platelet dysfunction and ultimately leading to renal impairment. Thus, analgesic coated suture can serve as a method to alleviate pain via local drug delivery not only in a way of promoting the pain relief efficacy, but also as minimizing the side effects possibly caused by conventional systemic drug exposure.

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