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Double-edged sword: Conservative functions of BioGlue in healing of tooth extraction wound

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ABSTRACT:

BACKGROUND: Healing refers to the replacement of damaged tissue by new bodily tissue to restore its normal form and function. Healing of extraction wounds constitutes a number of complex events for the restoration of tissue integrity. The use of N-Butyl Cyanoacrylate, a haemostatic agent and BioGlue in the healing of extraction wounds, prove to make the complex process of healing much more accelerated and efficient to re-establish functional and structural forms.

AIMS: 1.) To assess the role of BioGlue (N-Butyl Cyanoacrylate) in the healing extraction wounds.

2.) To compare wound healing in extraction wounds with and without BioGlue (N-Butyl Cyanoacrylate).

METHODS/MATERIALS: Extraction wounds were taken as as two groups, one without the BioGlue and the other, with BioGlue. The cyanoacrylate glue was administered to the extraction wound and was assessed for rate of wound healing.

RESULTS: we found enhanced reduction in the width of the extraction wound in the wound with BioGlue while comparing it to those without. We found an increased mean total inflammatory score in the 1st week, increased remodelling score in the 4th week as well as the total IPR score in the wounds with the BioGlue when compared to those without. The parameters of inflammatory scale in the first week that showed significant difference were tissue colour, edema, pain in the wounds with the BioGlue. The remodelling scale parameters that showed a significant difference is tissue colour in those wounds with the BioGlue. The Landry,Turnbull and Howley index at both the 1st and 4th week showed an increased healing score in the wounds with the BioGlue than when compared to those without the glue.

CONCLUSION: To our knowledge, the rates of healing of extraction wounds are significantly influenced by the administration of N-Butyl Cyanoacrylate. The supportive data of assessment of the same also has inferred that there is significant clinical reduction in post operative symptoms, reduced chance of clot dislodgement as well as better overall environment for healing

KEY WORDS: Extraction wounds. N-Butyl Cyanoacrylate, BioGlue, healing rate

INTRODUCTION:

Healing refers to the replacement of damaged tissue by new bodily tissue to restore its normal form and function. It should be understood that the healing of a wound is not an isolated solitary phenomenon, but actually a very complex series of biological events.[1]

The procedure of extraction is such that is encountered by every dentist in his/her practice. The understanding of the importance of thorough knowledge of technique to practice the same and the of the utmost is to understand the normal events or the sequence of healing.

A brief overview of the normal sequence of healing clinically is as follows, the immediate reaction after the extraction of teeth is coagulation and clot formation. After a week, we can see that the wound size has reduced but there is still erythema, organization of the clot, evidence of granulation tissue. In the second week, there is complete organization of the clot and no wound coverage is seen at this point. The third week, the clot is completely organized by matured granulation tissue and there is slight surface epithelialization. After the period of four weeks, the wound is completely epithelialized, and the last stage of bone deposition and remodeling takes place.[1] The formation of clot is considered to be the most important event in the healing of an extraction wound as it is important for wound contraction and delayed wound healing is resulted by the dislodgement of the same.

As discussed above, the process of forming a clot or simply haemostasis, is the most important aspect of healing. One such hemostatic agent as well as a bio glue is N-Butyl Cyanoacrylate (also known as n-BCA). It is blue in colour, liquid in form. It is insoluble in water. It is bacteriostatic and the usage does not cause any pain. It is significantly used in the medical field as a component of medical cyanoacrylate glues. They are in monomer form, soluble in methyl ethyl ketone, nitromethane, methyl chloride and acetone. Polymerization occurs when it comes in contact with blood and tissue fluids.[11]

There are other components available for use such as Isoamyl Cyanoacrylate and Octyl Cyanoacrylate. Isoamyl Cyanoacrylate provides weak bond strength and Octyl Cyanoacrylate has flexibility but offers a weak bond strength. The uniqueness of N-Butyl- Cyanoacrylate over the former products is that it offers a stronger bond, polymerized form exhibits excellent tensile strength and closure of wound edges and surgical wounds is very

effective. The closure of wound is rapid and is visible to the naked eye. The cosmetic outcome and functional outcome of such wound closure enhances wound contraction as well and increases epithelialization. [11][6]

The applications of this Bio glue are multitude in the field of medicine and dentistry. In the field of medicine, they are used as a tissue glue for simple lacerations on the skin for cosmetic use, to complex treatment of vascular structure bleeding, arteriovenous malformations (through angiography). In gastroenterology, it is used in the treatment of bleeding gastric and esophageal varices, duodenal varices as well as colonic varices. In the field of dentistry, they are used as substitute to sutures in alveoloplasty, closure of intraoral wounds in certain endodontic surgeries involving soft tissue reflection, extraction of third molars and mucogingival grafting. In such said procedures, there was reduced operative time, reduced post- surgical pain, and improved haemostatic property. [11]

The aim of the study was to assess role of Bio Adhesive in the healing of extraction socket.

MATERIALS & METHODOLOGY:

This prospective, longitudinal comparative, *in vivo* study was carried out in two stages- 1.) extraction and simultaneous administration of bio glue, 2.) patient follow-up to assess the rate of wound healing and comparison of the same.

The first stage was carried out in the Department Oral and Maxillofacial Surgery and the second was conducted in the Department of Oral Pathology and Microbiology at Subbaiah Institute of Dental Sciences, Shimoga. The Institutional Ethics Committee of Subbaiah Institute of Medical college and Research, approved this study on the 11th of May, 2021 (ref no: SUIMS/R&D/IEC/062/2021). For the study, 10 participants who needed several extractions for different conditions like periodontitis, caries, and orthodontic extractions were selected. Simple extractions were performed on each patient under local anaesthesia with the least amount of trauma.

The trial includes patients who are above the age of 18, are ready to give consent, and have no medical history that might hinder the process of wound healing.

Individuals with bleeding disorders, diabetes mellitus, high blood pressure, expecting mothers, and lactating women were excluded from the study.

A detailed and elaborate case history was recorded from the patient by the clinician. Valid written informed consent for the participation and administration of the Bio-glue was obtained from each patient. Investigations of RBS, Blood Pressure, bleeding Time and clotting time was checked to eliminate any co morbidities prior to any procedure.

All the patients were informed about the procedure, the purpose, advantages and drawbacks of this study. The patient was administered 1:80,000 Adrenaline in 2% lignocaine. A minimally traumatic extraction procedure was used. There were two sockets that were taken into consideration, one was left to heal without the influence of the Bio glue (group 1) while the other was administered the Bio glue (Endocryl) after extraction in to the socket (group 2). Both groups were measured for length and widest width of the wound. The group 2 sockets were thoroughly irrigated with saline and povidine iodine after curetting it for removal any soft tissue and then the cyanoacrylate glue was loaded into a disposable syringe from the vial and then injected on to the surface of the socket. While injecting, the adhesive did not polymerise in the needle or syringe. After the extractions, patients received post-extraction instructions and an analgesic prescription of Hifenac P. The patients were called for follow up after 1 week and 4 weeks.

The parameters taken for evaluating wound healing are

1.) Measuring the length and the widest width[8].

2.) IPR Scale [9] and

3.) Landry, Turnbull and Howley Index[10].

STATISTICAL ANALYSIS:

The data was collected, coded and fed in SPSS (SPPS version 23) for statistical analysis. The descriptive statistics included mean, standard deviation, frequency and percentages. Inferential statistics included independent t test and Chi square test for the comparisons. The level of significance was set at 0.05 at 95% Confidence Interval.

RESULTS:

The haemostasis was achieved instantaneously in the sockets where Endocryl was administered when compared to the other group. There is a clinically significant difference in the mean length at day 1, after week 1 and after 4 weeks.

There is a statistically significant difference in the mean width at day 1 (p=0.031), after 1 week (p=0.039) and after 4 weeks (p=0.031) between groups 1 and 2. There is a highly significant difference in the mean of the total inflammatory score at week 1 (p=0.003), total remodelling score at week 4 (p=0.00) and total IPR score to be highly significant as well (P=0.000) between groups 1 and 2.

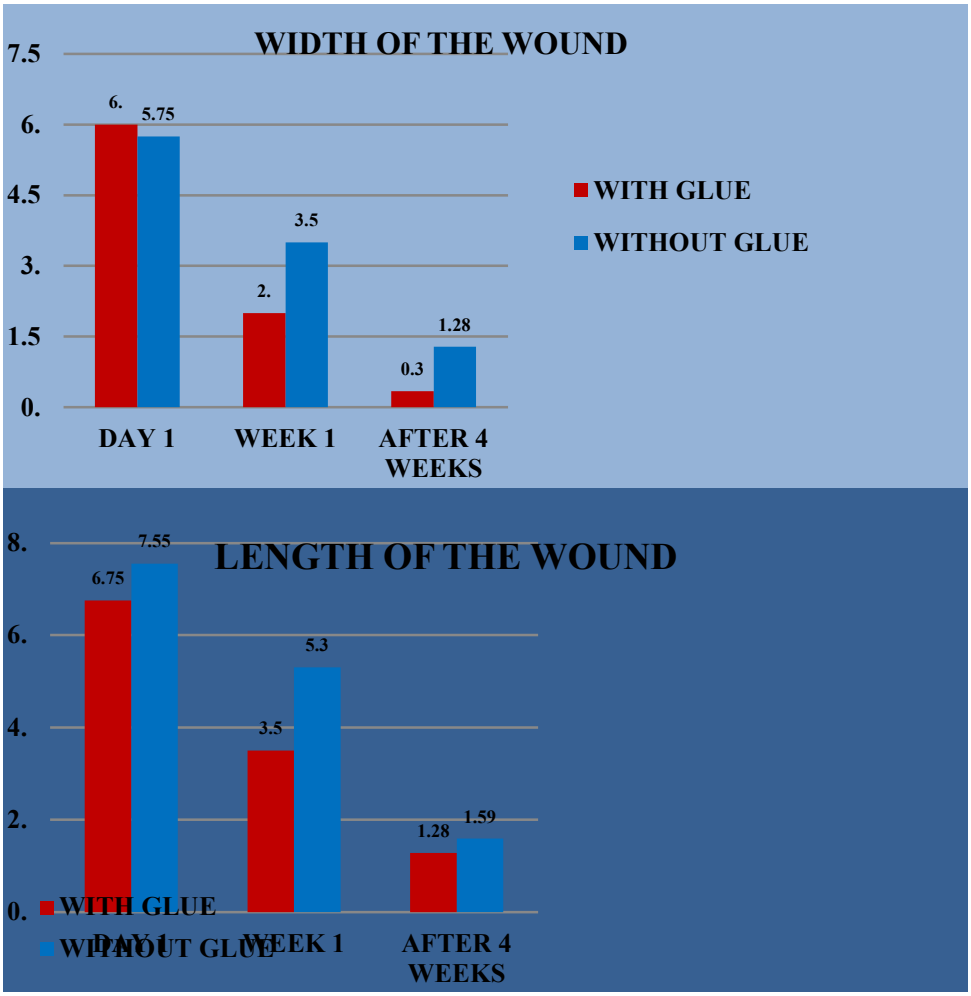
There is a highly significant difference in the frequency of occurrence of the score 1 in the inflammatory score, at week one in the following parameters: 1.) tissue colour(p=0.00) 2.) edema (p=0.001) 3.) pain (p=0.002).

There is a highly significant difference in the Landry, Turnbull and Howley Index at week 1 (p=0.00) and week 4 (p=0.00).

TABLE 1: Comparison of mean length and the width of the wound at day 1, after 1 week and after 4 weeks between the groups.

			MEAN	STANDARD DEVIATION	T	SIGNIFICANCE
LENGTH	Day 1	With glue	6.7500	2.15058	-0.928	0.540(NS)
		Without glue	7.5500	1.67415		
	Week 1	With glue	3.5000	.52705	-6.000	0.419(NS)
		Without glue	5.3000	.78881		
	Week 4	With glue	1.2800	1.27436	-0.549	0.814(NS)
		Without glue	1.5900	1.24940		
WIDTH	Day 1	With glue	6.0000	.66667	0.439	**0.031(S)**
		Without glue	5.7500	1.67083		
	Week 1	With glue	2.0000	1.41421	-2.875	**0.039(S)**
		Without glue	3.5000	.84984		

	Week 4	With glue	.3400	.46236	-2.826	**0.031(S)**
		Without glue	1.2800	.94493		



GRAPH 1: Comparison of the mean length of the wound between the two groups at day 1, week 1 and week 4.

GRAPH 2: Comparison of the mean length of the wound between the two groups at day 1, week 1 and week 4.

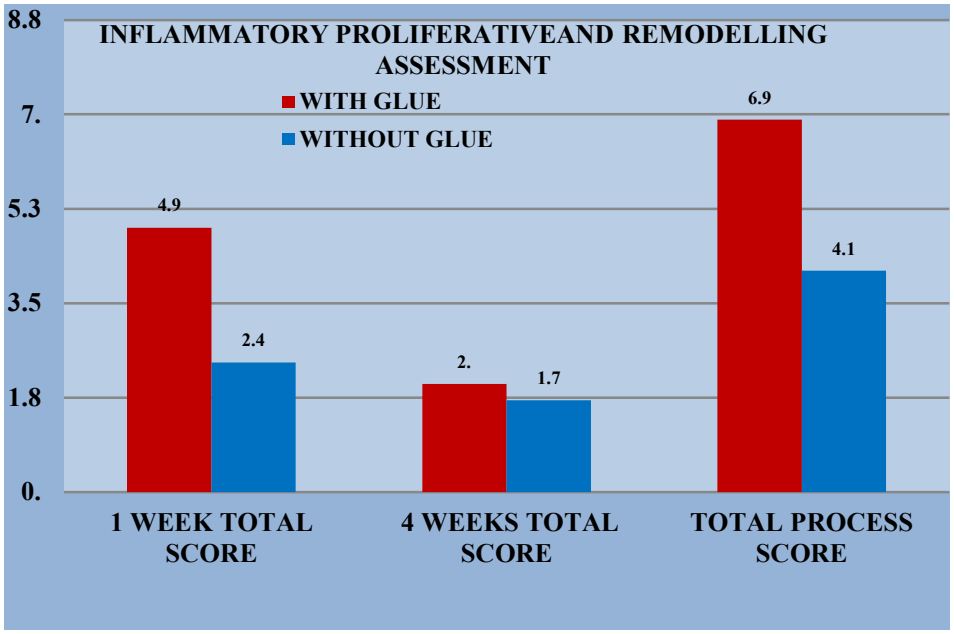


Table 2: Comparison of Inflammatory and Remodelling score after 1 week and after 4 weeks and the total IPR score between the two groups

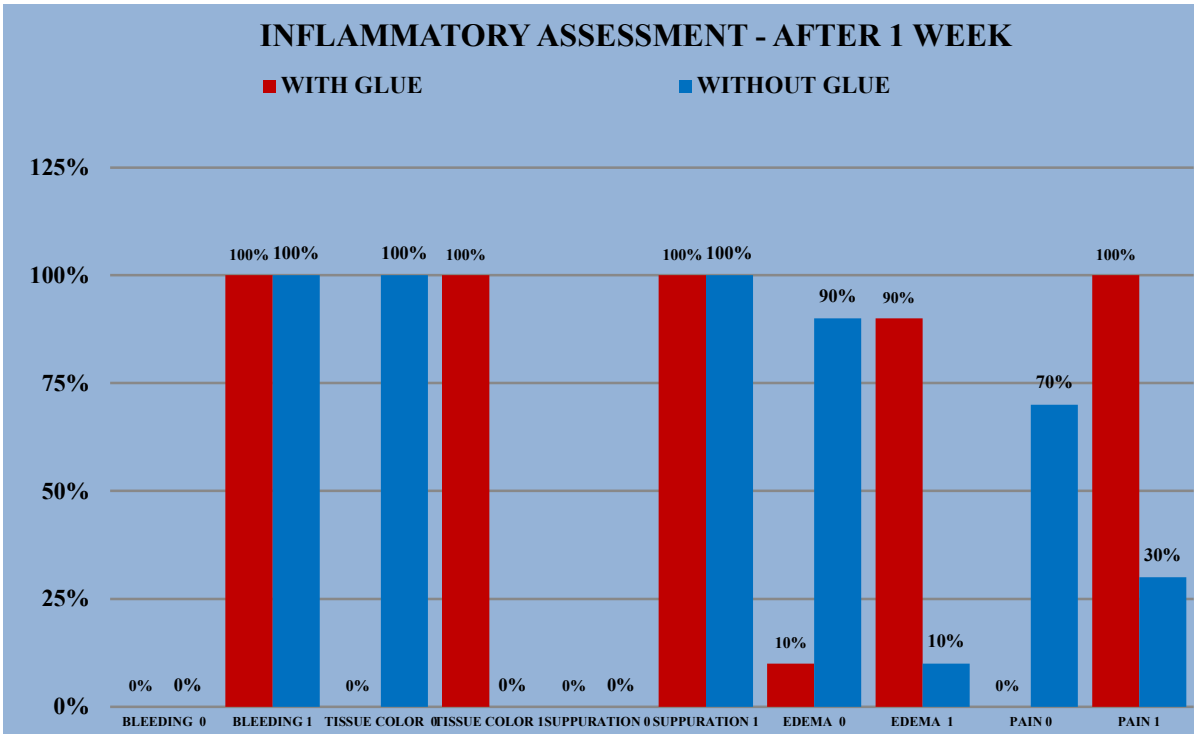
		MEAN	STANDARD DEVIATION	T	SIGNIFICANCE
AFTER 1 WEEK TOTAL SCORE	WITH GLUE	**4.9000**	**.31623**	13.056	**0.003(HS)**
	WITHOUT GLUE	**2.4000**	**.51640**		
AFTER 4 WEEK TOTAL SCORE	WITH GLUE	**2.0000**	**.00000**	1.964	**0.000(HS)**
	WITHOUT GLUE	**1.7000**	**.48305**		
TOTAL PROCESS SCORE	WITH GLUE	**6.9000**	**.31623**	13.627	**0.000(HS)**
	WITHOUT GLUE	**4.1000**	**.56765**		

GRAPH 3: Comparison of the INFLAMMATORY, PROLIFERATIVE AND REMODELLING (IPR) SCORE, at intervals of one week and 4 weeks between the two groups and the comparison of the total IPR SCORE between the two groups

TABLE 3: Comparison of frequency of the score 0 and 1 in inflammatory and remodelling scale between both groups.

			GROUPS		CHI SQUARE VALUE	SIGNIFICANCE
			WITH GLUE	WITHOUT GLUE		
ONE WEEK	BLEEDING	SCORE 0	0(0)	0(0)	-	-
		SCORE 1	10(100)	10(100)		
	TISSUE COLOR	SCORE 0	0(0)	10(100)	20.000	**0.000(HS)**
		SCORE 1	10(100)	0(0)		
	SUPPURATION	SCORE 0	0(0)	0(0)	-	-
		SCORE 1	10(100)	10(100)		
	EDEMA	SCORE 0	1(10)	9(90)	12.800	**0.001(HS)**
		SCORE 1	9(90)	1(10)		
	PAIN	SCORE 0	0(0)	7(70)	10.769	**0.002(HS)**
		SCORE 1	10(100)	3(30)		
AFTER 4 WEEKS	TISSUE COLOR	SCORE 0	0(0)	3(30)	3.529	0.105(NS)
		SCORE 1	10(100)	7(70)		
	PAIN	SCORE 0	0(0)	0(0)	-	-
		SCORE 1	10(100)	10(100)		

GRAPH 4: The comparison of mean Inflammatory scores 1 in each category after 1 week (bleeding, tissue colour, suppuration, edema, pain)



GRAPH 5: Comparison of remodelling score between the two groups for tissue colour and pain at interval of 4 weeks

LANDRY TURNBULL HOWLEY INDEX [10]

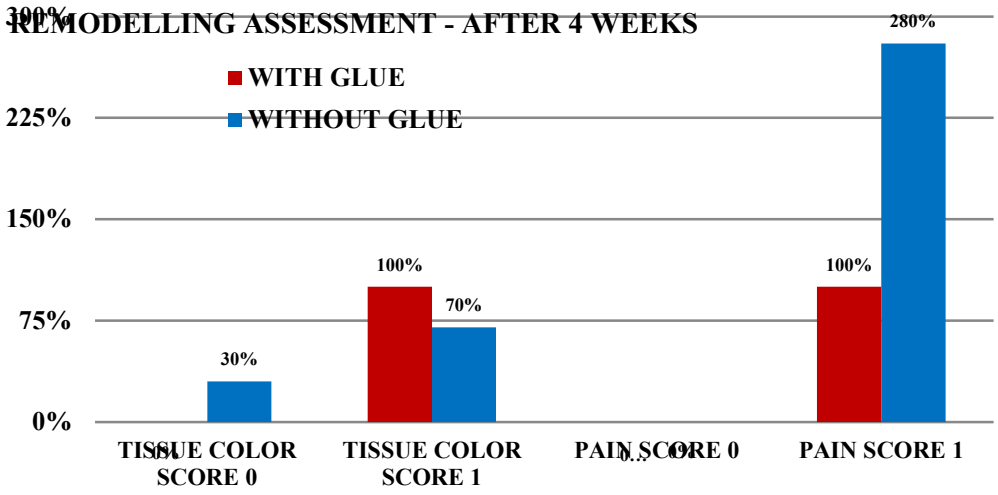
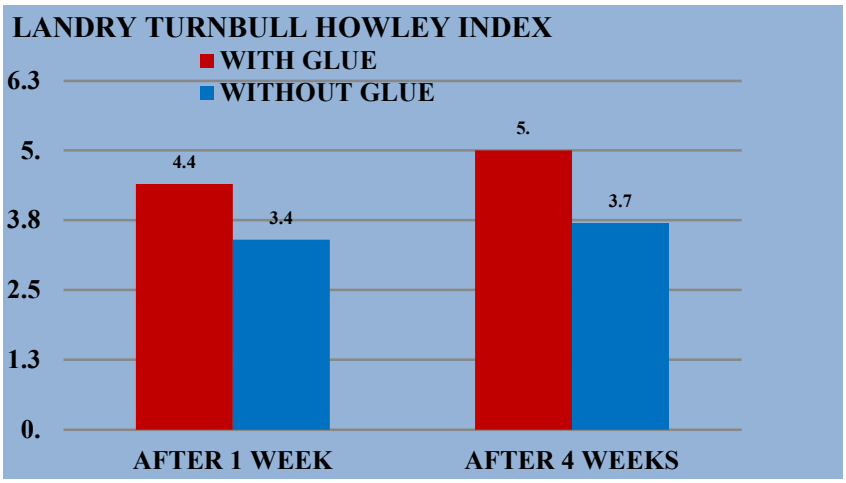


TABLE 4: Comparison of mean of Landry, Turnbull and Howley Index between both groups

		MEAN	STANDARD DEVIATION	T	SIGNIFICANCE
1 WEEK	WITH GLUE	4.4000	.51640	4.330	**0.000(HS)**
	WITHOUT GLUE	3.4000	.51640		
AFTER 4 WEEKS	WITH GLUE	5.0000	.00000	8.510	**0.000(HS)**
	WITHOUT GLUE	3.7000	.48305		



GRAPH 6: comparison of mean of Landry, Turnbull and Howley Index between both groups 1 and 2 at intervals of week 1 and week 4.

Discussion

Better structural support and increased soft tissue functional rehabilitation are provided by the significance of wound closure. Consequently, compared to traditional healing methods, early wound closure enables patients to take better care of their oral cavity.

In addition to its bacteriostatic properties in the oral cavity, which is home to a diverse array of oral flora, cyanoacrylate glue applied to the surface of a wound aids in the maintenance of a sterile environment, which in turn promotes healing in moist conditions.

The use of cyanoacrylate adhesive for bone repair dates back to the early 1970s. Soldiers with injuries during the Vietnam War (1996) were given haemostasis with cyanoacrylate spray. Adhesives such as n-butyl cyanoacrylate not only shortened the healing period compared to conventional techniques, but they also enhanced aesthetics and decreased the risk of infection. Although the early short-chain tissue adhesives were efficient, their quick breakdown into byproducts with severe tissue toxicity limited their application. Longer-chain cyanoacrylates, on the other hand, break down more slowly, preventing the buildup of harmful byproducts

in the tissues and making them suitable for topical skin closure.

Consequently, the first topical skin adhesive was approved for use by the US Food and Drug Administration in 1998. As topical skin adhesives, the following three cyanoacrylate compounds are currently in use: n-2-butyl cyanoacrylate (Endocryl, Histocryl, Indermil, GluStitch, Peri-Acryl, and LiquiBand), 2-octyl cyanoacrylate (Dermabond and SurgiSeal), and 2-ethyl cyanoacrylate (Epiglu).

When such adhesive was used, responses from patients to post-extraction symptoms like pain and discomfort were improved, and the assumptions of extractions being painful were generally reduced.

The formation and maintenance of the clot in the socket is the primary stage in the healing of extraction wounds. Cyanoacrylate exhibits rapid haemostasis, the formation of a hard barrier with maximum bond strength, and the creation of a water-resistant covering, all of which support keeping the clot in the socket without dislodgement. By acting as a barrier against dislodgment, the glue helps to avoid a dry socket

This glue can be inferred as a suitable aid to enhance the rate of healing in extraction wounds because it reduces the inflammatory response in reparative tissues and protects the underlying tissues, particularly in non-accessible areas of the third molar region where most clots get lost and undergo lysis.

This study focused on ten subjects who were selected via a rigorous and methodical process of detailing their case histories to guarantee that they satisfied the previously mentioned requirements. The study aimed to evaluate the healing rates of extraction wounds in groups 1 and 2. Both clinical and histological criteria have been used to evaluate the wound-healing process.

The results of the earlier research on rats to determine the impact of extraction wounds revealed that the extraction wounds treated with this cyanoacrylate exhibited the following characteristics, which are consistent with the clinical conclusions we have drawn from our investigation: 1.) The research indicates that the cyanoacrylate membrane that forms upon application exfoliates as granulation tissue forms and the wound contracts. 2.) In comparison to the control group, histologically, there is less inflammatory infiltration on the sockets treated with cyanoacrylate, and they shielded the underlying healing tissues from necrotic debris and other things. 3.) The histology results of the prior study demonstrated an increase in collagenization and epithelialisation in comparison to the control group. This was completely correlated in our study in terms of clinical outcomes, with group 2 showing quicker wound healing than group 1.

Future research directions:

Since even a basic extraction is a difficult and deadly treatment for patients with bleeding disorders, this work can be pursued and expanded upon to help the healing of extraction wounds in these patients. This product may be useful in mitigating the delayed wound healing and impaired phagocytic activity experienced by people with diabetes mellitus. To boost the healing activity of the cyanoacrylate and to increase post-extraction comfort, pregnant women who require extractions may be given this medication. Their exceptional tensile strength makes them suitable for a variety of wound closure operations, including periodontal surgery, the repair of soft tissue following oral and maxillofacial surgeries, apicectomy, and more. They have also been shown to be a good substitute for suture placement.

Conclusion

According to our findings, the application of N-Butyl Cyanoacrylate may cause a noticeable alteration in the rate at which extraction wounds heal. Immediately upon extraction, there is a faster contraction of the wound, stabilisation of the clot, and soft tissue closure with improved haemostasis. Additionally, the convenience of usage allows the surgeon to better care for the patient.

The clot is isolated from moisture and debris, which lowers the rate of inflammation and promotes the creation of granulation tissue. Additionally, the extraction site is typically in a more sterile environment, protected from

oral cavity germs and other sources. The price of cyanoacrylate glue in comparison to its regular use is undoubtedly a downside, but given the significant improvements in outcomes, this disadvantage is negligible. A more inferential result could be reached with a study with a larger sample size.

FINANCIAL SUPPORT AND SPONSORSHIP:

This study was sponsored by Rajiv Gandhi University of Health Sciences.

CONFLICT OF INTEREST:

No controversies were raised by this study because the results of this study correlate with the existing studies.

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