Comparative Evaluation of Cyanoacrylate Bioadhesive Material and Silk Sutures on Healing of Periodontal Flaps: A Systematic Review and Meta-Analysis.

Jasleen Thakker[1*], Shruti Karvekar[2], Vilas Pattar[3], Nivethitha D[4]

[1]Post graduate, Department of Periodontics, KAHER's KLE V.K Institute of Dental Sciences, Belagavi, Karnataka, India 590010. jasangle11@gmail.com*
[2]Faculty, Department of Periodontics, KAHER's KLE V.K Institute of Dental Sciences, Belagavi, Karnataka, India. 590010. shruti.karvekar@gmail.com
[3]Faculty, Department of Periodontics, Kaher's Kle VK Institute of Dental Sciences, Belagavi, Karnataka, India 590010. vilspat83@gmail.com
[4]Postgraduate, Department of Periodontics, Kaher's Kle VK Institute of Dental Sciences, Belagavi, Karnataka, India 590010. nivethithadivakar@gmail.com

***Corresponding contributor:** Dr Jasleen Thakker*
** KAHER's KLE V.K Institute of Dental Sciences, Belagavi, Karnataka, India 590010, Contact no.: +91 7506367111, E-mail: jasangle11@gmail.com*

KEYWORDS
Cyanoacrylates; Humans; Periodontal flap; Silk sutures; Tissue Adhesives, Periodontitis, Wound healing

ABSTRACT

***Background**:* Close post-operative adaptation of the periodontal flap onto the prepared root surface and the maintenance of this adaptation for a period is critical to the reestablishment of a healthy dentogingival unit. Applications of sutures require passage of a foreign material through tissue which elevates tissue reactivity. It also provides a pathway for the retention of microorganism onto the tissue which leads to further infection. So, in order to overcome the existing drawback with sutures, cyanoacrylate which is a biocompatible tissue adhesive can be used for the closure of the incised wounds. Hence, the current review aimed to assess the effectiveness of cyanoacrylate bioadhesive material in healing of periodontal flaps as compared to the conventional silk sutures.

***Materials and Methods**:* A systematic literature search was conducted in three databases: ProQuest, Google Scholar and PUBMED and a hand search of relevant scientific journals was performed for Randomized controlled trials. Studies were assessed for quality with the help of predetermined criteria which categorized the studies into high, medium and low quality. Random effect models were used for performing meta-analysis for Gingival index, Plaque index, VAS pain score, Wound healing index, Fibrosis, Vascularity and Inflammatory cells on the 7th day post-operative.

***Results**:* From 1101 initial studies, 14 were eligible for full-text review, with 8 RCTs included in the meta-analysis. The analysis favored cyanoacrylate bioadhesive material over silk sutures for the closure of periodontal flap with statistically significant improvement seen for Fibrosis, Inflammatory cells, Vascularity, Plaque index and Gingival index.

***Conclusion**:* Within the limitations of this review, the use of Cyanoacrylate bioadhesive material proved to be beneficial in improving the clinical and histological parameters when compared to Conventional silk sutures technique for the closure of Periodontal flap after surgery.

INTRODUCTION

The multifaceted disease referred to as periodontitis causes inflammation and breakdown of the teeth's connective tissue attachment. One of the most common procedures, especially for moderate to deep pockets, is the periodontal flap. In order to achieve primary wound healing, surgical pocket therapy entails raising a full thickness mucoperiosteal flap, debridement of diseased granulation tissue, and

root planing, followed by flap margin closure. In addition to promoting early tissue maturation and healing, primary closure of the site can ascertain wound stability.[1,2]

The flaps are routinely closed after surgery using materials such as silk, nylon, steel, catgut, and polyglycolic. The most preferred suture for closing oral wounds is braided silk. Sutures create the highest tissue response because they necessitate the passage of a foreign material through the tissue. Because of the "wicking" tendency, it can retain and allow bacteria to penetrate the tissues, serving as a reservoir for secondary infections. Suturing takes a lot of time, damages tissue, and elevates the risk of needlestick injuries. Removing sutures a week after surgery is inconvenient for the patient, and because silk sutures have a low knot strength, using absorbable sutures increases the risk of early absorption and wound opening, which can result in a gaping wound. Therefore, there is always a need for an alternative to sutures in order to get beyond such challenges.[3,4]

Coover et al. developed cyanoacrylates, which are tissue-adhesive materials, in 1959. The chemical formula for the cyanoacrylate compounds is $H_2C = C (CN) COOR$, where R can be any alkyl group, from methyl to decyl. Since cyanoacrylate bioadhesive materials are single-component, catalyst-free adhesives that may form a bond at ambient temperature in a matter of seconds, their use has surged in importance recently in comparison to traditional silk sutures.[5]

They are widely utilized in a variety of surgical applications in the fields of general and dental surgery due to this chemical characteristic. In the presence of trace amounts of moisture, the liquid monomer quickly polymerizes into a solid polymer in a matter of seconds. Cyanoacrylates create a continuous seal that effectively distributes the load and reduces scarring, in contrast to sutures, which leave tiny openings in the wound. These adhesives can also serve as a reservoir for antibacterial medication and a liquid bandage to protect the wound. These materials have the advantages of being quick to apply, comfortable for the patient, resistant to infection, and requiring no suture removal. Because of the polymer's strong electronegative charge and capacity to create a mechanical barrier that keeps out materials and organisms, cyanoacrylates are known to have bacteriostatic and hemostatic qualities in addition to their adhesive ones.[6,7]

An alternative to silk, nylon, or staples, cyanoacrylate is a more recent tissue adhesive material that is biocompatible and has a stronger tissue-binding ability, especially in moist conditions. Thus, the current review's objective was to comprehensively evaluate the superiority of cyanoacrylate bioadhesive material over traditional silk sutures in the healing of periodontal flaps.

MATERIALS AND METHODS

Protocol and registration

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist.[8] The registration of the study protocol was carried out at International Prospective Register of Systematic Reviews PROSPERO (Registration Number CRD42023428868).

The study was conducted with a focused question in the form of a specific PICO format “Is cyanoacrylate bioadhesive material more effective in healing of periodontal flaps as compared to the conventional silk sutures?”.

Population (P): Patients with age 18 to 64 years having moderate to severe periodontitis with a probing depth ≥6mm and no relevant systemic abnormalities.

Intervention (I): Periodontal flap surgery closed with cyanoacrylate bioadhesive material.

Comparison (C): Periodontal flap surgery closed with silk sutures.

Outcome (O): Visual analogue scores (VAS) for pain, Plaque index (PI), Gingival index (GI), Wound healing index (WHI), Vascularity, Fibrosis and Inflammatory cells, Papillary marginal attachment (PMA), Pocket probing depth (PPD), C-reactive protein levels (CRP), Number of colony forming units (CFU) and Bleeding index (BI).

Study design (S): Randomized controlled clinical trial

Inclusion criteria

All human randomized controlled trials with patients from age 18 to 64 years having moderate to severe periodontitis and a probing depth ≥6 mm with no significant systemic abnormalities. Studies that included PI, GI, PPD, PMA, VAS for pain, Chronic inflammation, Vascularity, Fibrosis, WHI, Levels of CRP, Number of colony forming units, BI, Presence of oedema, erythema and necrosis and any other modes of measurement used with any other relevant oral findings. Studies that included patients who underwent Periodontal flap surgery and published in English and with full text only up till December 2023.

Exclusion criteria

All observational studies, technical comments, letters to the editor, abstracts, in-vitro and animal research, and manuscripts that are indexed in databases without abstracts and case series. Studies that considered only one of the suture materials (Cyanoacrylate bioadhesive material, Conventional silk suture) for the closure of periodontal flap. Studies that included patients with active periodontal disease. Studies that included patients with any relevant systemic diseases or habit history.

Information sources and search strategy

The comprehensive data search of the scientific literature was performed through following databases: PubMed, Google scholar and ProQuest up till December 2023 in English language. Cross references and grey literature were checked for relevant articles. Hand searching of articles was done when the full texts of the relevant studies were not available through electronic database.
The search strategy was as follows: "periodontal flap" OR "periodontal pocket" OR "wound healing" AND "silk suture" OR "suture" AND "cyanoacrylate" OR "isoamyl 2 acrylate".

Selection of studies and data synthesis

The eligibility of the articles retrieved from the electronic search was evaluated by two independent examiners. The titles and abstracts were evaluated to eliminate irrelevant articles. Next, the full texts were independently assessed by the two examiners. Disagreements were resolved by discussion. Concordance between the two examiners was evaluated by the Cohen's kappa coefficient. Data were extracted according to predesigned forms. In case of missing data, correspondence was attempted with the corresponding author.
The primary outcomes included, PI, GI, WHI, Vascularity, Fibrosis, Inflammatory cells and VAS Pain scores while the secondary outcomes included, PMA, PPD, C-reactive protein, Number of colony forming units and BI.

Risk of bias assessment

The quality of included studies for five domains ("Assessing Risk of Bias in Included Studies, through Cochrane ROB 2 tool") was methodologically and independently evaluated by two review authors. Based on domains and criteria, the overall risk for individual research was rated as low, moderate, or high risk.[9]

Assessment of heterogeneity

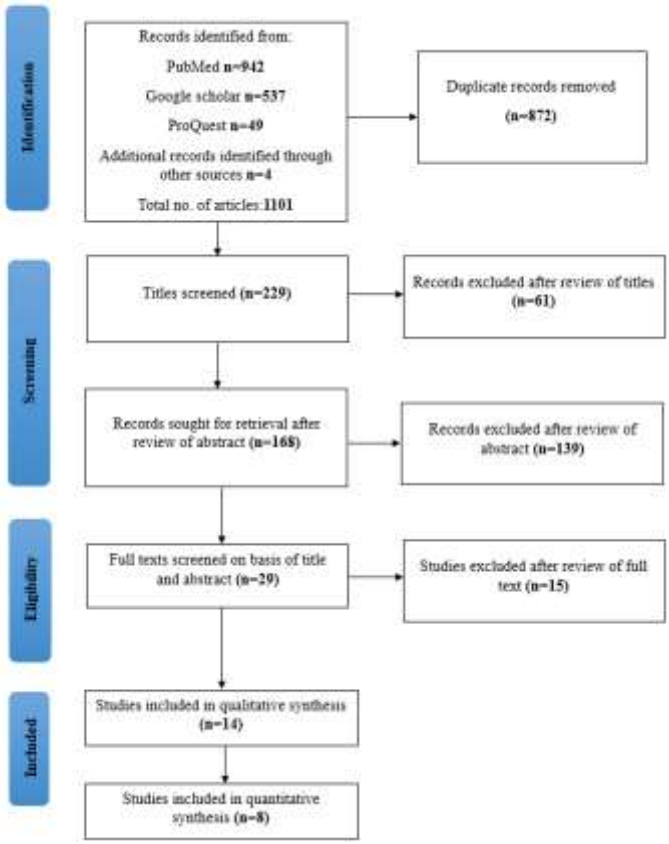
For continuous outcomes, a 95% CI and standardized mean difference (SMD) were computed (PI, GI, WHI, Vascularity, Fibrosis, Inflammatory cells, and VAS Pain scores). The Der Simonian Laird approach, a model for random effects, was applied. RevMan 5.3 (Cochrane Collaboration, Software Update, Oxford, UK) was used for all statistical analyses. A significance criterion of $p < 0.05$ was maintained. Cochranes' test for heterogeneity and the I^2 statistics were used to determine the significance of any differences in the pooled estimates of all the treatment effects from various studies. It indicates the proportion of overall variation among studies attributable to heterogeneity as opposed to chance. If p was less than 0.1, heterogeneity was deemed statistically significant. A manual for interpreting I^2 can be found in the Cochrane Handbook.

RESULTS

Selection of studies

After entering the search strategy, a preliminary screening was conducted. A total of 1101 publications were included in the primary screening; 229 of these were identified based on the study type and title. 15 articles were excluded from this review, after reviewing the full text, because they did not fulfil the inclusion criteria. As shown in the flowchart (Figure 1), 14 papers were deemed suitable for the review after duplicate articles and just abstracts were eliminated.

Figure no.1: PRISMA flow diagram



Characteristics of included studies

A total of 336 patients undergoing periodontal flap surgery were included. The age group of individuals incorporated in the studies that were included in this review was in the range of 18-60 years. All the included studies in this review had a split mouth design whereby two treatment groups were randomly assigned to either side of the mouth, with each participant acting as their own control. Table 1 presents the characteristics of the included studies.

Table 1: Characteristics of included studies

Author	Year of Publication	Sample size	Location of study	Sex (Male/ Female)	Age (Years)	Test group	Control group
Kulkarni et al.[11]	2007	24	Dept. of Periodontics and Dept. of Oral Pathology, S. D. M. College of Dental Sciences and Hospital, Dharwad	-	35-50	N-butyl-2-cyanoacrylate	3-0 black braided silk
Shah et al.[12]	2012	30	Department of Periodontics in Karnavati School of Dentistry, Uvarsad, Gujarat.	-	25-60	N-butyl-cyanoacrylate	3-0 black braided silk
Saquib et al.[13]	2018	30	Department of Periodontics, M.G.V Dental College and Hospital, Nasik, India	-	-	N-butyl-cyanoacrylate	3-0 black braided silk
Chandra et al.[14]	2021	40	Department of Periodontology, JSS Dental College and Hospital	M-23 F-17	20-60	N-butyl-cyanoacrylate	3-0 black braided silk

Sadatmansouri et al.[15]	2020	10	Periodontics department of the Faculty of Dentistry of Islamic Azad University of Medical Sciences, Tehran, Iran	M-3 F-7	-	N-butyl & 2-octyl cyanoacrylate, Glu-Stitch®GluStitch, Delta, BC, Canada	4.0 non-absorbable silk suture
Nambi et al.[16]	2020	20	Dept of Periodontics, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamilnadu, India.	-	30-50	Isoamyl-cyanoacrylate tissue adhesive (Amcrylate® 0.25 ml)	Silk sutures (Ethicon Mersilk #3-0 Black Braided Suture)
Khurana et al.[17]	2016	20	-	-	20-50	Isoamyl-2-cyanoacrylate	3-0 black braided silk
Vyas et al.[18]	2018	50	Ananta Institute of Medical Sciences and Research Centre, Rajsamand, Udaipur, Rajasthan, India	M-39 F-11	20-60	Isoamyl-2-cyanoacrylate	3-0 black braided silk
Mahajani et al.[19]	2019	20	Department of Periodontics, KAHER's KLE V K Institute of Dental Sciences, Belagavi	-	20-60	Cyanoacrylate tissue adhesive (Periacryl®90-HV)	3-0 black braided silk
Aeran et al.[20]	2022	30	Periodontology department, Seema Dental College and Hospital, Rishikesh, Uttarakhand	-	25-60	N-butyl-cyanoacrylate bioadhesive (@EPICLOS)	3-0 black braided silk (@TRUSILK)

Kaur et al.[21]	2020	10	Department of Periodontology, Sri Guru Ram Das Institute Of Dental Sciences and Research, Sri Amritsar.	-	20-40	Isoamyl-2-cyanoacrylate	3-0 black braided silk
Gudannavar et al.[22]	2018	10	Department of Periodontics, The Oxford dental college and hospital, Bangalore	-	-	Cyanoacrylate adhesive	Silk suture
Dr Ramu Vinayak P Menon et al.[23]	2020	12	Department of Periodontics, Amrita School of Dentistry, Cochin	-	35-50	Isoamyl-2-cyanoacrylate	Silk suture
Padhye et al.[24]	2011	30	Department of Periodontology, Government Dental College and Hospital, Mumbai	-	-	N-butyl-2-Cyanoacrylate	3-0 black braided silk

Table 2: Summary of primary treatment outcomes

AUTHOR	INTERVENTION	PI	GI	WHI	VAS PAIN SCORE	IC	VASCU-LARITY	FIBROSIS
AT BASELINE								
Saquib et al.[13]	Suture	0.71±0.14	0.66±0.08	-	-	-	-	-
	Cyanoacrylate	0.73±0.15	0.68±0.07	-	-	-	-	-
Nambi et al.[16]	Suture	1.57±0.18	-	-	-	-	-	-

	Cyanoacrylate	1.51±0.10	-	-	-	-	-	-
Padhye et al.[24]	Suture	4.113	2.1973	-	0.8333	1.4000	-	-
	Cyanoacrylate	4.0250	2.1593	-	0.3000	0.1000	-	-
AT 3 DAYS								
Chandra et al.[14]	Suture	1.3 ± 0.56	1.96±0.14	1.9±0.14	5.1 ± 0.9	-	-	-
	Cyanoacrylate	0.78±0.60	0.86±0.15	1.2±0.15	4.45±1.13	-	-	-
AT 7 DAYS								
Kulkarni et al.[11]	Suture	1.57±0.18	1.36±0.09	-	-	148.9±11.54	11.48±2.47	-
	Cyanoacrylate	1.14±0.26	1.02±0.12	-	-	94.25±9.23	9.00±2.13	-
Shah et al.[12]	Suture	1.93±0.62	-	-	-	1.90±0.73	1.50±0.52	1.80±0.63
	Cyanoacrylate	1.34±0.47	-	-	-	1.30±0.48	1.50±0.52	2.20±0.91
Saquib et al.[13]	Suture	2.61±0.21	1.60±0.09	1.58±0.16	-	1.93±0.59	2.33±0.18	1.86±0.83
	Cyanoacrylate	1.75±0.13	1.31±0.06	1.19±0.05	-	1.2±0.41	1.26±0.15	2.4±0.63
Chandra et al.[14]	Suture	1.1 ± 0.21	1.9 ± 0.21	1.8 ± 0.18	3.9 ± 1.5	-	-	-
	Cyanoacrylate	0.76±0.13	0.94±0.11	1.3 ± 0.13	3.1 ± 1.82	-	-	-
Sadatmansouri et al.[15]	Suture	3.9±0.82	-	3.3±0.53	4.7±1.34	-	-	-
	Cyanoacrylate	3.8±0.97	-	2.7±0.64	4.4±1.68	-	-	-
Nambi et al.[16]	Suture	1.95±0.29	-	2.3 ± 0.67	-	-	-	-
	Cyanoacrylate	1.43±0.19	-	1.8 ± 0.55	-	-	-	-
Mahajani et al.[19]	Suture	-	-	1.2±0.4	5.4±0.9	-	-	-
	Cyanoacrylate	-	-	2.1±0.8	1.8±1.2	-	-	-
Aeran et al.[20]	Suture	1.26±0.15	1.29±0.14	1.10±0.10	-	22.80± 8.71	6.86±3.52	-
	Cyanoacrylate	1.01±0.19	1.03±0.15	1.02±0.05	-	12.80 ±4.98	3.33±1.79	-

Kaur et al.[21]	Suture	1.45±0.75	-	-	-	-	-	-
	Cyanoacrylate	0.11±0.01	-	-	-	-	-	-
Gudaanavar et al.[22]	Suture	1.46±0.73	-	-	-	-	-	-
	Cyanoacrylate	0.10±0.00	-	-	-	-	-	-
Padhye et al.[24]	Suture	1.7397	1.5233	-	0.2333	0.7333	-	-
	Cyanoacrylate	1.3473	0.9433	-	0.0000	0.0000	-	-
Khurana et al.[17]	Suture		-	1.44	-	-	-	-
	Cyanoacrylate		-	1.00	-	-	-	-
AT 14 DAYS								
Chandra et al.[14]	Suture	0.8 ± 0.15	1.2 ± 0.15	1.4±0.16	0.65 ± 1.1	-	-	-
	Cyanoacrylate	0.77±0.09	0.95±0.13	1.2±0.12	0.90±1.12	-	-	-
Khurana et al.[17]	Suture		-	1.09	-	-	-	-
	Cyanoacrylate		-	1.00	-	-	-	-
AT 21 DAYS								
Kulkarni et al.[11]	Suture	1.31±0.21	0.94±0.49	-	-	102.1±21.35	9.13±2.70	-
	Cyanoacrylate	1.11±0.29	0.60±0.22	-	-	87.13±9.92	9.32±1.41	-
Shah et al.[12]	Suture	1.41±0.35	-	-	-	1.80±0.63	1.60±0.51	2.00±0.66
	Cyanoacrylate	1.36±0.48	-	-	-	1.60±0.69	1.70±0.67	2.00±0.81
Saquib et al.[13]	Suture	1.08±0.15	0.86±0.13	1.29±0.13	-	-	-	-
	Cyanoacrylate	1.04±0.09	0.94±0.13	1.08±0.09	-	-	-	-
Padhye et al.[24]	Suture	1.3610	1.1110	-	0.0000	0.0345	-	-
	Cyanoacrylate	1.2917	0.7268	-	0.0000	0.0345	-	-
AT 42 DAYS								
Kulkarni et al.[11]	Suture	1.21±0.24	0.57±0.19	-	-	59.00±24.59	8.62±1.59	-

	Cyanoacrylate	0.99±0.37	0.41±0.24	-	-	47.16±15.64	8.50±0.92	-
Shah et al.[12]	Suture	0.99±0.30	-	-	-	1.40±0.51	1.70±0.48	1.90±0.73
	Cyanoacrylate	0.98±0.50	-	-	-	1.40±0.51	1.60±0.51	2.10±0.73
Saquib et al.[13]	Suture	0.74±0.09	0.69±0.09	1.0	-	1.0±0	1.0±0	2.26±0.45
	Cyanoacrylate	0.74±0.09	0.69±0.07	1.0	-	1.0±0	1.0±0	2.4±0.50
Chandra et al.[14]	Suture	0.78±0.05	0.72±0.07	0.95±0.11	0.20±0.41	-	-	-
	Cyanoacrylate	0.81±0.09	0.76±0.05	0.93±0.15	0.05±0.23	-	-	-

Plaque index (PI), Gingival index (GI), Wound healing index (WHI), Visual analogue pain score (VAS), Inflammatory cells (IC), Vascularity and Fibrosis expressed as Mean ± Standard deviation at Baseline, 3 days, 7 days, 14 days, 21 days and 42 days' time interval.

Primary outcomes

The overall mean difference for VAS pain score on the 7th day was reported in 3 studies[14,15,19] which was -1.61 having a precision of -3.65 to 0.42. The results obtained were not statistically significant (p-value>0.05). (Figure No.2)

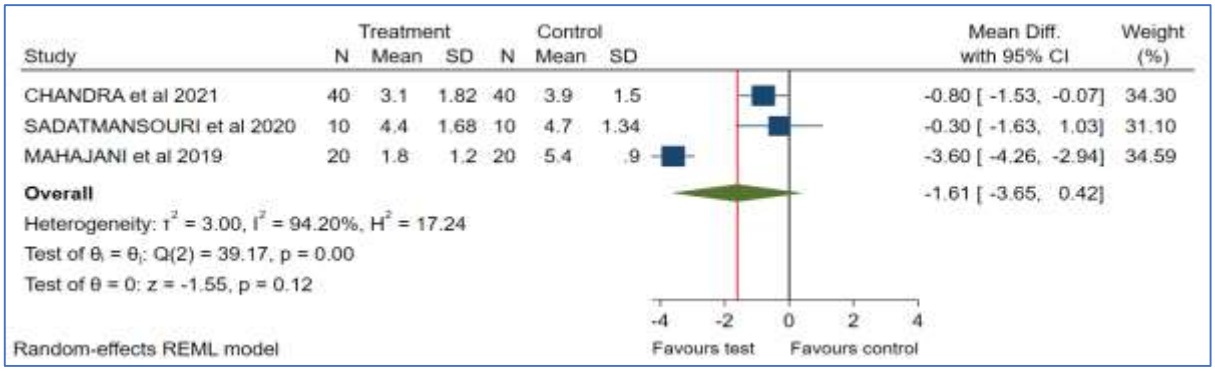


Figure no.2: Forest Plot for the mean VAS Pain score on the 7th day among the included studies.

The overall mean difference for Wound Healing I-ex on the 7th day was reported in 6 studies[13,14,15,16,19,20] which was -0.20 having a precision of -0.63 to 0.23. The results obtained were not statistically significant (p-value> 0.05). (Figure No.3)

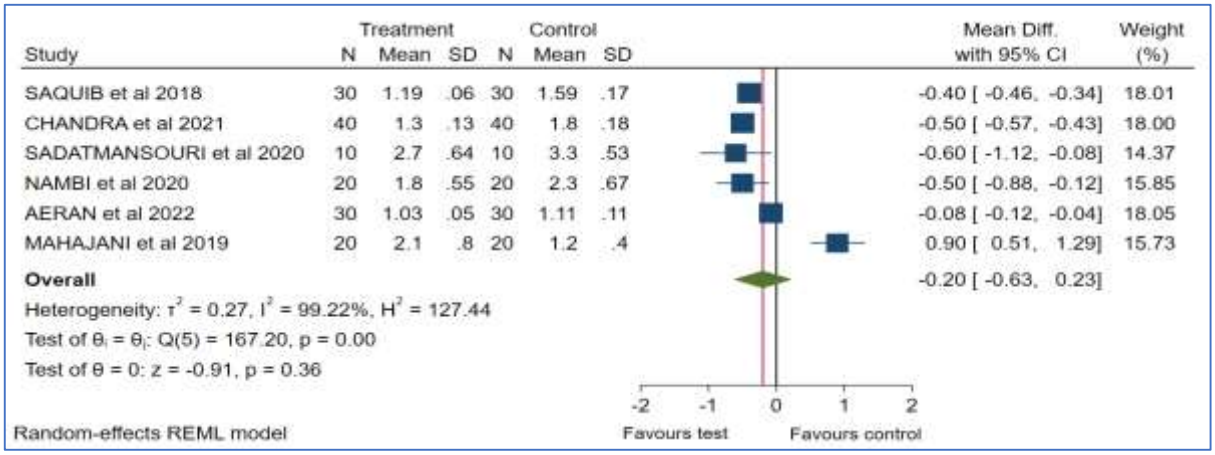


Figure no.3: Forest Plot for the mean Wound healing index on the 7th day among the included studies.

The overall mean difference for Fibrosis on the 7th day was reported in 2 studies[12,13] which was 0.49 having a precision of 0.20 to 0.74. The results obtained were statistically significant (p-value< 0.05). (Figure No.4)

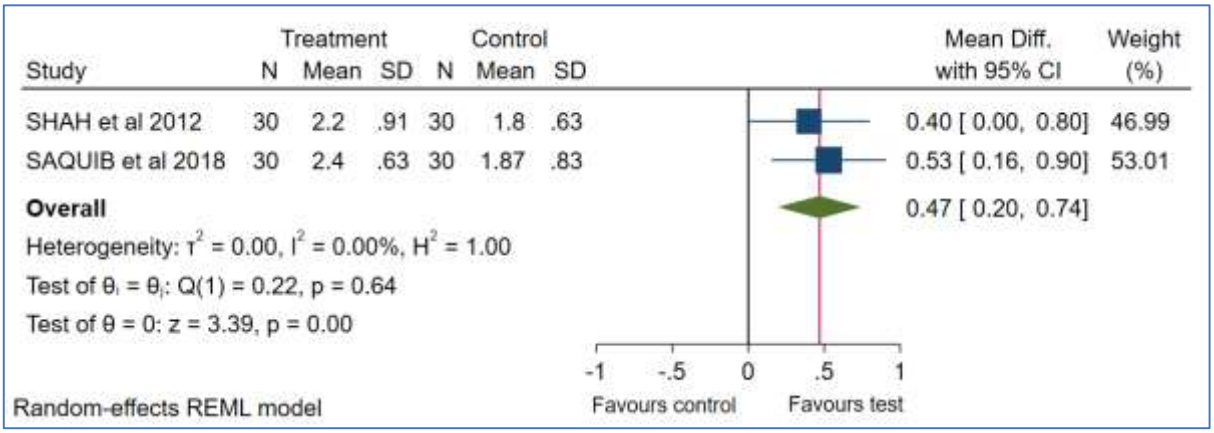


Figure no.4: Forest Plot for the mean Fibrosis on the 7th day among the included studies.

The overall mean difference for Inflammatory cells on the 7th day was reported in 2 studies[12,13] which was -0.68 having a precision of -0.88 to -0.48. The results obtained were statistically significant (p-value< 0.05). (Figure No.5)

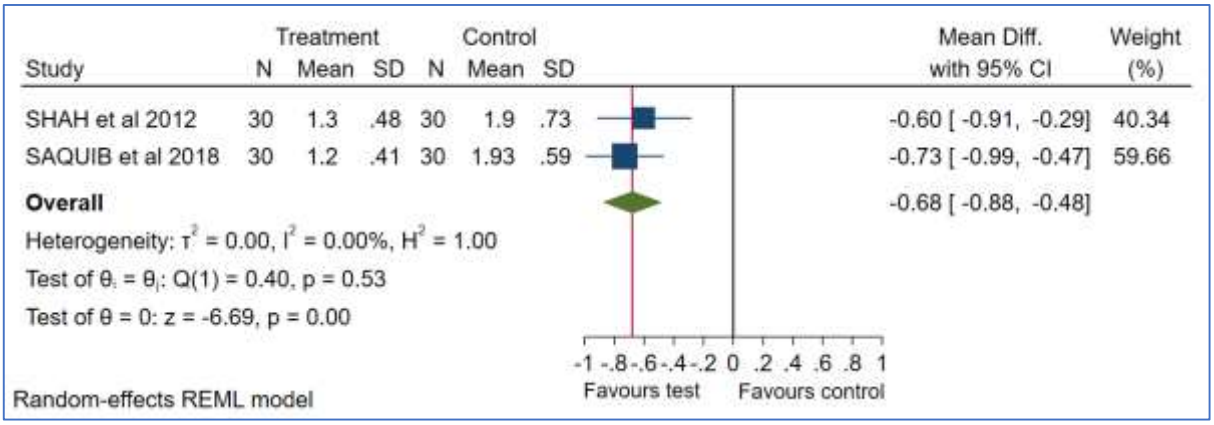


Figure no.5: Forest Plot for the mean Inflammatory cells on the 7th day among the included studies.

The overall mean difference for Vascularity on the 7th day was reported in 4 studies[11,12,13,20] which was -1.64 having a precision of -3.15 to -0.14. The results obtained were statistically significant (p-value< 0.05). (Figure No.6)

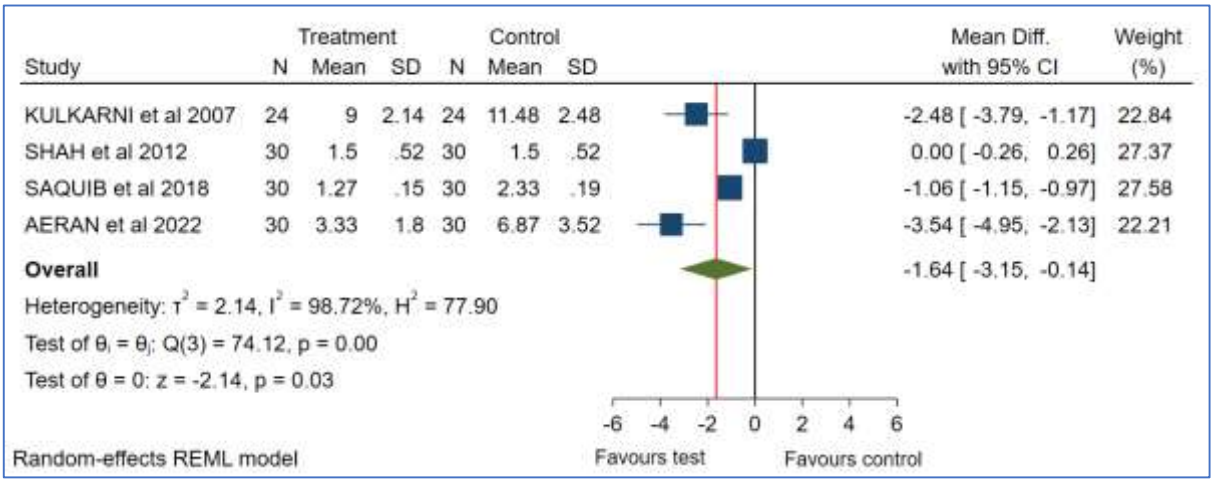


Figure no.6: Forest Plot for the mean Vascularity on the 7th day among the included studies.

The overall mean difference for Plaque index on the 7th day was reported in 8 studies[11,12,13,14,15,16,20,21] which was -0.55 having a precision of -0.78 to -0.33. The results obtained were statistically significant (p-value< 0.05). (Figure No.7)

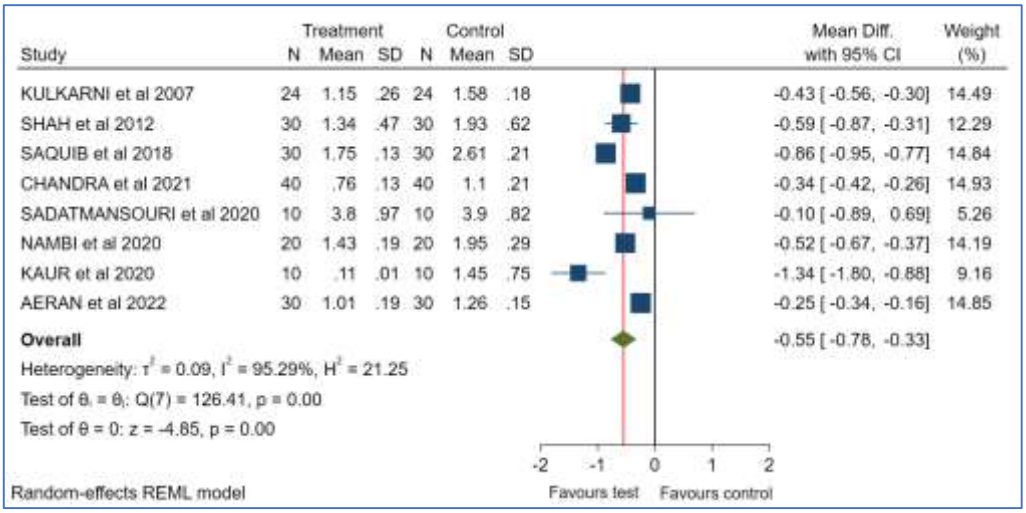


Figure no.7: Forest Plot for the mean Plaque index on the 7th day among the included studies.

The overall mean difference for Gingival index on the 7th day was reported in 4 studies[11,13,14,20] which was -0.46 having a precision of -0.79 to -0.13. The results obtained were statistically significant (p-value< 0.05). (Figure No.8)

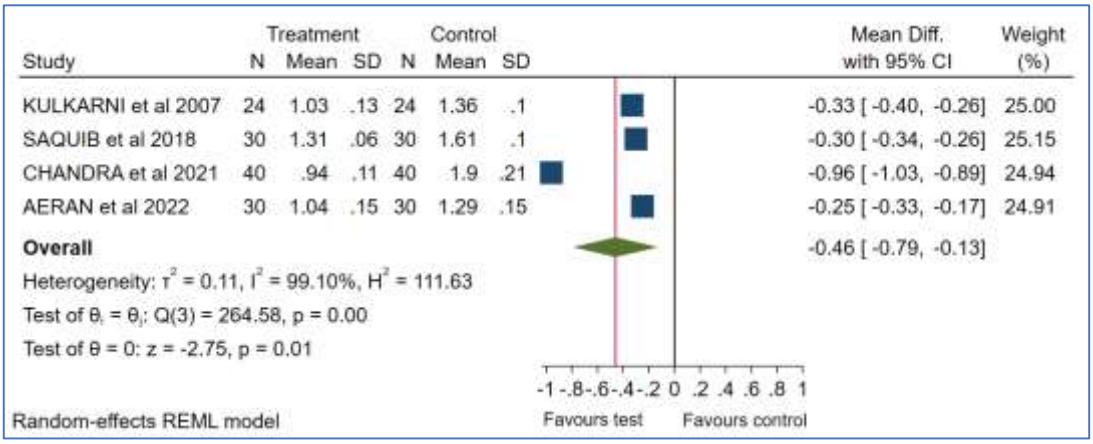


Figure no.8: Forest Plot for the mean Gingival index on the 7th day among the included studies.

A considerable heterogeneity (I^2) value ranging from 94% to 99% was observed with respect to VAS Pain score, Wound Healing Index, Vascularity, Plaque index and Gingival index on the 7th day, while a low heterogeneity (I^2) value 0% was observed with Fibrosis and Inflammatory cells on the 7th day. This can be attributed to varying sample size, different cyanoacrylate bioadhesive materials used and different sites used for surgical procedure for evaluating the clinical parameters. Table 2 represents the primary treatment outcomes

Secondary outcomes

Papillary marginal attachment was mentioned by 2 studies[12,20] at 1-week, 1 study at 3-week and 1 study[12] at 6-week intervals. Pocket probing depth was mentioned by 3 studies [17,18,24] at baseline, 1 study[24] at 3-week, 1 study[15] at 6-week and 2 studies[17,18] at 3-month intervals. C-reactive protein levels were mentioned by only 1 study[16] at baseline and Day 3 interval. Number of colony forming units was mentioned by 1 study[16] at baseline and 2 studies[16,19] at 1-week intervals.
Bleeding index was mentioned by 3 studies[17,18,24] at baseline, 3 studies[21,22,24] at 1-week, 1 study[24] at 3-week and 2 studies[17,18] at 3-month intervals. (Table 3)

Table 3: Summary of secondary treatment outcomes

SECONDARY CLINICAL OUTCOMES			
SR.NO	**AUTHOR**	**INTERVENTION**	**RESULTS**
PAPILLARY MARGINAL ATTACHMENT			
AT 7 DAYS			
1	Shah et al.[12]	Suture	1.80±1.54
		Cyanoacrylate	0.60±0.69
2	Aeran et al.[20]	Suture	71.26 ± 15.43
		C	50.53 ± 12.99
AT 21 DAYS			
1	Shah et al.[12]	Suture	0.90±0.99
		Cyanoacrylate	0.60±0.69
AT 42 DAYS			
1	Shah et al.[12]	Suture	0.90±1.37
		Cyanoacrylate	1.00±0.94
EPITHELIAL HEALING			
AT 7 DAYS			
1	Saquib et al.[13]	Suture	0.4±0.507
		Cyanoacrylate	0.66±0.488
AT 42 DAYS			
1	Saquib et al.[13]	Suture	0
		Cyanoacrylate	0
POCKET PROBING DEPTH			
AT BASELINE			
1	Padhye et al.[24]	Suture	5.4320
		Cyanoacrylate	5.5210
AT 21 DAYS			
1	Padhye et al.[24]	Suture	1.7083
		Cyanoacrylate	1.8250
AT 42 DAYS			
1	Sadatmansouri et al.[15]	Suture	2.5±0.67
		Cyanoacrylate	2.8±0.6
% IMPROVEMENT FROM BASELINE TO 3 MONTHS			
1	Khurana et al.[17]	Suture	68.90%
		Cyanoacrylate	71.10%
2	Vyas et al.[18]	Suture	70%
		Cyanoacrylate	72%
C-REACTIVE PROTEIN			
AT BASELINE			
1	Nambi et al.[16]	Suture	1.41 ± 0.34
		Cyanoacrylate	1.40 ± 0.32
AT 7 DAYS			
1	Nambi et al.[16]	Suture	0.92 ± 0.36
		Cyanoacrylate	0.44 ± 0.23
COLONY FORMING UNIT			
AT BASELINE			

1	Nambi et al.[16]	Suture	13.4 ± 0.6
		Cyanoacrylate	13.5 ± 0.5
AT 7 DAYS			
1	Nambi et al.[16]	Suture	18 ± 0.8
		Cyanoacrylate	11± 0.5
2	Mahajani et al.[19]	Suture	8545844.2±22066342.1
		Cyanoacrylate	613013.5± 2256324.3
BLEEDING INDEX			
AT BASELINE			
1	Kaur et al.[21]	Suture	No bleeding 60% Slight 40% Moderate 0% Severe 0%
		Cyanoacrylate	No bleeding 100% Slight 0% Moderate 0% Severe 0%
2	Gundannavar et al.[22]	Suture	No bleeding 50% Slight 50% Moderate 0% Severe 0%
		Cyanoacrylate	No bleeding 100% Slight 0% Moderate 0% Severe 0%
3	Padhye et al.[24]	Suture	0.7667
		Cyanoacrylate	0
AT 7 DAYS			
1	Padhye et al.[24]	Suture	0.1333
		Cyanoacrylate	0
AT 21 DAYS			
1	Padhye et al.[24]	Suture	0
		Cyanoacrylate	0
% IMPROVEMENT FROM BASELINE TO 3 MONTHS			
1	Khurana et al.[17]	Suture	99.20%
		Cyanoacrylate	100.00%
2	Vyas et al.[18]	Suture	95%
		Cyanoacrylate	99%

Papillary marginal attachment (PMA), Epithelial healing, Pocket probing depth (PPD), C-Reactive Protein (CRP), Number of colony forming units (CFU/ml) and Bleeding index (BI) expressed as Mean ± Standard Deviation and Percentages at various time intervals.

Quality assessment

The risk-of-bias graph and summary generated by the RevMan software (v5.3) are shown in Figures 9 and 10, respectively. The research was categorized into six areas, and each study's methodology was evaluated and given a risk level. Eight trials showed a low risk of bias, five showed moderate concerns, and one showed a high risk of bias out of the 14 included studies.

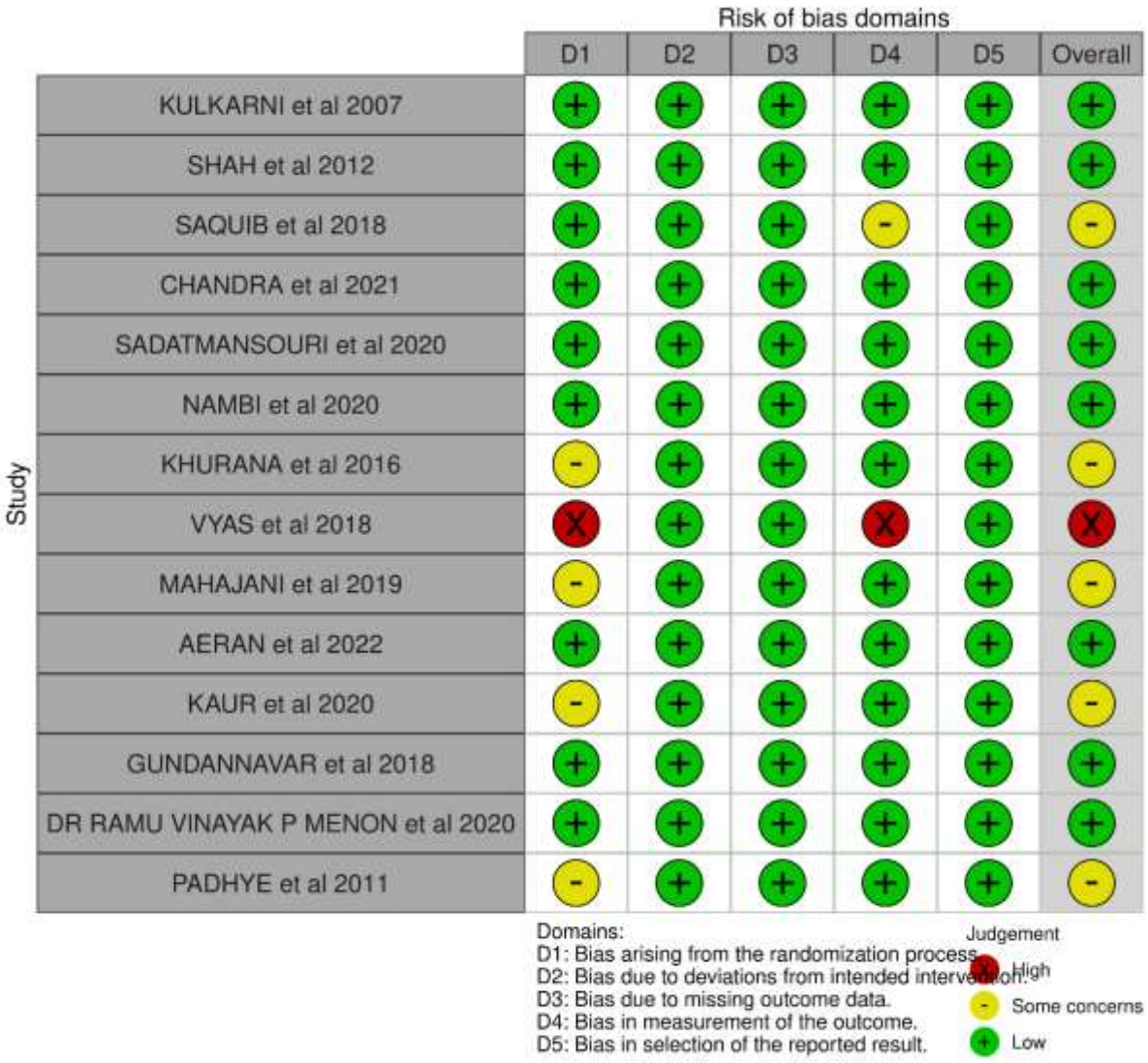


Figure no.9: Graph showing the summary of risk of bias: Review authors' judgments about each risk of bias item for each included study.

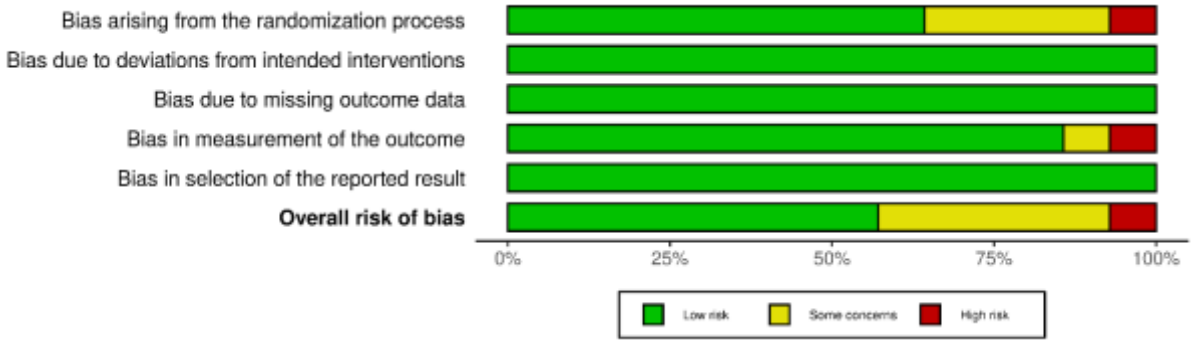


Figure no.10: Graph showing Risk of bias: review authors' judgements about each other risk of bias item present as percentages across all included studies.

DISCUSSION

The periodontal flap is one of the most routinely employed procedures, particularly in regards to deep periodontal pockets. Close postoperative adaptation of the flap onto the prepared root surface and the maintenance of this adaptation for a period of time holds the key to reinstating a healthy dento-gingival unit.[25] Which is why the current systematic review aimed to evaluate assess the effectiveness of cyanoacrylate bioadhesive material in healing of periodontal flaps as compared to the conventional silk sutures.

Among all the studies assessing the plaque index and gingival index, there was an increased plaque score at the suture site which was ascribed to the difficulty in oral hygiene maintenance post-surgery and the fact that they act as a sites of plaque accumulation owing to their multi-filamentous nature as compared to the cyanoacrylate bioadhesive material.

However, due to the removal of the suture threads after one week and the focus on maintaining oral hygiene, as reported by Kulkarni et al.[11] and Saquib et al.[13] in their respective studies, there was no difference in the plaque index and gingival index scores at 21 and 42-day intervals.

On the seventh day, the Wound Healing Index scores of the cyanoacrylate and suture sites differed significantly, with the cyanoacrylate sites showing a greater healing response than the suture sites This observation was ascribed by Kaur et al.[21] to the possibility that cyanoacrylate functions as a scab, preserving a moist surface that facilitates epithelial migration and averting subsequent infection.

There was no statistically significant difference observed at either site in the four trials that evaluated vascularity. This is explained by the fact that vessels proliferate as a natural aspect of the healing process. Shah et al.[12] and Saquib et al.[13] evaluated the connective tissue and reported that it organized over the course of the healing process. The total fibrosis in the cyanoacrylate and suture sites did not differ in a way that was clinically significant.

When the chronic inflammatory response and the overall cellularity were compared by four studies, cyanoacrylate site showed less inflammatory cell response as compared to suture site. Five authors reported a statistically significant reduction in the cyanoacrylate group suggesting that the less post operative pain and discomfort may be attributed to the properties of cyanoacrylate as it is painless, needleless, suture less, stress-free and easy to work with.[11,12,13,24]

In their assessments of papillary marginal attachment, Shah et al.[12] and Aeran et al.[20] were the only ones who found a significant difference between the two groups. They attributed this difference to the presence of silk in the tissues, which may have triggered the response because the body treated silk as a foreign protein, which had the potential to fragment the wound and increase the inflammatory response, as well as trauma during suturing.

Of the 14 included studies solely, Nambi et al.[16] assessed C-reactive protein levels which is an acute phase reactant which represents an early, non-specific reaction to a variety of injury. The more significant reduction in the CRP levels in the cyanoacrylate group was imputed to the lower plaque accumulation while the silk suture had a greater propensity for plaque accumulation.
According to Nambi et al.[16] and Mahajani et al.[19], there was a statistically significant difference in the total number of bacterial colonies between the two groups. The chemical structure of cyanoacrylates has an active double bond that may be able to combine with the free amino and/or hydroxyl groups of the bacterial cell wall to provide the antibacterial effect. Their bacteriostatic or bactericidal action may be augmented by the release of formaldehyde and cyanoacetate from the polymerization reaction that occurs after they are applied.
Khurana et al.[17], Vyas et al.[18] and Kaur et al.[21] reported a statistically significant reduction of bleeding index in the cyanoacrylate group than that of the silk suture group from baseline to 6 weeks and 3 months. The time required for closing the periodontal flap with the test and control materials was also assessed by Chandra et al.[14] They found that the control group needed a significantly longer suturing time (589.5 ± 82.23 seconds) than the test group (264.35 ± 37.98 seconds). Vyas et al.[18] studied the aesthetics factor between the sutured site and the site where isoamyl 2 cyanoacrylate was applied as securing material and concluded that cyanoacrylate was more aesthetically acceptable by all patient subjects.
Padhye et al.[24] in her study reported crater formation or a formation of an interdental depression in one patient on the Nectacryl side. This finding pointed out to the fact that the material should be placed above the wound edges and not under or between the edges.

LIMITATIONS AND FURTHER SCOPE

A limiting factor to the present review was that the included RCTs lacked pre- and post-treatment microbiological analysis for the periodontal flaps closed with cyanoacrylate bioadhesive material and silk suture, thus limiting the assessment of potential similarities in microbiological outcomes and reduction in periodontopathic bacteria. Additionally, secondary trauma was caused by the biopsy, and cyanoacrylate was placed superficially.
Hence, there is a need for methodologically well-designed, long-term randomized controlled clinical trials with a larger sample size to validate the antimicrobial activity of cyanoacrylate tissue adhesives and examine the impact of confounding factors like smoking, diabetes mellitus, or alcohol consumption and uncooperative patients on the effectiveness of the treatment to establish the application of cyanoacrylate bioadhesive material as a minimally invasive and effective alternative to the conventional silk suture for the closure of periodontal flaps.

CONCLUSION

When closed with silk sutures and cyanoacrylate bioadhesive material, periodontal flaps heal normally, uneventfully, and with primary intention. According to the current review, using cyanoacrylate bioadhesive material as opposed to silk sutures led to improved clinical and histological recuperation and decreased postoperative inflammation. Therefore, it can be stated that cyanoacrylate bioadhesive material can be advocated as a viable substitute for conventional silk sutures for the closure of periodontal flap.
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