Introduction of fibrin adhesive system (tissucol) in periodontal surgery part I: Suture substitution and wound healing

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Abstract:

The present investigation was undertaken to study the efficacy of fibrin adhesive system (tissucol) as a substituting material to the traditional suturing, and to compare the clinical findings obtained in case of traditional suture, thus, two groups each of 21 adult periodontitis patients of nearly equal age, were subjected to the repositioned flap, apically repositioned flap, modified Widmann flap and free gingival graft surgical procedures. Haemostatic time (H.T.), flap adaptation time (F.A.T.), postoperative discomfort time (P.O.D.T.) (pain and swelling) and clinical healing achievement time C.H.A.T. of tissucol group (T.G.) were compared to those of suturing group (S.G.).

This study showed that fibrin adhesive system provides rapid haemostatic action and excellent flap adaptation. Its introduction shortened significantly the clinical healing period of wounded area and shortened the postoperative time.

Keywords:

Tissucol, fibrin adhesive system, periodontal surgery, substituting material, suture substitution.

Introduction:

All periodontal flap surgery depends on flap reflection, then flap replacement, and later on immobilization with suture , silk suture were used traditionally , although , the surgeons consider it as an additional irretentive factor, time consuming during surgery , and could prolongs bleeding on chair , also prolongs healing process later on . Any looseness of the stitches means losing the goal of surgery to gain a collagenous reattachment with major patient sufferness. Any hazard placement of periodontal pack under the flap margin could give a negative consequences. Thus since Bergel 1909 [1] many essays have been done to fined a suitable material able to substitute the stitches with as less as possible of side effects , uncomfortability, disagreeability, unfavorability and complexity for both patient and surgeon as well. Cyanoacrylate [2] had been used for a while , suggested as a surface homeostatic and stabilizing material with precautions about unfavorable inflammatory reaction when become in contact with the alveolar bone . Fluecrylate [3] gave a better result in flap fixation with less possible toxicity and less inflammatory reaction, again with precaution about contacting the alveolar bone.

A celluloid adhesive band [4] had been used for the same purposes. A modified celluloid band [5], these materials exhibited a weak adhesion without inflammatory reaction.

The natural physiologic adhesion of flap still in choice, the

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coagulation process seemed to be in the first line of investigations.

The fibrinogen have been used since Bergle 1909 [1], Harvey 1916[6], then Tarlov 1943 [7] as a successful haemostatic agent. However, the light concentrations of fibrinogen used at that time didn't give a suitable adhesion. The first successful experimentation on rabbit [8,9] showed a positive anaestomosis of sectioned nerves when a concentrated fibrin has been used . Bartolocci 1982 [10], have used a commercial lyophilized fibrin-fibrinogen as a hemostatic and flap immobilizing agents. Miller 1983 [11] applied the fibrinogen for graft fixation.

The use of GTR (guided tissue regeneration) procedures with absorbable or non-absorbable collagen membrane have been introduced recently to periodontal surgery with wide limitations in use and some difficulties in practice [12,13,14].

Tissucol , is a commercial fibrin seal , composed essentially from plasma fibronectin, fibrinogen, factor XIII (fibrin stabilizing factor) and thrombin, able to activate the fibroblasts and to provide an extra cellular adhesive matrix for their migration, and able to form a covalent linkage between fibrin and collagen [15]. This product have been experimented and studied as a haemostatic and as a bioadhesive material widely, over the majority of the surgical branches on humans, but rarely on periodontal surgery. It has been studies successfully in thoracic surgery [16], Head and neck surgery [17], splenic surgery [18], cardiovascular surgery [19-21], ear nose and throat [22], Neurosurgery [23,24], used as a vascular sealer with artificial heart valve [25], and in skin graft [26]. It has been tested successfully about its negative ability in transmission of HBS and HIV [27].

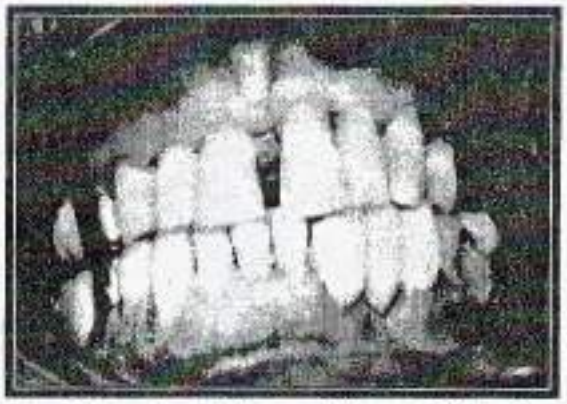
The aim of this study is to investigate the bioadhesive and haemostatic qualities of tissucol in periodontal surgery on human, compared with that of traditional suturing. The clinic wound healing following tissucol application and to be compared with that following traditional suturing.

Material and method:

A. Tissucol group (T.G.)

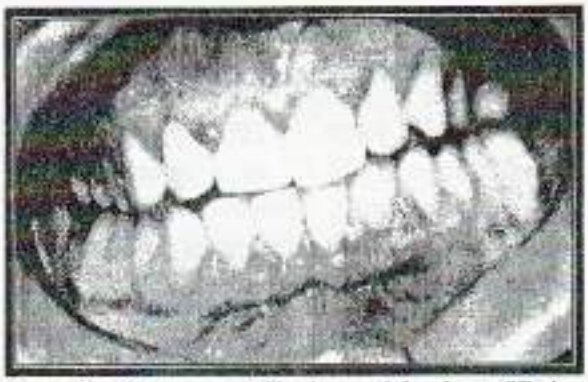
Figures (A to D).

A_1: Repositioned flap with deep periodontal pocket, upper anterior teeth.



A_2: Flap adaptation and immobilization with tissucol.

A_3: About one month later good healing.

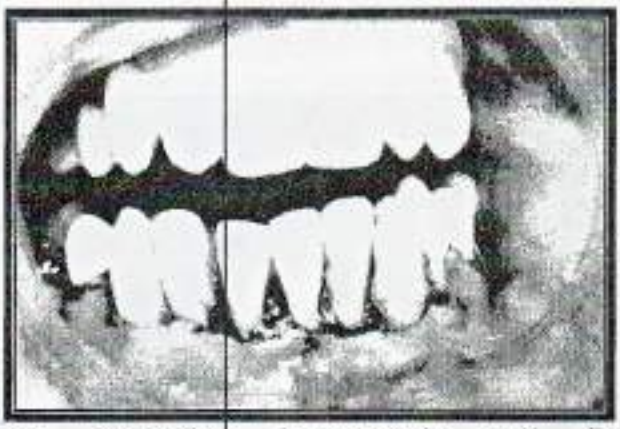


B_1: Shallow vestibule with insufficient attached gingiva associated with gingival inflammation and marginal enlargement (chronic) at lower anterior area.

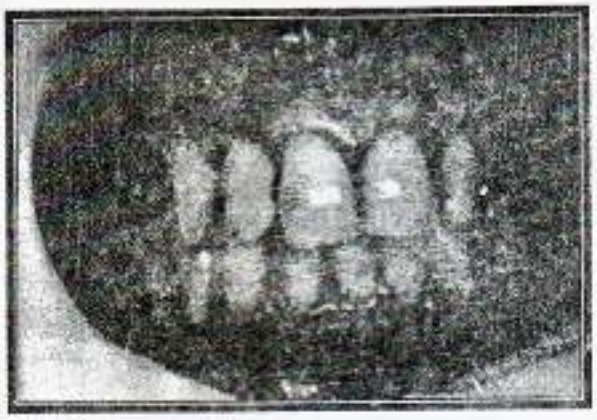
B_2: Tissucol application during apically repositioned flap.

B_3: 35 days later, good healing.

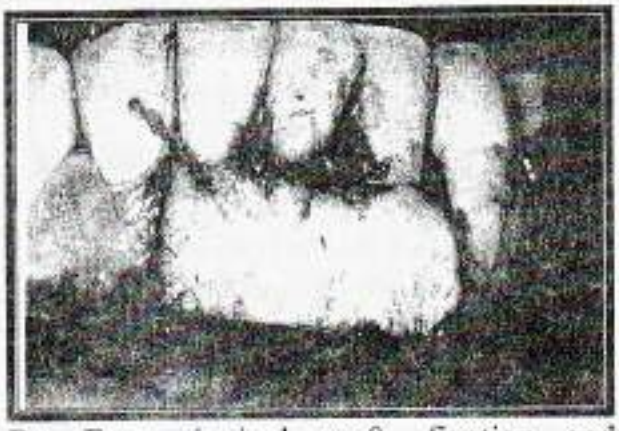
C_1 : Irregular gingival enlargement with thin attached gingiva, shadow of alveolar bone easily noticed, with generalized shallow horizontal bone loss.(Lower anterior area)



C_2: Immediate haemostatic and flap immobilization.



C_3: One month later.



D_1: Free gingival graft, fixation and immobilization with tissucol.

D_2: 45 days later, good healing.

D_3: 3 months later, complete healing and organization.

Twenty one patients, 10 men and 11 women, age 16-55 year. Incorporated in this group, were examined clinically and radiological, they have had chronic adult periodontitis, all were indicated for flap or graft surgery. The clinical data collected for each patient included age, sex, general health, reported bleeding time, clotting time, HBS negative and HIV negative, surgical technique, area of surgery and the number of teeth involved. 4-5 single rooted teeth have been selected.

The surgical procedures proceeded in this study were, repositioned, apical repositioned, modified Widmann and free gingival graft. Granulation tissue debridement and mechanical root planning have been performed with new Gracy hand instruments (Hu-friedy – immunity, USA, and GC – American, USA) according to usual surgical protocol of periodontal flap surgery.

Tissucol components were prepared using a water bath at 37°C, slow solidification manner were used in order to gain time for flap adaptation.

Two components fibrin sealant (heat treated) tissucol material prepared according to the manual of instruction supplied. The lyophilized powder, which after reconstitution gives 1ml of tisseel solution contains:

Clottable protein	75-115 mg
Thereof fibrinogen	70-110 mg
Plasma fibronectin (CIG)	2-9 mg
Factor XIII	10-50 U
Plasmogen	40-120 mg
A protinin solution (bovine)	3000 KIU/1ml
Thrombin 4 (bovine) (slow solidification)	4 IU / 1ml
Thrombin 500 (bovine) (rapid solidification)	500 IU/ 1m ml
Calcium Chloride Solution	40 mmol/l

The tisseel lyophilized mixed with a protinin solution to get tisseel solution, (first component), the lyophilized thrombin mixed with calcium chloride solution to get thrombin solution (second component), these two preparations must done separately in water bath at 37°C.

A simultaneous application by the Duploject applicator (provided), the totality of wound area, flap borders, crevicular and interdental areas, the exposed alveolar bone, root surfaces were completely covered with the bioadhesive material. Flaps were replaced and adapted by a gentle digital adaptation to the required position.

After finishing taking the records, washing with warm normal saline has been performed several times. The patients were clinically supervised on chair during the first 30 minutes after tissucal application, then at the first, second third and forth day successfully, then at the second, and third week, then once a month during the following 6 months.

All patients were tested for HBS and HIV; they appeared negative before, one month after surgery, and 6 month later.

Time records have been performed by a sport stop watch (seiko), haemostatic time (H.T.) measured in seconds from the moment of tissucol application till the blood oozing stopped definitively.

Flap adhesion time (F.A.T) measured in seconds from the moment of digital adaptation of the flap till the moment of complete fixation and immobilization of the flap as tested by tweezers on the flap borders. Post operative discomfort time (P.O.D.T.) was measured in days as concluded from the daily visit during the first week after surgery as based on patient interrogation and clinical findings P. O. D. T. includes pain time and swelling time, the clinical health achievement time C.H.A.T. was measured in days from the day of operation till the day when the clinic examination reveals a complete healing of wounded area, and the healthy appearance of gingiva easily been clinically distinguishes.

B- Suturing Group (S. G.)

Twenty one patients, 11 men, 10 women, age 22-51 years, involved in this group, they were examined clinically and radiologically, they have had a chronic adult periodontitis. A similar clinical data as tissucol group were collected and recorded, the surgical area were selected as similar as possible to those chosen in tissucol group. The surgical procedures applied were identical to that of tissucol group.

After the soft tissue debridement and mechanical root planning, the flaps have been sutured by means of a continuous interdental suturing technique, 3/0 black silk (Ethicon), semicircular triangular tip needle have been used. After recording all data, several washes with warm normal saline have been done. Suturing time was measured from the

moment of first stitches till the moment of the last knot done. Suturing as well as tissucol preparation and application were done by the author.

All our patients in both groups have a normal bleeding time, normal clotting time; they were in good general health, with normal hematologic picture.

Results:

The average age of the total sample (42 patients) was 30.88±4.7. In tissucol group, the average age was 30.8±4.3, and that of suture group, the average age was 30.95±3.26. There was no significant variation of age variable in both groups.

The time required for haemostatic and flap adaptation and adhesion with tissucol bioadhesive was 164.43 ±30.3 seconds (Table A), while haemostatic and suturing time was considerably longer, scored 607.14±67.9 seconds, the difference was largely significant ($P<0.01$) (Table B), the sutured tissues exhibited a marked inflammatory signs with bleeding points, pain with bleeding during suture removal was noted, while the bioadhesived gingiva appeared with much less inflammatory signs, without bleeding or any discomfort during pack removal.

Table (A): Tissucol group.

No.	Age Sex	Surgical Procedure	H.T.	F.A.T	P. O. D. T.		C. H. A. T.
					Pain	SW	
1	26 F	F.G.G.	60	50	1	-	23
2	23 F	R.F.	80	60	-	-	21
3	21 M	F.G.G.	110	55	1	1	30
4	23 M	R.F.	90	60	1	-	24
5	55 M	R.F.	55	60	-	-	27
6	23 F	R.F.	40	120	-	2	25
7	27 M	R.F.	43	90	1	3	22
8	24 F	R.F.	62	180	-	2	28
9	32 M	F.G.G.	52	120	1	2	35
10	37 M	A.R.F.	82	60	2	3	35
11	31 M	A.R.F.	91	60	1	1	24
12	21 F	A.R.F.	72	60	1	1	35
13	46 F	M.W.F.	75	120	-	-	28
14	29 M	M.W.F.	32	120	-	-	29
15	25 F	M.W.F.	34	120	1	-	26
16	26 M	M.W.F.	48	60	-	-	25
17	29 M	M.W.F.	61	120	-	-	26
18	36 F	M.W.F.	72	60	-	2	27
19	29 F	M.W.F.	58	120	1	1	35
20	42 F	M.W.F.	82	180	-	-	30
21	42 F	M.W.F.	89	190	2	1	36
	30.8±4.3			98.33± 20.57	0.62± 0.3	0.91 ± 0.5	28.14± 3.4

Abbreviations:
H.T.: Haemostatic time in seconds
F.A.T.: Flap adhesion time in seconds
P.O.D.T: Post Operative discomfort time in days
Pain: pain duration in days
SW: Swelling duration in days
C.H.A.T.: Clinical healing achievement time in days
P.O.T: Post operative time (months)
R.F: positioned Flap
A.R.F: Apically Repositioned flap
M.W.F.: Modified Widmann flap
F.G.G.: Free Gingival Graft.

Table (B): Suturing group.

	Age Sex	Surgical Procedure	Suturing time seconds	P. O. D.		C.H.A.T.
				Pain	Swelling	
1	26M	R.F.	510	2	2	32
2	33F	R.F.	510	2	2	36
3	46F	R.F.	510	2	3	37
4	26M	R.F.	480	2	3	30
5	27M	R.F.	420	2	3	39
6	32F	R.F.	480	2	2	32
7	27F	F.G.G.	870	2	2	34
8	25M	A.R.F	750	2	3	37
9	34M	A.R.F	780	3	3	30
10	30F	A.R.F	690	3	3	34
11	51F	A.R.F	720	2	3	36
12	32F	F.G.G.	900	3	3	40
13	30M	A.R.F	840	3	3	38
14	35M	M.W.F.	630	2	3	38
15	22M	M.W.F.	540	2	2	39
16	23M	M.W.F.	480	2	2	33
17	35F	M.W.F.	570	2	2	32
18	36F	M.W.F.	570	2	2	30
19	29M	M.W.F.	600	1	3	39
20	27M	M.W.F.	450	2	2	37
21	24F	M.W.F.	450	1	2	30
	30.95±3.26		607.14±67.9	2.1±0.25	2.43±0.23	36.19±3.8

Postoperative pain was absent in 9 patients of tissucol group, others showed a slight superficial pain started after the disappearance of anesthesia, may or may not continued interruptedly for about one day and/or recurrent at the second day, while in suturing group the patient complained from a longer duration of pain, the mean pain time score in T.G. was 0.62±0.3 days, in S.G., the pain scored 2.1±0.25 days, the difference insignificantly deviated in their variance ($P < 0.05$). The post operative swelling was common in all patients of S.G., it varied from slight to well developed clinical swelling, their score was 2.43±0.23 days, 10 patients of T.G., didn't recognize any swelling, the other 11 patients showed a slight elevation of check or lip, their score was 0.91±0.5 days, the difference is deviated significantly in their variance ($P<0.05$).

The clinical healing achievement time of T.G. appeared significantly shorter than that of S. G. ($P<0.05$) this time scored in T. G. 28.14±3.4 days, while that of S. G. scored 36.19±2.0 days.

T.G. patients showed excellent, rapid clinical healing without any evidences of retard or immediate allergic reactions.

The inter group compares of findings revealed that the mean patients age were indifferent significantly there were insignificant decrease in postoperative pain time, while swelling time as well as clinical healing achievement time were decreased significantly ($P<0.05$) with the utilization of tissucol bioadhesive.

Discussion and conclusion:

The traditional suturing may be time consuming and difficult,

especially, in relative inaccessible areas. Many stenches, moreover, causes a considerable information during the early healing period. Suture as a material could act as a foreign body, and could interfere with the reattachment and regeneration process of flaps or even could lead to a tissue necrosis [28] Healing with fibrous regeneration requires an interaction between fibroblasts and the vital remainders of collagen fibers [29], this interaction is carried out by the formation of a fibrin linkage with the original collagen fibers, which followed by a subsequent replacement of the fibrin linkage by a new collagen [30]. Plasma fibrin, a multifunctional glycoprotein has attracted much interest in the content of the wound healing [31]. Fibronectin, has an opsonic activity before macrophage which could be important for biological debridement of wounds [32]. Fibrin with factor XIII, able to stimulate fibroblasts adhesion and growth. The fibronectin is covalently linked to fibrin and collagen by factor XIII. Thrombin, able to convert fibronectin into fibrin and to activate factor XIII during the final stage of blood coagulation and also to stimulate the fibroblasts growth and collagen synthesis [16]. Indeed, several evidences suggest that the initial events in periodontal wound healing are of critical importance in determining whether or not the healing by connective tissue regeneration is likely to occur [28].

Tissucol a fibrin adhesive system of which plasma fibronectin, fibrinogen, factor XIII, and thrombin are essential constituents, it is a naturally occurring tissue adhesive with haemostatic properties [33].

Earlier studies [7,17-25,27] suggested that tissucol enhance and promote regenerative wound healing . Bosch [34] reported that the osteogenic potential was enhanced significantly by tissucol. It has been cleared that the application of the bioadhesive material able to shortening the bleeding time and to promote a rapid haemostatic (Table A and table B).

It gives a good and accurate flap adhesion and immobilization, these two clinical factors the rapid haemostatic and the excellent adhesive quality, are the essential factors leading to a high surgical performance, shortening the operation time, shortening the postoperative discomfort time, playing a possible great role in clinical healing quality, and could provide a connective tissue regeneration [17]. Tissucol provides a close contact between flap and underneath structures due to the creation of a thin, well formed and sticky blood clot [5,26]. In contrast, the traditional suturing is an additional factor increases bleeding possibility, flap distortion, increases the inflammatory responses during the early healing period which leads to increase the postoperative discomfort [29], the poor immobilization of the flap as result of loose stitches could lead to a thick blood clot underneath the flap, this condition leads to a prolonged regeneration process with high risk of epithelial invasion and gingival distortion [4].

The clinical healing achievement time (C.H.A.T) significantly reduced with the bioadhesive tissucol ($P<0.05$), tissue healing appeared smoothly progressed, naturally organized without surprises of flap border detachment or any unsuitable sulcus depth, the gingival margin and papillae were sealed intensively against the crown and / or root surface , the gingival tissues distributed uniformly in covering the alveolar bone .

A statistical compares in variance of data was made between the

two groups revealed that the differences were significant ($P<0.05$, $P<0.01$) in the all categories except that of age and, pain time. This result could suggest that the tissucol bioadhesive make the periodontal surgery easier for operator and more tolerable for patients, it provides a short operation time with minor postoperative discomfort, accelerated clinical wound healing, short and perfect haemostatic excellent adhesion and immobilization of flap and graft with a fibrous reattachment of gingival tissues.

The complex process of wound healing and repair of periodontium is not sufficiently understood. The extrapolation of previous data and present data would suggest that the bioadhesive system could accelerate wound healing and repair periodontal fibers in such a way to provide a thin, homogenous equally distributed blood clot underneath a perfectly sealed flap with excellent immobilization which insure a fibrous regeneration of gingival and periodontal tissues.

GTR with collagen membrane has shown promising results [35], the non-absorbable membrane requires a second surgical procedure for redrieval of the membrane, these membranes are therefore associated with an increased probability of surgical complications such as exposure and infections [36,37]. The use of absorbable membrane reduces the incidence of such complications and eliminate the need for second surgery. The use of collagen membrane have been shown effective in inhibiting epithelial migration and promoting new connective tissue attachment also enhances the ability to augment tissue thickness [38,39]. Histological , is based on the ability of collagen to attract fibroblasts and facilitate clotting by aggregating platelets to act as haemostatic [40,41], in spite of its advantages, the GTR still limited to certain cases, [42], in contrast with tissucol, which can be used widely in all periodontal surgery and it could be the successful solution for the GTR limitations .

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