Introduction of fibrin adhesive system (tissucol) in periodontal surgery; part II : clinical pocket reduction and attachment regeneration

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Abstract:

The major goal of periodontal therapy is to eliminate the periodontal pockets and to create a connective tissue attachment. Forty two patients with periodontal pockets subdivided into 2 groups, Tissucol group, 21 patient were treated surgically with introduction of Tissucol bioadhesive material, other 21 patients were also treated surgically their flaps were sutured according to the traditional suture technique. The result showed that there were a significant gain in the pocket depths reduction and attachment levels in both groups, but that of Tissucol group is superior than that of suturing group. The patients were followed for six months, the stability of the gain in Tissucol group still significant, while that of suturing group showed a significant loss in pocket depth reduction and attachment level during the six months of follow up. The result suggested that the tissucol help in creation of connective tissue attachment and preventing the invasion of epithelial growth. The role of oral hygiene were also taken in consideration , as long the oral hygiene kept in healthy state level as the gain in pocket depth and attachment level maintained stable .

Keywords:

Periodontal pockets, connective tissue attachment, Tissucol bioadhesive material,

Introduction:

At present time , the conventional treatment of the periodontal pockets aimed to the regeneration of the periodontal connective tissues , the healing by the regenerative attachment requires an interaction between fibroblasts and the planned or demineralized root surfaces [1] , this interaction is carried out by the formation of a fibrin linkage with the collagen of the root surfaces , which followed by a subsequent replacement of the fibrin linkage by collagen fibers . Regeneration of the connective tissues from a fibroblasts populations arising either from gingival tissues or periodontal tissues could impaired due to the behaviors and kinetics of the junctional epithelium which during the early critical phase of healing tends to proliferate apically along the root surfaces , thus precluding the contact between fibroblasts population and root surfaces [2-5] .

Regeneration of the collagenous connective tissues of the periodontal apparatus obtained either as a new attachment after the demineralization of the root surfaces by citric acid or as a reattachment after the mechanical debridement and elimination of old infected cementum [6] . Regeneration

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process needs a denudation of the radical dentin as well as the activation and enhancement of fibroblasts , osteoblasts and cementoblasts [2,7] .

During the last two decades , many trials have been done to get a regenerative connective tissue attachment , included inventions and modifications in the surgical technology [1,3,4,8-14] , introduction of a synthetic materials [11,15-21] and the introduction of a natural occurring biologic materials [2,13,22-25], in order to enhance the connective tissue regeneration and at the same time to prevent the disagreeable epithelial growth to invade into the area of contact between the periodontal fibrous tissue and the tooth/root surfaces . This epithelial invasion could lead to an epithelial or mixed attachment [1,26].

Plasma fibronectin , a multi-functioned glycoprotein has attracted much interest in the context of the healing process [27] because it activates fibroblasts and provide an extra cellular adhesive matrix for their migration [28] . When incorporated in clotting plasma serves as a substrate for the activity of factor XIII by forming covalent linkage with fibrin and collagen [29] . Fibronctin has opsonic activity for macrophages as a scavengers which could be important for biologic debridement of non-needed tissular remainders in the wounded area [29,30] .

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 , have the ability to activate fibroblasts and other formative cells [31,32] .

The aim of this study was to investigate the reduction in probing depth of periodontal pockets and the attachment level stability over six months after the introduction of Tissucol and to be compared with the pocket depth reduction and attachment level stability obtained after traditional suturing over the same period of observation .

Material and method:

A- Tissucol Group (T.G)

Twenty one patient , 10 men and 11 women , aged 16-55 years , incorporated in this group , were examined clinically and radiologically , they have had a chronic periodontitis with pocket depth ranged from 4-10mm , the clinical data collected for each patient included age , sex , general health , gingival inflammations according to the Gingival bleeding index (GBI) [33] , plaque index (Pl.I)[34] probing depth of pockets , attachment level [35], bleeding time , clotting time , HBs and HIV negatives . Area of surgical procedures and the number of teeth involved were also recorded . The area of surgical procedure were selected according to the deepest pocket measurements recorded clinically and radiologically . Attachment level and probing depth have been recorded immediately before surgery as a base line records , then first , second , third and sixth months successfully . Granulation tissue debridement and mechanical root planning have been performed with new Gracy hand instruments (Hu-friend – immunity, USA, and GC – American, USA) according to usual surgical protocol of periodontal flap surgery. Tissucol components were prepared using 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 Tissucol solution contains:

Clottable protein	75-115mg
Thereof fibrinogen	70-110mg
Plasma fibronectin (C1G)	2-9 mg
Factor XIII	10-50 U
Plasmogen	40-120mg
Aprotinin solution (bovine)	300 KiU/ml
Thrombin 4 (bovine) slow solidification	4 IU/1ml
Calcium Chloride solution	40 mmol/L

Tisseel lyophilized mixed with aprotinin 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 , pocket spaces , cervicular and interdental areas , the exposed alveolar bone , and root surface were completely covered with the bio-adhesive material , flaps were replaced and adapted by a gentle digital adaptation to the required position . Probing depth and attachment level measurements were performed with WHO CPTN probe , as well as the Gingival bleeding index ((GBI) and Plaque index (PII)).

B- Suturing group (S.G.):

Twenty one patients , 11 men and 10 women aged 22-51 year , involved in this group , they were examined clinically and radiologically , they have had a chronic adult periodontitis with probing pockets depth ranged from 4-10mm . 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 those of Tissucol group .

After soft Tissue debridement and mechanical root planning , the flaps have been sutured by means of a continuous interdental technique , 3/0 black silk (Ethicon) , semicircular triangular tip needle have been used , several washes with warm normal saline have been performed as Tissucol group . All surgery, suturing, Tissucol applications were done by the author.

All our patients in both groups have normal bleeding time, normal clotting time , good general health , with normal hematologic picture , negative HBs , and HIV .

The statistical analyses in this study based upon the t-test and student Fisher test [36]

Results:

The average age of the total sample (42 patient) was 30.88±4.7. In Tissucol group , the average age was 30±4.3 , and that of suturing group was 30.95±3.26 . There were no significant variations of age variables, the bleeding time and clotting times variables. GBI and PLI were insignificantly deviated in both groups when compare the base lines data with that of the follow up period , as well as when comparing GBI and PLI data of T.G. with that of S.G. (Table 1 , 2) .

Table (1): GBI, Patients means average.

	Baseline	First month	2nd month	3rd month	6th month
T.G.	0.59	0.48	0.51	0.65	0.71
S.G.	0.65	0.61	0.65	0.7	0.82

- Insignificant deference with baseline data.

Table (2): Plaque index , patients means average.

	Baseline	First month	2nd month	3rd month	6th month
T.G.	0.13	0.18	0.18	0.12	0.12
S.G.	0.12	0.15	0.13	0.15	0.18

- insignificant deference with baseline data .

A- Tissucol group; T.G.: (Fig.1)

Probing depth records of operated areas showed a significant decrease in depth, one month as well as 6 months postoperative when compared to the baseline records (Table 3 and 6).

Table (3): The gain in probing pocket depth in mm .

	First month	2nd month	3rd month	6th month
T.G.	3.69	3.54	3.55	3.5
S.G.	3.5	3.28	3.14	2.94

About 3.7mm gain of pocket depth was obtained at the first months which decreased up to 3.5mm at the sixth months , this loss (5.1%) was insignificant ($P>0.05$) . A significant difference were also obtained in attachment level one and six months postoperatively when compared to the base line records ($P<0.05$) (Table 6), about 3.63mm gain was obtained at the first month which decreased up to 3.28 at the sixth month , this loss (9%) was insignificant . The postoperative records were significantly indifferent when data compared to each other in GBI , PLI , probing pocket depth and attachment level , this result could suggest an adequate attachment stability . (Table 3, 4, 5, 6), all our patients didn't show neither immediate nor retarded allergies.

Table (4): The gain in attachment level in mm .

	First month	2nd month	3rd month	6th month
T.G.	3.63	3.58	3.38	3.28
S.G.	2.68	2.58	2.45	2.32

Table (5): Percentage of loss in pocket depth and attachment level between first month and sixth month data .

	Pocket depth	Attachment level
T.G.	0.19 mm 5.1%	0.35mm 9%
S.G.	0.56mm 16%	0.36mm 13%

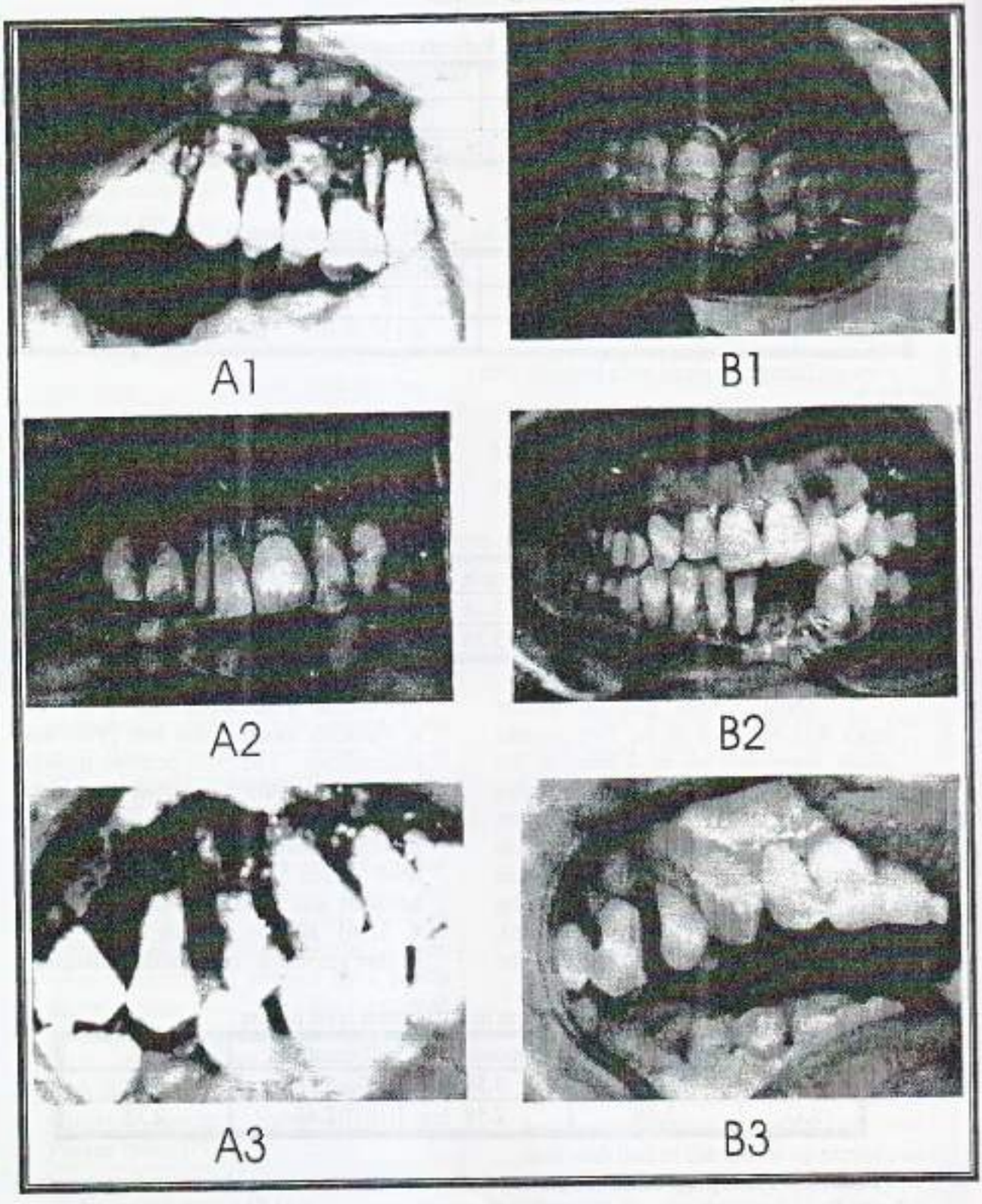

Fig.(1): Examples of cases treated with tissucal bioadhesive material A1, 2, 3, :during surgery; B1, 2, 3, :six months later

Table 6

Changes in probing depth and attachment level (patient means) Tissucol group .

No	P.P.D baseline	P.P.D 1 month	P.P.D 2 month	P.P.D 3 month	P.P.D 6 month	A.L. baseline	A.L. 1 month	A.L. 2 month	A.L. 3 month	A.L. 6 month
1	4.75 ± 0.11	2.38 ± 0.24	2.60 ± 0.25	2.58 ± 0.34	1.92 ± 0.45	5.7 ± 0.21	2.7 ± 0.21	3.0 ± 0.21	3.2 ± 0.31	3.3 ± 0.41
2	4.62 ± 0.21	2.88 ± 0.22	2.58 ± 0.34	2.50 ± 0.27	1.80 ± 0.40	5.78 ± 0.2	2.9 ± 0.27	2.9 ± 0.33	2.9 ± 0.18	2.9 ± 0.22
3	3.91 ± 0.18	1.2 ± 0.1	1.28 ±0.12	1.8 ± 0.18	1.76 ± 0.31	6.6 ± 0.12	3.5 ± 0.21	3.5 ± 0.41	3.6 ± 0.13	3.8 ± 0.12
4	6.21 ± 0.21	3.15 ± 0.31	3.50 ± 0.38	3.70 ± 0.35	3.00 ± 0.16	7.8 ± 0.81	3.8 ± 0.31	3.8 ± 0.31	3.8 ± 0.73	3.9 ± 0.83
5	7.37 ± 0.30	2.95 ± 2.33	2.80 ± 0.19	2.44 ± 0.14	2.3 ± 0.13	7.56 ± 0.22	2.1 ± 0.31	2.2 ± 0.31	2.3 ± 0.52	2.5 ± 0.06
6	8.56 ± 0.19	3.00 ± 0.01	3.00 ± 0.02	3.00 ± 0.01	3.00 ± 0.01	6.6 ± 0.01	2.3 ± 0.41	2.0 ± 0.03	2.0 ± 0.53	2.1 ± 0.02
7	6.78 ± 0.31	3.15 ± 0.31	3.14 ± 0.26	3.38 ± 0.32	3.00 ± 0.37	5.8 ± 0.09	2.8 ± 0.81	2.8 ± 0.31	3.1 ± 0.18	3.1 ± 0.10
8	5.5 ± 0.27	2.2 ± 0.22	2.6 ± 0.25	2.38 ± 0.24	2.50 ± 0.27	6.67 ± 0.11	3.1 ± 0.11	0.31 ± 0.22	3.5 ± 0.01	3.5 ± 0.51
9	6.12 ± 0.21	2.3 ± 0.11	2.8 ± 0.21	2.36 ± 0.11	2.45 ± 0.10	6.22 ± 0.31	3.8 ± 0.11	3.8 ± 0.32	3.8 ± 0.21	3.6 ± 0.17
10	4.88 ± 0.3	3.1 ± 0.01	3.28 ± 0.10	2.95 ± 0.34	2.1 ± 0.31	4.2 ± 0.51	2.3 ± 0.18	2.3 ± 0.23	2.5 ± 0.81	2.8 ± 0.28
11	4.95 ± 0.12	1.2 ± 0.01	1.3 ± 0.03	1.3 ± 0.04	1.3 ± 0.04	4.4 ± 0.35	2.1 ± 0.11	2.2 ± 0.11	2.6 ± 0.11	2.6 ± 0.53
12	4.89 ± 0.22	2.2 ± 0.16	2.2 ± 0.17	2.4 ± 0.12	2.5 ± 0.08	6.4 ± 0.28	2.6 ± 0.81	2.8 ± 0.18	3.0 ± 0.32	3.1 ± 0.15
13	5.5 ± 0.28	2.3 ± 0.16	2.8 ± 0.31	2.8 ± 0.03	2.5 ± 0.18	6.7 ± 0.17	2.7 ± 0.31	2.7 ± 0.12	3.1 ± 0.23	3.2 ± 0.13
14	6.38 ± 0.13	2.5 ± 0.33	2.5 ± 0.33	2.8 ± 0.11	2.8 ± 0.17	7.8 ± 0.15	3.7 ± 0.01	3.7 ± 0.11	3.7 ± 0.12	4.0 ± 0.11
15	6.82 ± 0.20	3.1 ± 0.33	3.2 ± 0.33	3.3 ± 0.20	3.5 ± 0.35	8.2 ± 0.1	3.8 ± 0.22	3.8 ± 0.10	4.1 ± 0.31	4.3 ± 0.29
16	5.60 ± 0.17	2.8 ± 0.22	2.5 ± 0.22	2.4 ± 0.31	2.4 ± 0.03	9.16 ± 0.2	5.50 ± 0.14	5.5 ± 0.81	5.7 ± 0.30	5.8 ± 0.10
17	8.80 ± 0.20	3.1 ± 0.27	3.3 ± 0.38	3.4 ± 0.31	3.4 ± 0.9	7.89 ± 0.6	2.98 ± 0.29	3.0 ± 0.35	3.2 ± 0.13	3.3 ± 0.22
18	10.44± 0.25	4.4 ± 0.14	4.4 ± 0.16	4.5 ± 0.22	4.5 ± 0.36	10.2 ± 0.38	6.0 ± 0.35	6.0 ± 0.35	6.1 ± 0.13	60.1 ± 0.18
19	8.53 ± 0.13	3.1 ± 0.21	3.3 ± 0.33	3.3 ± 0.21	3.5 ± 0.27	8.4 ± 0.12	4.1 ± 0.25	4.2 ± 0.27	4.5 ± 0.14	4.6 ± 0.21
20	7.88 ± 0.17	3.8 ± 0.01	3.7 ± 0.01	3.5 ± 0.01	3.5 ± 0.01	8.78 ± 0.22	5.7 ± 0.20	5.7 ± 0.37	6.0 ± 0.31	6.51 ± 0.22
21	6.92 ± 0.21	4.1 ± 0.08	3.88 ± 0.29	2.82 ± 0.19	3.78 ± 0.20	9.9 ± 0.14	6.1 ± 0.11	6. 2 ±0.31	6.8 ± 0.21	6.8 ± 0.21
	6.43 ± 0.76	2.74 ± 0.33	2.889 ±0.33	2.88 ±0.32	2.93 ± 0.34	7.18 ± 1.6	3.55 ± 0.56	3. 6 ± 0.58	3.8 ± 0.06	3.9 ± 0.57

Intragroup differences between base line and 1 month were significant $P < 0.05$.

Intragroup differences between base line and 6 month were significant $P < 0.05$.

B- Suturing group ; S.G.:

As in the precedent group probing depth as well as attachment level records of operated areas showed a significant decrease ($P<0.05$), when compare the baseline records with the first month and sixth month postoperative data.

The gain in pocket depth was 3.5mm at the first month , decreased up to 2.94 at the sixth month , this loss (16%) were significant ($P<0.05$) , the gain in attachment level was 2.68mm , at the first month , then decreased up to 2.32mm at the sixth month , this loss (13%) was significant , ($P<0.05$) (table 3, 4 , 5 , 7)

No significant differences were observed in GBI , PLI , pocket depth and attachment level records when comparing the post operative data successfully with each other . The significant difference were obtained between the first and sixth months data in amount of gain in pocket reduction and attachment level .

A statistical comparism in variance [36] between the data of T-G and that of S-G showed that the base line records were significantly indifferent , the postoperative records showed a significant variations in privilege to T.G. group with the exception of GBI and PLI ($P<0.05$) .

Discussion and conclusions:

In periodontal flap surgery, the final healing depends upon the selective cell repopulations of the region adjacent to the prepared root surfaces by epithelial cells, gingival connective tissue cells , endosteal cells , and periodontal ligament cells [37,38] . Indeed , several lines of evidences suggested that the initial events in periodontal wound healing are of a critical importance in determining whether or not healing by connective tissue regeneration is likely to occur [8] . Predictable periodontal regeneration following periodontal surgery is a major goal of therapy [1,2,31] . Surgery aimed to create a new attachment or a reattachment of periodontal connective tissues, the eventual debridement of infected connective tissue with a chemical or a mechanical root planning could perform the basic conditions for connective tissue regeneration [4]. Attachment regeneration requires an interaction between fibroblasts and root surface in an attempt to confer a selective advantages upon fibroblasts over epithelial cell in order to overcome the epithelial growth during healing events and to enhance the connective tissues regeneration [3,4,9,10] .

The guided tissue regeneration (GTR) procedure with collagen membrane either absorbable or non absorbable [10] has been introduced to periodontal surgery in order to obtain a regenerative connective tissue attachment and to prevent the epithelial invention [11] . Even the GTR has shown a promising result , especially when associated with the absorbable collagen membrane , its action based on the ability of collagen membrane to attract fibroblasts and facilitate clotting by aggregating the platelets to act as hemostat [10,13,39,40] so it was effective in inhibiting epithelial migration and promoting new connective tissue attachment [17,41] , GTR still associated with surgical complications such as exposure and infections in addition to the technical difficulties [42] .

Table 7

Changes in probing depth and attachment level (patient means) Suturing group .

No	P.P.D baseline	P.P.D 1 month	P.P.D 2 month	P.P.D 3 month	P.P.D 6 month	A.L. baseline	A.L. 1 month	A.L. 2 month	A.L. 3 month	A.L. 6 month
1	5.47 ± 0.02	3.0 ± 0.11	3.11 ± 0.18	3.28 ± 0.28	3.6 ± 0.20	7.25 ± 0.45	4.00 ± 0.12	4.20 ± 0.25	4.35 ± 0.32	4.65 ± 0.31
2	6.42 ± 0.12	3.1 ± 0.25	3.6 ± 0.20	3.8 ± 0.10	3.8 ± 0.2	7.50 ± 0.48	4.0 ± 0.22	4.30 ± 0.27	4.64 ± 0.35	4.84 ± 0.14
3	4.21 ± 0.14	2.1 ± 0.22	2.6 ± 0.33	2.7 ± 0.11	3.1 ± 0.01	7.70 ± 0.71	4.22 ± 0.12	4.28 ± 0.18	4.33 ± 0.31	4.83 ± 0.31
4	6.56 ± 0.39	4.8 ± 0.13	5.1 ± 0.13	5.5 ± 0.22	5.7 ± 0.22	9 3 ± 0.80	5.33 ± 0.18	5.50 ± 0.31	5.7 ± 0.29	5.9 ± 0.19
5	7.73 ± 0.57	4.9 ± 0.22	5.3 ± 0.17	5.3 ± 0.18	5.3 ± 0.17	9.5 ± 0.32	5.5 ± 0.33	5.8 ± 0.19	5.8 ± 0.33	5.9 ± 0.20
6	8.65 ± 0.31	5.7 ± 0.71	6.0 ± 0.13	6.0 ± 0.33	6.1 ± 0.11	10.6 ± 0.32	6.00 ± 0.30	6.20 ± 0.20	6.30 ± 0.45	7.2 ± 0.33
7	7.68 ± 0.22	5.11 ± 0.11	5.11 ± 0.14	5.4 ± 0.22	5.4 ± 0.23	6.75 ± 0.31	4.4 ± 0.33	4.5 ± 0.22	4.8 ± 0.17	4.9 ± 0.21
8	5.70 ± 0.18	2.1 ± 0.16	2.1 ± 0.22	2.2 ± 0.71	2.4 ± 0.41	5.51 ± 0.22	4.0 ± 0.22	4.3 ± 0.12	4.8 ± 0.02	5.0 ± 0.01
9	6.8 ± 0.01	3.0 ± 0.18	3.3 ± 0.17	3.11 ± 0.11	3.5 ± 0.31	5.73 ± 0.33	4.5 ± 0.17	4.5 ± 0.12	4.8 ± 0.22	4.82 ± 0.28
10	4.34 ± 0.09	2.1 ± 0.28	2.5 ± 0.08	2.6 ± 0.55	2.7 ± 0.27	5.08 ± 0.12	4.3 ± 0.37	4.3 ± 0.22	4.31 ± 0.13	4.33 ± 0.13
11	4.44 ± 0.19	2.0 ± 0.29	2.0 ± 0.02	2.2 ± 0.11	2.3 ± 0.22	5.32 ± 0.30	4.0 ± 0.22	4.0 ± 0.12	4.0 ± 0.37	4.11 ± 0.27
12	5.98 ± 0.27	2.1 ± 0.22	2.9 ± 0.11	3.1 ± 0.67	3.2 ± 0.32	4.95 ± 0.92	4.2 ± 0.4	4.33 ± 0.45	4.3 ± 0.20	4.33 ± 0.21
13	6.55 ± 0.36	3.0 ± 0.24	3.0 ± 0.28	3.2 ± 0.08	3.2 ± 0.09	5.09 ± 0.8	4.9 ± 0.35	4.9 ± 0.33	5.0 ± 0.9	5.09 ± 0.8
14	8.63 ± 0.51	3.3 ± 0.29	3.3 ± 0.26	3.6 ± 0.15	3.7 ± 0.15	4.50 ± 0.39	3.5 ± 0.34	3.5 ± 0.22	3.5 ± 0.29	3.5 ± 0.3
15	8.62 ± 0.57	4.1 ± 0.17	4.1 ± 0.20	4.2 ± 0.25	4.3 ± 0.42	8.11 ± 0.11	5.5 ± 0.28	5.5 ± 0.30	5.8 ± 0.33	5.8 ± 0.28
16	6.5 ± 0.42	3.3 ± 0.11	3.4 ± 0.15	3.6 ± 0.17	4.0 ± 0.04	9.11 ± 0.22	6.5 ± 0.58	6.6 ± 0.61	6.6 ± 0.16	6.76 ± 0.22
17	8.2 ± 0.32	4.4 ± 0.56	4.4 ± 0.55	4.5 ± 0.19	4.5 ± 0.27	10.51 ±0.25	6.0 ± 0.9	6.0 ± 0.35	6.1 ± 0.73	6.1 ± 0.21
18	9.2 ± 0.23	4.2 ± 0.30	4.2 ± 0.22	4.0 ± 0.37	5.0 ± 0.37	9.9 ± 0.19	6.1 ± 0.6	6.1 ± 0.070	6.0 ± 0.11	6.0 ± 0.08
19	8.35 ± 0.11	4.1 ± 0.16	4.3 ± 0.11	4.3 ± 0.22	4.6 ± 0.22	9.16 ± 0.27	6.1 ± 0.38	6.1 ± 0.39	6.20 ± 0.31	6.18 ± 0.16
20	8.78 ± 0.91	4.2 ± 0.2	4.2 ± 0.18	4.5 ± 0.61	5.1 ± 0.01	9.32 ± 0.34	5.1 ± 0.3	5.3 ± 0.81	5.29 ± 0.14	5.17 ± 0.13
21	9.65 ± 0.14	4.3 ± 0.18	4.5 ± 0.28	4.7 ± 0.21	5.3 ± 21	8.88 ± 0.36	5.3 ± 0.53	5.5 ± 0.41	5.7 ± 0.16	5.88 ± 0.28
	7.07 ± 0.73	3.57 ± 0.51	3.79 ± 0.49	3.93 ± 0.49	4.13 ± 0.49	7.61 ± 2.1	4.93 ± 0.89	5.034 ± 0.88	5.16 ± 0.86	5.29 ± 0.9

Intragroup differences between base line and 1 month were significant $P < 0.05$.

Intragroup differences between base line and 6 month were significant $P < 0.05$.

The regenerative connective tissue attachment didn't limited to the fibroblasts activation only , but to osteoblasts and cementablasts activation too [7,25,43] . Cementoblast engineering [42] confirm the selective behavior of periodontal cells and support the role of cementoblasts in periodontal regeneration .

Tissucol able to form a ground substrate for cellular growth of fibroblasts , asteoblasts and cementoblasts [24,25] , the plasma factors stimulate fibroblasts adhesion and growth , fibronectin covalently linked to fibrin and collagen by facto XIII , thrombin able to convert fibrinogen into fibrin and factor XIII to its active form during the final stage of blood coagulation and to stimulate fibroblast growth and collagen synthesis [31] . A cellular dermal matrix [21] and Enamel matrix [22] have been experienced recently , showed an increase in gingival margin thickness and increased keratinization with a significant gain in attachment level , their use is limited to only a gum recession cases . Bioabsorbable materials other than collagen [41] like polydioxanan and polylectide acetyltributyl citrate have been used in infrabony pockets in association with GTR , these synthetic chemical materials showed gain 81% in bone level with stability for 5 years , without acting on fibrous attachment . Synthetic Oligo peptides [16] have been also used as periodontal ligament's cells activator , showed that the synthetic peptides mimicking cells binding domain of fibronectin might be a potential tool for arranging a biologically attractive environment for periodontal ligament cells which would enhance periodontal regeneration efficacy . A selective adhesion and proliferation of periodontal ligament cells showed essential to obtain a predictable periodontal regeneration [17-21] . Tissucol , as it is a liquid , able to cover all the areas and spaces even the meticulous lodges , sticky enough to adhere firmly to the underneath tissues and to form a rapid ground substrate for a thickness – controlled blood clot . Beside the natural occurring constituents of tissucol , able to activate the fibroblasts , osteoblasts and cementoblasts and perform the cellular adhesion to form a connective tissue network [25] . The rapid coagulation and the rapid closure of the wound opening could help in forming an attentive and perfect seal of flap borders which could prevent the epithelial migration in apical direction [2,32,23] . Tissucol could give a uniformly distributed blood clot all over the wounded area . While stitches may give an irregular thickened blood clot , depending upon areas of tissue loss and flap adaptation . In addition , the looseness of stitches on gingival margin creates a loss of flap adhesion that could open the way to the epithelial invasion in between the flap and root surfaces [8] . The gain in pocket depth and attachment level after the introduction of Tissucol is significantly superior to that followed the traditionally sutured pockets . This results could suggest that tissucol adhesive material could give a successfully pocket reduction and connective tissue attachment .

During the follow up period , there were 5% loss in pocket depth gain in Tissucol group , while in the traditionally sutured pockets the loss was 16% , this difference appeared significant ($P<0.05$) . The attachment level data showed that the loss in gained

attachment were reduced 9% during the follow up period in Tissucol pockets , and 13% in sutured pockets .

This result could suggest a gradual loss in stability , which could be due to inevitable looseness of stitches on flap borders , leading to an epithelial migration and result in an partial epithelial attachment .

This difference appeared significant ($P<0.05$) , even though could suggest an epithelial migration occurred at the coronal part of the sutured flap which couldn't tolerate and resist the oral bacterial challenges .

The advantages of Tissucol in obtaining a significant gain in pocket depth and attachment level were maintained during the following 6 months by means of a successful oral hygiene measures . The stability of attachment positively depends upon the maintenance procedures and oral hygiene control , we cannot neglect the importance of the preventive measures and oral hygiene performance . As the gingival diseases initiated as a result of plaque accumulation , the recurrence of these diseases also occurs due to the same causes . Even though any gain in pocket depth could maintained as long as the oral hygiene is kept in a healthy level , taking in consideration the connective Tissue attachment is more resistant to the bacterial challenge than the epithelial or mixed attachment .

The long term attachment and pocket stability could be suggestedly related to the oral hygiene performances , with a condition that the flap border sealed attentively and perfectly .

Our result could be due to two reasonable procedures , firstly ; the enhancement of tissuler regenerator and creation of connective Tissue attachment by Tissucol constituent as a result of fibroblast and endosteal cell activation and a rapid homeostasis that could prevent the epithelial invasion . Secondly ; by the prevention measures in keeping the oral hygiene in a healthy state level .

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