

Introduction of polyvinyl pyrrolidone (PVP) In the non surgical periotherapy of Rapidly progressive periodontitis

Al-Juboury Abdullatif*
Al-Mousilly M. Maiada

Received 15/2/2005 ; accepted 23/5/2005

الخلاصة

إن العلاج غير الجراحي في التهابات جنيب السن يعتمد على البكتيريا المسببة للمرض. هناك أكثر من 46 نوع مختلف من الزمر البكتيرية وقد استعمل التتراسايكلين , دوكسيسايكلين أو منوسايكلين أما داخلياً أو موضعياً مع التدرج الاعتيادي والتخطيط الجذري إضافة إلى عدد من المعجمات ومنها الكلور هيكسيدين. نوع A ونوع B هي نوعان معقدة من المرض يتطور بسرعة فائقة ويوضح وجود زمر بكتيرية معقدة غير أنه لم يعرف بعد غير العلاج الجراحي لهذه الحالة. في هذه الدراسة أستعمل الـ PVP كمادة معقمة وذات فعالية كبيرة وواسعة الطيف لقتل البكتيريا والفطريات والفيروسات , بتركيز قليل (3%) لغسل الجيوب السنية مع التدرج الاعتيادي والتخطيط الجذري. خضع للعلاج 8 مرضى يعانون من النوع المتطور أو المتقدم لالتهاب جنيب السن (3 مرضى نوع A و 5 نوع B). أستمر العلاج لمدة 6 أشهر متضمنة 12 جلسة علاجية لكل مريض , جلسة واحدة في الأسبوع للشهر الأول ثم أثنان في الشهر خلال الأشهر الثلاثة التالية وبعدها مرة في الشهر خلال الشهرين الأخيرين. أظهرت النتائج تحسناً سريرياً ملحوظاً في قياسات نرف اللثة , إزدياد عمق الجيوب السنية وتحرك الأسنان كما أظهرت نتائج الأشعة تكويناً عظمياً جديداً. تدل نتائج الدراسة أن فعالية الـ PVP في علاج أمراض جنيب السن قد تجعله العقار المرجو في علاج هذه الأمراض فضلاً عن كونه مأموناً , سهل الأستعمال سريرياً ومتوفر بسعر زهيد.

ABSTRACT

The non surgical periotherapy are based on the bacteriologic back ground of periodontal diseases. More than 46 different verulant species were composing the bacterial flora. Tetracycline, doxycyline, minocycline were used systemically and / or topically in association with conventional scaling and root planning, as well chlorhexidine and wide variety of antiseptics were used. Rapidly progressive type A and type B being a complex disease showing a specific entity and a complex bacterial flora, a curative non surgical remedy not yet well realized.

The polyvinyl pyrrolidone (PVP) a highly effective wide broad spectrum bactericidal, fungicidal and virocidal antiseptic used in low concentration (3%) as an intrapocket irrigation solution accompanied with conventional ultrasound scaling and root planning. Eight patients having rapidly progressive periodontal (3 of type A , 5 of type B) were involved in this study, 12 therapeutic sessions were performed during 6 months. Once a week, in the first month, twice a month in the next 3 months, then once a month in the later 2 months. The result showed a significant improvement of the clinical parameters, gingival bleeding index (GBI), clinical pocket depth (CDD) and clinical tooth mobility (CTM) and with radiologic evidences of bone formation.

The result suggests that PVP could be the promising effective, safe, clinically applicable, easy to use, and cheap remedy of complex periodontal diseases.

*Dental Department, AL-Yarmouk University College.

INTRODUCTION:

As the microbial colonies is the major causative factor of the initiation of periodontal diseases in general term, the pathogenic courses and duration of these diseases have some variations. The rapidly progressive periodontitis (RPP) appeared with a specific entity and specific bacterial flora⁽¹⁻⁶⁾ type B rapidly progressive (aggressive periodontites) appeared with severe acute clinical signs of gingival inflammation with plaque deposits in contrast with the rapidly progressive type A which appeared clinically with almost very slight gingival inflammation and slight plaque deposits⁽⁷⁾. Both diseases associated with common characteristics in their bacteriological findings, a rapid and severe bone loss with deep pocket formation leading to tooth mobility which some times reported as the first sign of the disease and the major chief complaint of the patient^(7,8). The periotherapy of established periodontitis is either an antibacterial chemotherapy associated with conventional root planning or a surgical elimination of the infected tissues and correction of periodontal apparatus, or a combination of both^(9,10). Basically the remedy started with oral hygiene performance, initial preparation, surgical intervention if needed, then oral rehabilitation and finally a maintenance program. These rules may be inapplicable on all cases, especially those of Rapidly progressive, juvenile and destructive type periodontitis, due to its specific entity and courses⁽⁵⁻⁸⁾. A wide variety of chemical agents have been proposed and used in prevention, and/or treatment of gingival and periodontal diseases, some of them gave promising results in some cases^(6,11,12) or showed a short duration success^(13,14). Ultrasound scaling showed, since its introduction in periotherapy, a successful preventive, curative procedure and been helpful device in periodontal therapy⁽¹⁵⁾. Root planning which is the essential factor in the regenerative process of fibrous reattachment could be performed either with a flap surgery or with a rigorous ultrasonic scalar⁽¹⁶⁾ when associated with an irrigation could remove the microbial pocket contents and cleans the intra pocket chamber, in addition to its ability to remove the infected epithelial lining of pockets⁽¹⁷⁾. Polyvinyl pyrrolidone (PVP) is an iodophor complex of iodine with a surface-active agent. commercialized as povidone-iodine, available in markets as aerosol, ointment, antiseptic gauze pads, skin cleaner (liquid or foam), solution and swab sticks. The amount of free iodine is low, but it is released as the solution is diluted. PVP is less irritant and less likely to produce hypersensitivity than tincture of iodine⁽¹⁸⁻²⁰⁾. Gram positive and Gram negative micro organisms were highly susceptible to PVP, as well as acid-fast bacteria, spores and lipophilic viruses were also susceptible in moderate concentrations⁽²¹⁾. Fungi and amebic cysts were as well even in low concentrations. HIV and HBV could be destroyed within 2-10 minutes in vitro by 75mg/l⁽²²⁾. The aim of this study is to investigate the influence of ultra sound scaling and root planning associated with irrigation of 3% concentration of PVP solution on the clinical parameters of rapidly progressive periodontitis cases type A and type B.

MATERIALS AND METHODS:

Eight patients diagnosed as having rapidly progressive periodontitis according to the clinical findings and radiologic examination (3 of them were of type A and 5 of type B(7)).

Type A cases were all females aged from 17–22 years. Type B cases consisted of 2 females and 3 males aged from 35–38 years. All patients appeared with good general health according to their health record.

Gingival bleeding index (GBI)⁽²³⁾ Clinical pocket depth (CPD)⁽²⁴⁾, Clinical tooth mobility (CTM)⁽²⁵⁾, and radiologic bone loss were recorded before and six months after periotherapy .

The remedy protocol included an ultrasound scaling and root planning associated with simultaneous intra-pocket irrigation of 3% concentrated PVP solution, once a week during the first month, then twice a month during the following 3 months, and once monthly for another 2 months. Mean of GBI/person, CPD/person, and CTM/person were calculated before therapy as a baseline record and then 6 months post therapy.

The intra pocket irrigations performed by means of blind plastic needle and disposable plastic syringes, in addition to the scale jet, the container of the ultrasound scaler filled up with PVP solution, to be used Instead of water spray.

Means per group, (Type A, 3 patients and type B, 5 patients) were also calculated separately for GB1, CPD, and CTM. True periodontal pockets exceed 4mm in mean were 98 (32 for type A and 66 for type B), CTM according to modified miller index⁽²⁵⁾ were 87 tooth, 14 for type A and for 73 type B.

OPG and periapical x-ray were used in the diagnosis and to observe the results. Statistical analyses based upon T and F tests were done.

Polyvinyl pyrrolidone (PVP) commercialized as povidone-iodine (Merk) solution was diluted up to 3% . Each 100mg contains as excipient:

Non-oxynol-9-glycerol, Dihydrated sodium of hydrogenophosphate, Monohydrate citric acid. Iodine 3mg/100mg of excipient, Distilled water up to 100ml.

The patients have been informed to withdraw and give up mouth washes and systemic antibiotics during the period of study. Conventional brushing and tap water mouth wash are allowed. patients taken systemic antibiotics for any reason or have used antiseptic mouth washes or those having thyroid problem were excluded. Retained roots and tooth mobility more than grade 3 with nonvitality or associated with periapical abscess were extracted. Vital tooth associated with deep periodontal abscess were induced this study. Carious teeth were treated. No wire splinting was used for immobilization of mobile teeth.

RESULTS :

Clinical finding:

Clinical improvement observed in type B patients with disappearance of clinical inflammatory signs, gingiva appeared healthy, o bleeding tendency with probing, color changed to pink, halitosis were disappeared, gingival consistency appeared thickend with noticeable fibrous bulk of margins with keratinization .False pockets were highly reduced .

Total GB1 were significantly reduced (P<0.05) from 1.89±0.91 up to 0.888±0.212. GB1 of type A was reduced significantly as well as that of type B. (P<0.05).

Table 1 . GBI

	Base line	6 month later	Amount of difference	Percent of difference	T and F test
Type A	0.69±0.13	0.323±0.15	0.367	53.188%	P<0.05
Type B	2.289±0.88	1.07±0.66	1.219	53.255%	P<0.05
Total	1.89±0.91	0.888±0.212	1.002	53.01587%	P<0.05

The percentage of improvement among all patients was 53.015% (type A=53.188%, and type B=53.255%).

Total clinical pocket depth (CPD) were also reduced significantly (P<0.01) from 7.7±1.8 mm up to 4.33±1.3 mm, CPD of type A showed a significant confidence P<0.01, and that of type B showed confidence P<0.05.

Table 2 . Clinical pocket Depth (CPD).

	Base line	6 month later	Amount of difference	Percent of difference	T and F test
Type A	7.3±202	4.25±2.1	3.05	41.780%	P<0.01
Type B	8.1±2.01	5.02±2.3	3.08	38.0247%	P<0.05
Total	7.7±1.8	4.33±1.3	3.37	43.766%	P<0.01

Total clinical tooth mobility (CTM) significantly reduced (P<0.01) from 2.68±0.879 up to 1.2±0.99. The significant confidence type A was P<0.01, and that of type B was P<0.05.

Table 3 . Clinical tooth mobility (CTM).

	Base line	6 month later	Amount of difference	Percent of difference	T and F test
Type A	2.6±0.8	0.8±0.38	1.8	69.23%	P<0.01
Type B	2.7±0.89	1.4±0.45	1.3	48.148%	P<0.05
Total	2.68±0.879	1.2±0.99	1.48	55.224%	P<0.01

Radiologic findings:

Showed a noticeable bone formation around teeth specially the multi-rooted, increase in opacity of alveolar bone and lamina dura, which could suggest a new bone deposits.



Fig.1.A.
CRATER – LIKE BONY LESION INVOLVING THE TWO-THIRDS OF THE ROOT OF THE FIRST LOWER RIGHT BICUSPID.

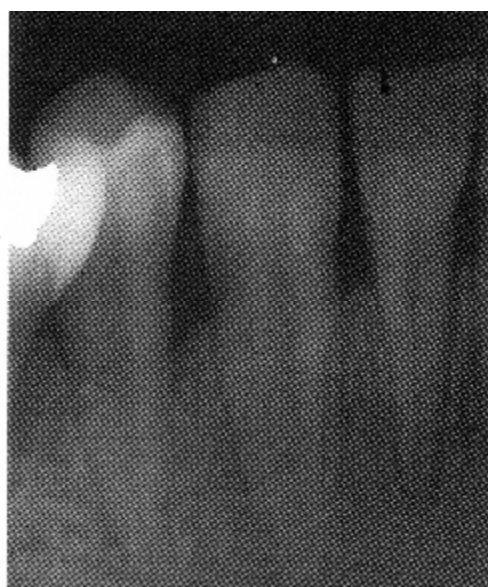


Fig.1.B.
SIX MONTHS LATER . HEALING OF LESION WITH OSSEOUS REPAIR AROUND THE FIRST LOWER RIGHT BICUSPID.



Fig.2.A.
*FIRST LOWER RIGHT MOLAR . BONY
DESTRUCTION INVOLVED THE ENTIRE
FURCATION AND MESIAL BONE WALL.*



Fig.2.B.
*SIX MONTH LATER . OSSEOUS REPAIR IS
VISIBLE ON THE MESIAL AND IN THE
INTERRADICULAR AREA OF THE FIRST LOWER
RIGHT MOLAR .*



Fig.3.A.
*INFRA BONY LESION , WITH WIDENING OF
PERIODONTAL CHAMBER OF THE FIRST
UPPER RIGHT CENTRAL INCISOR .*



Fig.3.B.
*SIX MONTHS LATER . VISIBLE BONE FORMATION
SUPPORTING THE FIRST UPPER RIGHT CENTRAL
INCISOR , THINNING THE PERIODONTAL
CHAMBER .*



Fig.4.A.

BONE LOSS ASSOCIATED WITH INFRABONY LESION INVOLVING THE UPPER RIGHT BICUSPID AND MOLARS

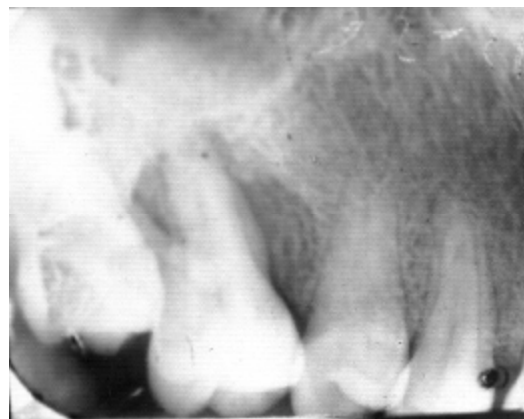


Fig.4.B.

SIX MONTHS LATER . BONE FORMATION IS VISIBLE IN THE INTERDENTAL ALVEALOS AS WELL OF THE INTER RADICULAR SEPTUM OF THE UPPER RIGHT FIRST MOLAR , BONE AROUND THE BICUSPID IS AUGMENTED CLOSE TO THE COMENTOENAMEL JUNCTION .

DISCUSSION:

Since the Fifties of last century, the periotherapy takes three essential directions, preventive for the non established periodontitis, surgical or the non-surgical remedy for the established periodontitis⁽²⁶⁾. The non-surgical periotherapy based upon the bacteriological findings⁽²⁷⁾ and on the susceptibility of the causative micro organisms to the antimicrobial drugs⁽²⁸⁾ given systemically, topically used or both⁽²⁹⁾. The surgical periotherapy based upon the ideology of excusion of the infected tissues and modify the environment to get the best condition for rehabilitating process with rigorous maintenance follow up⁽⁸⁾.

In spite of the technical limitations and the disadvantages of the surgical choices, still for more than century considered as the essential remedy^(28,30). The preventive periotherapy showed a successful measures for gingivitis and non-established periodontitis⁽³¹⁻³³⁾. But it failed to prevent juvenile periodontitis or rapidly progressive periodontitis to take place⁽³⁴⁾. Juvenile and rapidly progressive type A always associated with clean mouth, little or no plaque deposits, with simple clinical gingival inflammation^(2,34). Since the beginning of eighties, a periotherapeutic protocol have been realized. It organized according to the etiologic, bacteriologic, histologic, pathologic and immunologic backgrounds of the usual adult type periodontitis^(3-5,35-37). The rules of this protocol insist to perform a conventional scaling, and root planning with hand instruments, ultra sound scalers or citric acid demineralization⁽²⁶⁾, surgical intervention to eliminate the periodontal pocket and to regenerate a fibrous reattachment, then a maintenance phase⁽¹⁰⁾ with a rehabilitation procedure to restore the occlusion⁽³⁸⁾, a huge natural, synthetic and chemical materials have been experimented in association with surgery to improve and ameliorate the results^(11,15,39), to obtain a fibrous reattachment and to prevent the epithelial invasion in between flap and planned root surfaces⁽⁴⁰⁻⁴²⁾ and finally to stabilize the post surgical periodontium in healthy level as long as possible^(39,43,44).

On the same line, some expensive natural or synthetic materials have been used to obtain bone-build in order to compensate the pathologic bone loss and/or to enhance bone building^(26,45-48).

Under the limitations of indications and contraindications of the periodontal surgery the authors were directed toward a non-surgical remedy^(9,10) the basic protocol includes a subgingival scaling with antiseptic mouthrinse under a systemic cover of antibiotics specially tetracycline⁽⁴⁹⁻⁵¹⁾.

A subgingival irrigation of antiseptic or antibiotic solutions have been experimented as a topical bactericidal therapy in association with scaling and root planning showed a promising results^(9,29,52-55). Chlorhexidine gluconate 0.2%⁽⁵⁶⁻⁶¹⁾ have been used as subgingival, intra pocket irrigation with or without surgery, the result showed a significant reduction in bacterial flora and a clinical improvement, but the recolonization of treated pocket by bacteria is often. Although it create a fibrous attachment and significant pocket reduction specially when accompanied with mechanical root planning. Hydrogen peroxide 1-3% solution^(31,32,58,59,62) studied widely as a bactericidal antiseptic mouth rinse and subgingival irrigation, reduces the bacterial colonies and showed a temporary significant clinical cure especially on gingivitis and help in tooth whitening. Stannous floride, sanguinarin⁽⁵⁵⁾ and aluminum chloride^(63,64) have also been used, they showed efficacy when irrigated with pressure in the periodontal pocket. Warm normal saline, and distilled water have demonstrated as effective subgingival cleaners, their results when used with jet irrigator device significantly equivalent to that obtained with antiseptic solutions^(31,65) these results suggested that the physical influence of washing the pockets able to eliminate the aerobic and anaerobic bacterial flora and perform the field for an immunologic repair process which result in a visible clinical improvement.

Tetracycline a broad spectrum bactericidal antibiotic was widely used in the treatment of juvenile periodontitis and the aggressive periodontitis (type B rapidly progressive) as a systemic adjunctive and as a topical intra-pocket filler^(29,49,50,53,66) or as an irrigation solution^(53,54).

Metronidazol^(67,68) as well as Doxycyclin^(30,69,70) were also administered systemically or topically as subgingival irrigations in the treatment of adult type, juvenile and rapidly progressive as wall as in cases of acute necrotizing ulcerative gingivitis, their administration based upon the fact that a broad spectrum bactericidal agent able to eliminate the majority of the intra pocket bacterial flora which is a collection of many bacterial associations. The results of these studies showed a significant improvement in clinical periodontal parameters when the systemic or topical administration accompanied with scaling and root planning, even a significant attachment gain were observed^(50,51,54,60,70). Systemic administration of antibiotics without scaling and root planning appeared useless^(30,49,51,69,72) while the topical application or intra pocket irrigations of antibiotics or antiseptics appeared more effective either with or without root planning⁽⁷³⁾.

Intrapocket micro organisms able to penetrate the epithelial lining of the pockets⁽⁷⁴⁾ and the alveolar bone^(8,62) these micro organism can colonize the bone surfaces or even the deeper layers of cancellous bone especially in cases of aggressive periodontitis^(75,76).

Topical subgingival hyaluronic acid gel was administered recently as an adjunctive to scaling and root planning, but the result showed a negative influence on microbial flora and a positive significant increase in the sulcus fluid flow rate leading to physical washing action⁽⁷¹⁾.

Rapidly progressive periodontitis is an aggressive periodontal brake-down associated with the presence of a specific bacterial colonies including Actinobacillus Actinomyces temcomitance (AAT), B. gingivalis, B. melaninogenicus⁽⁷⁷⁾ black-pigmented backterioide⁽⁷⁸⁾ prevotella intermedia, porphyromonas gingivalis tanerella forsythensis^(71,79) Fuso-bacterium nucleatum⁽⁶⁷⁾, spirochetes, protheromonas gingivalis⁽³²⁾. A novel single-strand circulating DNA virus has been recently isolated and named as TT virus (TTV). It has been demonstrated that peripheral blood cells harbors (TTV) DNA, was first identified in the gingival tissues and was found to be significantly associated with the presence of periodontitis⁽⁸⁰⁾. Recent evidences showed that at least 46 different combinations of the assessed periodontal pathogens were isolated in subjects with periodontitis, and at least 10 different antibiotics regimens might be required to specifically target the various pathogen complexes⁽⁶⁾.

The specific entity and the specific bacterial flora either type A or type B⁽⁷⁾ did an obstacles facing a successful curative therapy. Severe and rapid bone loss leads to a rapid tooth exfoliations⁽⁷⁷⁾ are oftenly characteristics thus the surgical interference in this conditions perhaps leads to more bone loss and more tooth loss.

Although the bacterial flora of juvenile, rapidly progressive aggressive types of periodontitis showed wide resembleness⁽⁸¹⁾. The curative therapy for these destructive diseases is still not yet well realized^(6,34). Scaling and root planning under a heavy dose of systemic tetracycline^(29,54), doxycycline^(60,69,70) metronidazol^(50,68) or minocycline⁽¹⁷⁾ showed limited positive results^(8,30,58,72), topical application of these antibiotics or an antiseptic mouth rinses showed a questionable result resembles that obtained with normal saline irrigation associated with root planning^(31,56,57,62). Experimental therapy showed a promising positive result, but still conserved in the experimentation field which could not be yet applied clinically as a conventional therapy. Tooth discoloration, disagreeable test is usually associated with mouth rinses or subgingival irrigations^(32,62,82).

Scaling and root planning seemed to be effective in reduction of the bacterial flora and eliminate the necrotic cementum as well as the infected epithelial lining of pockets^(8,10,76), which results in improvement of clinical parameters. Ultrasonic device seemed to be superior to the hand instrumentation^(36,83,84,85) with less possibility to induce blood bacterimia⁽⁷⁴⁾, chronic periodontitis patients undergoing an episode of subgingival scaling showed a significant elevation in circulating endotoxine following treatment and may significant in terms of the relationship between periodontal diseases, bacterimia and cardiovascular diseases⁽⁸⁶⁾. Actual knowledge agreed that ultrasound scaling and root planning in association with deep intrapocket irrigation could perform the parameters of a promising non-surgical curative therapy^(15,65,84). The physical effect of washing the periodontal pocket with a jet device or pestol-jet could eliminate the bacterial colonies, and improve the gingival healing, but for a short time due to the recolonization of the pocket by the bacteria which already penetrated the pocket wall and colonized the adjacent surfaces of alveolar bone, epithelial lining and cementum^(76,87).

The bactericidal effect of antiseptics or antibiotics when used as subgingival irrigations seemed to be unable to act on the bottom of deep pockets, it seemed to need a long duration exposure with bacteria or a higher concentration was suggested^(9,69,74) taking in consideration the increased tissulor damages associated with augmented concentration^(57,62). Conditioning the diseased cementum with tetracycline may induce an intense inflammatory response⁽⁸⁸⁾. The bactericidal action of systemic antibiotics seemed to be week, it could enhanced when accompanied with scaling and root planning, but its duration still shortly effective^(6,17,30,69,70).

Tetracycline, Doxycycline and Minocycline^(17,70) showed 4-8 µl/ml concentration in the gingival fluid after 24h when 1 gram/day have been taken⁽⁸⁸⁾ this concentration is effective bactericidal when associated with conventional scaling and root planning, it appeared useless when administered alone^(44,53). The complex bacterial flora of RPP pockets could need highly effective bactericidal subgingival irrigating solution, with save topical use, or at least 10 different antibiotic regimens might be required to specifically target the various pathogen complex⁽⁶⁾.

Polyvinyl pyrrolidone PVP, is a disinfectant solution highly effective against the majority of microorganisms, the totality of gram negative and gram positive aerobic, anaerobic, acid fast bacteria were highly susceptible to a low concentration of PVP. Spores, lipophilic viruses, fungi and amoebic cyst were also susceptible⁽¹⁸⁾ the amount of free iodine is low but it is released as the solution is diluted, nevertheless it retains the activity of iodine⁽⁸⁹⁾.

PVP is less irritating and less likely to produce skin hypersensitivity⁽¹⁹⁾ acts as rapidly as chlorhexidine with a broader spectrum of action including sporicidal⁽²⁰⁾, virocidal even against HIV and HBSA⁽²¹⁾. Its content of citric acid perform an additional bactericidal action⁽²²⁾ and demineralizing the necrotic cementum⁽⁹⁰⁾, it may fulfil the requirement of an ideal topical, anti-microbial agent for aggressive periodontatis conditions.

Our result showed a significant improvement in clinical parameters, reduction in GBI with gain of 1.002 (equal to 53.015%), pocket depth were reduced significantly (3.77 mm = 43.766%). Tooth mobility also significantly reduced (1.48 = 55.224%). Radiographs showed evidences of bone formation around the bi-wall and tri-wall pockets when compared to the baseline x-rays film.

Conclusion:

Within the limit of this study and based on the current literature, the results demonstrate that a rigorous scaling and root planning could perform mechanical root planning, elimination of infected epithelial lining and able to scotching the subjacent bone surfaces, thus eliminate the microbial field and prepare the periodontium to a reattachment possibilities, intra pocket irrigation performs a washing mechanism.

In addition to its effective wide broad spectrum bactericidal and veridical actions, PVP could perform a long acting exposure with low concentrations and thus provide bone formation. A save, effective, clinically applicable, easy to use and cheap remedy of complex periodontitis could be proposed.

REFERENCES:

- 1- Dzik J L, Socranisky S S , Haffajee A D. The predominant cultivable flora of active and inactive sites of destructive periodontal diseases. *J clin. Periodontal*, 1988 , 15 : 316-323.
- 2- Durant B M, Perdrix G, Delalande J. une entite clinique; La parodontite aggressive. *J de parodontology*. 1984; 3 : 89-101.
- 3- Davenport jr. R H, Simpson D M, Hassel T M. Histometric comparisom of active and inactive lesion of advanced periodontities. *J periodontal* 1982; 53 : 285-291 .
- 4- Harold Loe. Specificite microbienne dans la maladie parodontale. *J de parodontology* 1982; I : 305-319.
- 5- Helderman WVP. Aspects microbiologic dans l'etiologie et le contról de la maladie parodontale. *J de parodontology* 1982; I : 321-332.
- 6- Thomas B, Karola P, Benjamin E, Thomas F. Specific Antibiotics in the treatment of periodontitis - A proposed strategy. *J periodontal* 2004; 75 : 169-175.
- 7- Suzuki J B, Charon J A. Classification of the periodontal diseases. *J de parodontology* 1989; 8 : 31-51.
- 8- Saxen L, Asikainen S, Sandholm L, Kari K. treatment of juvenile periodontitis without antibiotics. *J clin. Periodontal* 1986; 13 : 714-719.
- 9- Cadet J, Burnel G. Non surgical treatment. A long term study. *J de parodontology* 1989; 8 : 81-88 .
- 10- Isidor F, Karring T. A long term efficacy of surgical and non surgical periodontal therapy, clinical study over 5 years. *J periodont Res*. 1986; 21 : 462-472.
- 11- Peter E, Diana-Mario K, Bernadette P., Harold S, Christof D. Guided tissue regeneration with bioabsorbable barrier. II long-term results in infrabony defects. *J periodontal* 2004; 75 : 957-965.
- 12- Bral M, Brownstein CN. Antimicrobial agents in the prevention and treatment of periodontal diseases. *Dent clin. North Am* 1988; 32 : 217-241.
- 13- Yu-kang T, Mark S, G, Gareth SG, Ian H M, Kenneth AS, Newell WJ. The application of Multilevel modeling in the analysis of longitudinal periodontal data-part I : Absolute level of disease. *J periodontal* 2004; 75 : 127-136.
- 14- Yu-kang T, mark S G, Gareth S G, Ian H M, Kenneth AE, Newell WJ. The application of multilevel modeling in the analysis of longitudinal periodontal data - part II : Changes in disease level over time. *J periodontal* 2004; 75 : 137-145.
- 15- Anton S, Frank S, Mohammad B, George E R, Nicole B A; Jurgen B. Periodontal treatment with an Er : YAG laser compared to ultrasonic instrumentation : A pilot study. *J periodontal* 2004; 75 : 966-973.
- 16- Luciana M, Denise CA, Bruno BB, Marcelo DC, Getúlio RNF, Marco ZC, Francisco HN, Enilson AS. Locally delivered doxycycline as an adjuvative therapy to scaling and root planning in the treatment of smokers : A clinical study. *J periodontal* 2004; 75 : 464-469.

- 17- Paquette DW, Hanlon A, Lessem J, Williams RC. Clinical relevance of adjunctive minocycline microspheres in patients with chronic periodontitis : secondary analysis of a phase 3 trial. *J periodontal* 2004; 75 : 531-536.
- 18- Bertram GK, Basic and clinical pharmacology, 7th ed. Appleton and lange, 1998; 804-807.
- 19- Wood PR. Cross infection control in dentistry, mosby year book, 1992, 110-120.
- 20- Viljanto j. Disinfection of surgical wounds without inhibition normal wound healing. *Arch surg.* 1980; 115 : 253-261.
- 21- Reams GJ. practical application of infection control in endodontics, *J endodontics* 1995; 21 : 281-285.
- 22- Maki DG. Prospective randomized trial of povidon-iodine, alcohol, and chlorhexidine for prevention of infection associated with control venous and arterial catheters, *Lancet*, 1991; 238 : 339-347.
- 23- Ainano J, Bay I. problems and proposals for recording gingivitis and plaque. *Int. Dent. J* 1975; 25 : 229-235.
- 24- Clark DC, Chin Quec T, Bergeron MJ. Reliability of attachment level measurement using the CEJ and a plastic stent. *J periodontal* 1987; 58 : 115-117.
- 25- Miller SC. Textbook of periodontal, 3rd ed. Philadelphia, Blakiston. 1950.
- 26- Ramfjord SP, Caffesse RC, Morrison EC, Hill RW, Kerry GS, Appleberry EA, Nissle RR, Stults OI. A comparative study of 4 types of periodontal treatment. 5 years Observations. *J clin. Periodontal* 1987; 14 : 445-452.
- 27- Miller W.D. The microorganisms of the mouth. S S white ed. Philadelphia 1890; pp333.
- 28- Weanhaug I. The gingival pocket. Anatomy, pathology deepening and elimination. *Odontol TSKR* 1952; 60 suppl; pp 186.
- 29- Goodson JM, Hogan PE, Duncan SL. Clinical response of periodontium after treatment with local application of antibiotics. *J periodontal* 1985; suppl., special issue : 81-87.
- 30- Gulnur E, Gul A, Timo S, Hanne L, Levent K, Haluk B. The effect of adjunctive low. dose doxycycline therapy on clinical parameters and gingival crevicular fluid matrix metalloproteinase-8 levels in chronic periodontitis. *J periodontal* 2004; 75 : 106-115.
- 31- Philstrom BL, Wolff L.F., Bashar M, Scheffer EM, Jensen J.R., HeppliDM, Baudt CL. A conventional oral hygien with saline solution and hydrogen peroxide. A comparative study. *J periodontal* 1987; 58 : 291-313.
- 32- Hatice H, Martha N, Martha W, Thomas EVD. Efficacy of a fluoridated hydrogen peroxide-based mouth rinse for the treatment of gingivitis : A randomized clinical trial. *J periodontal* 2004; 75 : 57-65.
- 33- Karen W, Anita F, Kathy D, Jan H, Aaron RB, Robert DB. One and 3-minuts plaque removal by a Battery-powered versus a manual tooth brush. *J periodontal* 2004; 75 : 1107-1113.
- 34- Zambon JJ, Christersson LA, Genco RJ. Diagnosis and treatment of juvenile periodontitis. *JADA* 1986; 113 : 299.
- 35- Hill RW, Ramfjord SP, Morisson EC, Appleberry EA, Caffesse RG Kerry OJ, Nissle RR. Comparative results of 4 types of periodontal treatment over 2 years. *J. periodontal* 1981; 52 : 655-616 .
- 36- Benfinati MP, Montisami MT, Benfinati SP, Nathanson D. Electron microscope study of radicular surfaces treated with hand instruments and ultrasound scalor. *Int. review of periodontic and Rest. Dents.* 1987; 2 : 50-67.
- 37- Benjamin TK, Nicola JM, Jason E, Jonathan P, peter NG. Study of Bacterial viability within human supra gingival dental calculus. *J periodontal* 2004; 75 : 23-29.
- 38- Carranza F A Jr. Glickman's clinical periodontology, 6Th ed. 1984; Sander's company, ISBN 0-7216-2441-3. USA.
- 39- Al-Juboury A L. Introduction of fibrin adhesive system (tissucol) in periodontal surgery, part I : Suture substitution and wound healing. *Mustansiria dental journal* 2004; I : 218-227.
- 40- James GW, Therry G, Margaret H, Connic D, John MI, James S. The clinical effect of a cellular matrix on gingival thickness and root coverage compared to coronally positioned flap alone. *J periodontal* 2004; 75 : 44-56.
- 41- Yasuko S, Masahiro K, Noboru O, Masoto T, Yoshinori K. Enhanced cementum formatron in experimentally induced cementum defects of the root surface with the application of recombined basic fibroblasts growth factor in collagen gel in vivo. *J periodontal* 2004; 75 : 243-248.

- 42- Roselyn CD, Andrew D, Franco C, Timothy P M John SM, Lawrence CP, Laura R, gene RH, Mansoor J. Lysophosphatidic Acid modulates the regenerative responses of human gingival fibroblasts and enhances the action of platelet derived growth factor. *J periodontal* 2004; 75 : 297-305.
- 43- George H P. effect of periodontal therapy in smokers and non-smokers with advanced periodontal diseases : Results after maintenance therapy for a minimum of 5 years *J periodontal* 2004; 75 : 839-843.
- 44- Cern AG, Murat OA, murat AK. Alteration in location of the mucogingival junction 5 years after coronally repositioned flap surgery. *J periodontal* 2004; 75 : 893-901.
- 45- Carlos EN, Leah B, Shireley SH, Simona FH, Alexander V. Bone apposition in surgical bony defect following orthodontic movement : A comparative histomorphometric study between root-and periodontal ligament-Damaged and periodontally intact Rat molars. *J periodontal* 2004; 75: 1013-1019.
- 46- Nada BAH, Edmond Ch, Hala T, Nadim M. Combined bone grafting and orthodontic treatment of an iatrogenic periodontal defect : A case report with clinical reentry. *J periodontal* 2004; 75 : 31-321.
- 47- David ED, Alan JM, Howard TM, charles AP, brian LM. Osseous surgery for crown lengthening : A. 6 months clinical study. *J periodontal* 2004; 75 : 1288-1294.
- 48- Chang-Sung K, Seong-Ho Ch, Jung-Kiu Ch, Kyoo-Sung Ch, IK-Sang M, Ulf MEW, Chong-kwan K. periodontal repair in surgically created intrabony defects in dogs : influence of the Number of bone walls on healing response. *J periodontal* 2004; 75 : 229-235.
- 49- Charon J. Proye M. Usage des tetracycline en parodontie. *Journal de parodontologie* 1982; I : 99-110.
- 50- Slots J, Rosling BG. The suppression of the pathologic flora by the tetracycline in juvenile periodontitis. *J clin. Periodontal* 1983; 10 : 465-486.
- 51- Lindhe J, Liljenberg B, Adielsson B. The effect of long term Tetracycline on the periodontal diseases in ma n. *J clin. Periodont* 1983; 10 : 590-601.
- 52- Eakle WS, Ford C, Boyd RL. Amount of penetration of local irrigation in periodontal pockets. *J clin. Periodontal* 1986; 13 : 39-44.
- 53- Minabe M, Takeuchi K, Tomomatsu E, Hori T, umemoto T. The clinical influence of local application of tetracycline attached to collagen film. *J clin. Periodontal* 1989; 16 : 291-296.
- 54- Terranova VP, Francetti LC, Hic S, Diflorio RM, Lyall RM, Genco RJ. Biochemical approach of periodontal repair, treatment of radicular surfaces with tetracycline facilitate the growth and adhesion of fibroblasts on the dentinal surfaces. *J. periodontal Res.* 1986; 21 : 330-337.
- 55- Joël IT, Raphaëls S. subgingival irrigation, a critical review of different protocol of experimentation. *journal de paradontologie* 1988; 7 : 65-78.
- 56- Lander PE, Newcomb GM, Seymour GJ, powell RN. The clinical antimicrobial effect of subgingival irrigation of chlorhixidin in advanced periodontitis. *J clin. Periodontal* 1986; 13 : 74-80.
- 57- Oosterwall PJM, Miky FHM, Van Denbrink ME, Renggli H. Determination of active concentration of digluconate of chlorhixidine, aminofloride gel, and stannous floride gel on the subgingival bacteria. in vitro. *J periodontal Res.* 1989; 24 : 155-160.
- 58- Wattes E.A. , Newman HN. Clinical effect of simplified oral hygien system included subgingival chlorhixidin irrigation on chronic periodontitis *J clin. Periodontal* 1986; 13 : 666-670.
- 59- Wennstrom JL, Dahlen G, Grondahl K, Heyl L. subgingival antimicrobial irrigation of periodontal pocket; bacteriologic and radiologic observations. *J clin. Periodontal* 1987; 14 : 773-580.
- 60- Centa A, Barthet P, Benque EP, Elefterion A. The influence of irrigation of chlorhixidine solution on the gain of attachment. *J periodontal* 1987; 6 : 243-248.
- 61- Corinne B, Philippe C. Emploi sous-gingival de chlorhexidine dans le treatment des paradontites. *J de paradontologie* 1987; 6 : 357-362.
- 62- Wikesjo VME, Reynolds HS, Christersson LA, Zambonjj, Genco RJ Effect of subgingival irrigation on Actinobacillus Actinomyces temcomitance. *j clin. Periodontal* 1989; 16 : 116-119.
- 63- Fourel J, Roig R. Ultrasonic curettage with irrigation of aluminium chloride in the treatment of adult periodontitis. *J de parodontologie* 1987; 6 : 325-336.

- 64- Roig R, Fourel J. A preliminary clinical and histologic study of the action of aluminum chloride on gingival inflammation. *J de parodontologie* 1987; 6 : 41-46.
- 65- Cobb CM, Rodgers RL, Kinoy W.J. Ultrastructural study of periodontal pocket after subgingival mechanical irrigation in vivo. *J periodontal* 1988; 59 : 155-163.
- 66- Rosling BG, Slots J, Webber RL, Christersson LA, Genco RJ. The microbiological and clinical effects of a topical-subgingival antimicrobial treatment of periodontitis in man. *J clin. Periodontal* 1983; 10 : 487-514.
- 67- Lindhe J, Liljenberg B, Adielson B, Borjesson I. The use of metronidazole as an investigating method in periodontal diseases in man. *J clin. Periodontal* 1983; 10 : 100-110.
- 68- Maria P, Carmelo GA, Aida B, Italo FA. Meta analysis of local metronidazole in the treatment of chronic periodontitis. *J periodontal* 2004; 75 : 830-838.
- 69- Gulmur E, Gül A, Timo S, Hannel K, Haluk B. The effect of adjunctive low-dose doxycycline therapy on clinical parameters and gingival crevicular fluid matrix metallo- proteinase-8 level in chronic periodontitis. *J periodontal* 2004; 75 : 106-115.
- 70- Philip M, Arthur FH, John Novak M, Brayan SM, Bruce LP, Robert Sc, Clarence LT, John D, Thomas EVD, Clay BW, Mark HB. Subantimicrobial dose doxycycline enhance the efficacy and root planning in chronic periodontitis. A multicenter trial. *J periodontal* 2004; 75 : 1068-1076.
- 71- Yi-xu, Hofling K, Fimmers F, Frentzen M, Jervoe-Storn M. Clinical and microbiological effects of topical subgingival application of hyaluronic acid gel adjunctive to scaling and root planning in the treatment of chronic periodontitis. *J periodontal* 2004; 75 : 1114-1118 .
- 72- Rams TE, Keys PH. Approach in periodontal pathology : effect of tetracycline on the subgingival flora. *JADA* 1983; 107 : 37-41.
- 73- Blomlöf L, Lind Skag S, Appelgren R, Jonsson B, Weintraub A, Hammanstrom L. New attachment with or without cementum elimination. *J clin. Periodontal* 1987; 14 : 134-143.
- 74- Saglie R, Newman MG, Carranza jrFA, Pattison GL. Bacterial invasion of gingival connection tissue in advanced periodontitis. *J periodontal* 1982; 53: 217-229.
- 75- Carranza jrFA, Saglie R, Newman MG, Valentin PL, An electron-microscope study of micro organisms invading the periodontal tissue of juvenile periodontitis. *J periodontal* 1982; 54 : 598-17.
- 76- Liakoni H, Barber R, Newmann HH. Bacterial penetration of periodontal pocket's soft tissues. *J clin. Periodontal* 1987; 14 : 22-28.
- 77- Slot's J, Hoftstram C, Rosling B, Dahlan G. Detection of Actinobacillus Actinomyces Temcomitance and bacteroid gingivalis in the prelevements of subgingival plaque by indirect fluorescent antibodies. *J periodontal Res.* 1985; 20 : 613-621.
- 78- Schultz-Handt S D, Bruce MA, Bibby BG. Bacterial factor in non-specific gingivitis. *J Dent. Res.* 1954; 33 : 454.
- 79- Yang HW, Huang YF, Chou MY. Occurrence of porphyromonas gingivalis and Tannerella Forsythensis in periodontal diseased and healthy subjects. *J periodontal* 2004; 75 : 1077-1083.
- 80- Rotendo R, Maggi F, Nieri M, Muzzi L, Bendinelli M, Pini Prato GP. TT virus infection of periodontal tissue : A controlled clinical and laboratory pilot study. *J periodontal* 2004; 75 : 1216-1220.
- 81- Yang HW, Asikainen S, Dogan B, Suda R, Lai CH. Relationship of Actinobacillus Actinom yest Temcomitance serotype b to oggressive periodontitis : frequency in pure cultured Isolates. *J periodontal* 2004; 75 : 592-594.
- 82- Flora L, Gjerm M, Rolla G, and Waerhang J. Side effects of chlorhexidine mouth washes. *Scand Dent. Res.* 1971; 79 : 149-168.
- 83- Cecchi L, Melliccioni GA, Comparison of the efficacy of manual and ultrasound root planning in the eviction of radicular surface endotoxine in vitro. *J periodontal* 1988; 59 : 398-402.
- 84- Rosenberg E-S, Gressberg DE, Hammond B. Incidence of scaling and root planning on the microbial flora associated with periodontal diseases. *Review Int. periodont and Rest. Dent.* 1989; 1 : 23-33.
- 85- Folwaczny M, Markel U, Mehl A, Hickel R. Influence of parameters on root surface roughness following treatment with a magnetostrictive ultrasonic scalar : An in vitro study. *J periodontal* 2004; 75 : 1221-1226.

- 86- Ide M, Jagdev D, Coward PY, crook M, Barely GR, Wilson R.F. The short-term effects of treatment of chronic periodontitis on circulating levels of endotoxin, C-reactive protein, Tumor necrosis factor- α , and interleukin-6. *J periodontal* 2004; 75 : 420-428.
 - 87- Newman GM, Sanz M, Nachnani ST, saltini C, Anderson L. Effect of 0.12% chlorhexidine on bacterial recolonization following periodontal surgery. *J periodontal* 1989; 60 : 577-581.
 - 88- Haddad YH, Karake L, Stabhalz A, Soskolne A, Shapira L Tetracycline conditioning Augments the in vivo inflammatory Response induced by cementum extracts. *J periodontal* 2004; 75 : 388-392.
 - 89- Larson E. Guidelines for use topical antimicrobial agents. *Am J infect. Dis. control* 1988; 16 : 233-249.
 - 90- Daly C.G. The antibacterial effect of citric acid during the root planning. Study in vitro. *J clin. Periodontal* 1982; 9 : 386-392.
-