Preventive Periodontal Regimen in Papillon-Lefèvre Syndrome

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Abstract

Purpose: The purpose of this study was to evaluate the effect of a comprehensive preventive program, based on mechanical plaque control and local and systemic antibacterial measures, on periodontal health and preservation of permanent teeth in patients with Papillon-Lefèvre syndrome (PLS).

Methods: Thirty-five consecutive PLS patients (median age=7 years; range=3-19 years) were treated and followed every third month over 3 to 7 years. Visible plaque, bleeding on probing, periodontal pockets ≥5 mm, and number of lost permanent teeth were registered at the first visit and during the follow-up period. Due to severe periodontal inflammation, all primary teeth were extracted prior to the eruption of the first permanent tooth. Tooth-brushing was supported by comprehensive periodontal care and local and systemic chemotherapeutics (chlorhexidine and amoxicillin/metronidazole) on individual indications.

Results: Subjects treated strictly according to the program from their early years showed significantly fewer signs of periodontal disease and lost fewer permanent teeth than patients who started the program at an older age ($P<.05$). This was especially true if signs of periodontal disease had emerged when the treatment started. Compliance with the treatment protocol had a significant impact on the presence of plaque, bleeding surfaces, periodontal pockets, and number of lost permanent teeth.

Conclusions: Early treatment and compliance with the preventive program were the major determinants for preserving permanent teeth in young PLS patients. (Pediatr Dent 2005; 27:226-232)

KEYWORDS: PAPILLON-LEFÈVRE SYNDROME, PERIODONTAL DISEASE PERIODONTAL INFLAMMATION, PREVENTIVE TREATMENT, CHILDREN

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Papillon-Lefèvre syndrome (PLS) is characterized by erythematous palmoplantar hyperkeratosis and severe periodontal disease. Dermatological as well as oral signs vary considerably between affected subjects.[1] The condition is inherited as an autosomal recessive trait[2] and linked to mutations of the cathepsin C gene.[3,4] Cathepsin C is a lysosomal cysteine protease that activates several granule serine proteases expressed in bone marrow-derived effector cells of myeloid and lymphoid series.[5] These proteases are implicated in a variety of immune and inflammatory processes, including cell-mediated cytotoxicity, phagocytic destruction of bacteria, local activation and deactivation of cytokines and other inflammatory mediators, and extracellular matrix degeneration.[6] Cathepsin C is normally expressed in palmar, plantar, and gingival epithelium,[7] but its involvement in epithelial desquamation or its significance in gingival epithelium is unknown.[8] While several cathepsin C gene mutations have been identified,[9] the correlation to the disease's phenotypic expression is still obscure.

The aggressive periodontal inflammation leads to premature loss of primary and permanent teeth. Clinical observations and investigations have led to various theories regarding possible etiologic mechanisms, including altered immune response,[10-13] underlying tissue pathology,[14,15] and virulent and aggressive periodontal flora. *Actinobacillus actinomycetemcomitans* is a periopathogen of key importance in periodontal infections and has often been identified in periodontal lesions in PLS patients.[15-19] Others, however, have found flora without any particular periodontal pathogens.[20,21]

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Since the etiology of the periodontal inflammation in PLS is unknown, various treatment regimens have been suggested. Mixed results have been shown by previous studies investigating treatments such as systemic use of antibiotics or retinoids, chlorhexidine rinses, oral hygiene regimens in combination with extraction of all deciduous teeth prior to eruption of the first permanent tooth, extraction of permanent teeth with severe periodontal inflammation, and scaling and root planing when used on their own.[17,18,22-29] Furthermore, in most reports the number of patients is few and may be considered as case reports rather than systematic evaluations of intervention.

The aim of this prospective study was to investigate the effect of a comprehensive preventive treatment program, based on mechanical plaque control as well as local and systemic antibacterial measures, on periodontal health in young PLS patients.

Methods

Patients

The study group consisted of 35 consecutive patients referred to the Department of Dentistry, King Faisal Specialist Hospital and Research Centre (KFSH & RC), Riyadh, Saudi Arabia, between 1996 and 2000. The median age was 7 years (range=3 to 19 years), and all subjects had the PLS diagnosis confirmed by genetic screening and/or clinical examination. The patients had either primary, mixed, or partially dentate permanent dentitions.

Study design

At the initial visit, oral and dermatologic examinations were conducted, as described later. The patients were subjected to a standardized treatment program, as summarized in Table 1. The program emphasized meticulous plaque control via thorough tooth-brushing, conservative periodontal care, and local and systemic antimicrobial measures with chlorhexidine rinses and antibiotics, respectively. Every patient with a primary dentition expressed severe periodontal inflammation. To eliminate any foci of infection, all primary teeth were extracted at least 6 months prior to the first permanent tooth erupting. For the same reason, permanent teeth with advanced periodontal disease were also extracted. During the follow-up period, the patients were recalled for checkups and re-evaluations every third month or more frequently if their oral condition required closer monitoring. For patients with primary teeth present when the preventive regimen started, baseline data were not collected until the first permanent tooth erupted. As outlined later, the endpoint measures were:

1. presence of visible plaque;
2. bleeding surfaces;
3. number of lost permanent teeth;
4. presence of pathological periodontal pockets.

To be included in this evaluation, a follow-up period of at least 3 years—with 2 years of permanent teeth present—was required. All the patients' parents signed an informed consent for the treatment, and older children also gave their consent.

Oral examination

The dermatological and oral examinations were carried out as previously described.[30] All oral examinations were performed in a dental office by one of the authors and included bitewing and panoramic radiographs at baseline and then yearly. The examination included recording of visible plaque index[31] (VPI) and bleeding on probing[32] (BPO). VPI and BPO were expressed as a percentage of total number of tooth surfaces. Extracted permanent teeth were recorded, and measurements of periodontal pocket depths in

Table 1. Standardized Dental Treatment Protocol for Patients With Papillon-Lefèvre Syndrome

Primary dentition
Oral hygiene instructions and prophylaxis every third month
Extraction of teeth with advanced periodontal disease
Extraction of all primary teeth at least 6 months prior to eruption of the first permanent tooth
Antibiotics for 2 weeks post extractions to avoid postoperative complications
Recommended antibiotics: amoxicillin or amoxicillin + clavulanic acid with a dose of 20-50 mg/kg/day or 20-40 mg/kg/day, respectively, in divided doses every 8 hours
Permanent dentition
Oral hygiene instructions and prophylaxis every third month
Mouthrinses with chlorhexidine gluconate 0.2% twice daily
Teeth with *moderate periodontal disease* (bone loss <30% of root length, probing pocket depths <5 mm)
Dental scaling and prophylaxis once a month
Systemic antibiotic treatment for 4 weeks
Recommended antibiotics: amoxicillin 20-50 mg/kg/day+metronidazole (15-35 mg/kg/day) in divided doses, every 8 hours[43]
Teeth with *advanced periodontal disease* (bone loss >30% of root length, ≥5 mm pocket depths)
Extraction

Table 2. Median and Distribution of Visible Plaque Index (VPI) and Bleeding on Probing (BOP) Scores, Mean Number (±SD) of Periodontal Pockets and Lost Permanent Teeth at Initial Examination of Young Papillon-Lefèvre Syndrome Patients

Group	VPI				BOP				Periodontal pockets ≥5 mm		Extracted permanent teeth	
	Median	Score*			Median	Score*						
		0	1	2		0	1	2	Yes/No*	Mean±SD	Yes/No*	Mean±SD
1 (N=13)	38%	4	5	4	17%	4	5	4	0/13	-	0/13	-
2 (N=22)	63%	5	4	13	41%	3	1	18	16/6	7.3±12.2 (0-54)	13/9	4.4±5.2 (0-18)

VPI and BOP measured as percentage of present permanent surfaces. Group 1=patients who were initially examined and had treatment started prior to the eruption of the first permanent tooth. Group 2=patients who were initially examined and had treatment started after the eruption of the first permanent tooth. VPI scores: 0=0%-24% of permanent tooth surfaces; 1=25%-49% of permanent tooth surfaces; 2=≥50% of permanent tooth surfaces. BOP scores: 0=0%-9% of permanent tooth surfaces; 1=10%-19% of permanent tooth surfaces; 2=≥20% of permanent tooth surfaces.
*Values denote number of patients.

millimetres were made using a periodontal probe (WHO-CPITN-E, Henry Schein, Melville, NY). The registrations were made on the mesial, distal, buccal, and lingual sites of all erupted permanent teeth. Pocket depths ≥5 mm on fully erupted teeth were considered to be pathological. Pockets ≥5 mm on erupting teeth were considered pathological only when combined with severe periodontal inflammation in association with granulation tissue and/or pus emerging from the periodontal pocket. The radiographs were primarily used for treatment planning and evaluation and, to some extent, to verify the occurrence of proximal bone destruction.

Compliance

The adherence to the treatment protocol during the follow-up period was scored as "complier" or "noncomplier" by 2 of the authors independently, based on plaque index and review of charts. Any discrepancies in scoring were discussed before reaching consensus. An acceptable compliance was scored when the patient exhibited mainly good oral hygiene and cooperated with any pharmaceutical treatment over the follow-up period. Noncompliance was considered when patients showed poor adherence to the treatment protocol and had recurrent no-shows for dental clinic appointments.

Statistical analysis

The data were processed with the SPSS (v. 11.5, SPSS Inc, Chicago, Ill) software and presented descriptively. For odds ratio (OR) calculations, dichotomised data ("presence" vs "nonpresence" of pathological periodontal pockets and "compliance" vs "noncompliance") were used. Values of $P<.05$ were considered statistically significant.

Results

Due to the wide age range, the subjects were subgrouped into 2 groups, according to dental age at treatment start. Group 1 consisted of 13 patients with a median age of 5 at their initial examination. They were examined and had their regular follow-ups started prior to the eruption of the first permanent tooth. Group 2 included 22 patients, with a median age of 8 at the initial examination, who were examined and had their treatment started after their first permanent tooth erupted. As a natural consequence of the criteria used, the median age was lower in subjects with earlier diagnoses (group 1). Group 1 children had no pathological periodontal pockets and no permanent teeth extracted at the initial examination (Table 2). In group 2, 16 patients had deep periodontal pockets and 13 of the 22 patients had permanent teeth extracted at the initial examination. This group of patients showed significantly poorer oral hygiene and gingival health at baseline compared to group 1 (Table 2). The onset of periodontal inflammation typically involved the first permanent molars.

The patients were treated and followed for 3 to 7 years, with a mean follow-up time of 5.3 years. The median age, number of permanent teeth lost during follow-up, and presence of pathological periodontal pockets at the final examination are presented in Table 3. In total, 107 permanent teeth were lost during the follow-up and all but 8 were lost in group 2 (OR=6.6; 95% CI=1.2 to 37; $P<.05$). Only 1 of 13 patients in group 1 (8%) developed pathological pockets compared to 9 of 21 (43%) in group 2. Thus, the odds ratio for a positive outcome from the treatment program, when initiated before the eruption of the first permanent tooth, was 9 (95% CI=1 to 82.5; $P<.05$). Oral hygiene and gingival health levels at the final examination are given in Table 4. Group 2 patients exhibited significantly less visible plaque compared to group 1 at the final follow-up ($P<.05$), and group 2 patients showed a significant improvement in their oral hygiene at the final examination in comparison to the initial examination ($P<.05$). No difference was found regarding the scores for bleeding on probing between groups 1 and 2.

Treatment protocol compliance had a strong impact on plaque presence, number of bleeding surfaces, and pathological periodontal pockets, as shown in Tables 5 and 6. Compliance was considered acceptable for 23 cases, and 21 of these showed no clinical signs of periodontal pockets ≥5 mm at the study's conclusion. This was in clear contrast to the patients with less favorable compliance who exhibited a significantly increased risk of periodontal disease (OR=31.5; 95% CI=4.5 to 221.9; $P<.001$). Noncompliers had an average of 11.3 permanent teeth

Table 3. Median Age, Follow-up (FU) Time, and Selected Outcome Measures at Final Examination of Young Papillon-Lefèvre Syndrome Patients

Group	Age at the final examination (median range)	FU time (ys) (mean range)	No. of teeth present at final examination (mean range)	Teeth lost during FU		Periodontal pockets (≥5 mm) at final examination	
				Yes/No*	Mean±SD	Yes/No*	Mean±SD
1 (N=13)	9 (7-18)	5.1 (3-11)	11.8 (5-25)	2/11	0.6±1.7 (0-6)	1/12	0.3±1.1 (0-4)
2 (N=22)	15 (9-23)	6.9 (3-12)	15.2 (0-28)	12/10	5.0±5.7 (0-17)	9/12†	3.4±5.4 (0-17)

All patients were treated according to the preventive program (Table 1). Group 1=patients who were initially examined and had treatment started prior to the eruption of the first permanent tooth. Group 2=patients who were initially examined and had treatment started after the eruption of the first permanent tooth.
*Denotes No. of patients.
†One patient lost his last 16 teeth during FU and was edentulous at the time of the final examination. All teeth, in this study, were extracted due to severe periodontal disease.

extracted at the final follow-up examination, compared to an average of 3.5 permanent teeth among the compliant patients ($P<.05$).

Discussion

This study was undertaken to investigate whether or not a comprehensive preventive program could contribute to the preservation of permanent teeth in young PLS patients. The result was affirmative for this group of children. Single gene disorders like PLS are characterized by a variety of expressions wherein the phenotype can be modified by environmental factors.[33] Considerable heterogeneity has been described regarding oral manifestations in PLS patients.[1,2]

In the past, the effects of various oral treatment regimens have been reported, although the significance of this heterogeneity on the outcome has rarely been considered. In addition, many of these studies dealt with a very small number of patients. This cohort consisted of 35 consecutive patients and is, to the authors' knowledge, the largest group of young PLS patients to be investigated in a single institution in relation to the outcome of a treatment protocol. No control group of PLS patients could be included, as it would have been unethical to withhold treatment according to best practice. The fact that, for various reasons, a number of PLS patients had problems keeping to the program allowed the authors to subgroup the subjects into compliers and noncompliers, which enabled evaluation of the effects of the preventive program by comparing the 2 groups. Bearing this in mind, any conclusions must be drawn with caution.

All patients in this study had a history of severe periodontal inflammation affecting the primary dentition. Despite this, 11 of the 35 patients had not lost any permanent teeth or expressed any pathological periodontal pocketing in the permanent dentition at this study's completion. Nine of these 11 patients had been treated according to the protocol since the eruption of their first permanent tooth (group 1), while the other 2 had permanent teeth already erupted when the treatment was initiated. Thus, it appears that young PLS patients who were treated with this systematic treatment protocol from an early age (group 1) lost fewer permanent teeth and showed less signs of periodontal disease compared to the patients that began the same treatment later in life (group 2), when signs of periodontal disease in the permanent dentition had already emerged.

The mean age of group 1 patients was less than that for group 2. It is possible that these younger patients might yet develop periodontal disease, as is consistent with reports of late-onset periodontitis in PLS patients.[34,35] Therefore, before reaching a final conclusion, it is necessary to compare in 6 years the oral status of group 1 children with that recorded for group 2 children at the end of this study. At that time, the median age of the 2 groups will be the same. The authors' experience has been that PLS patients are less prone to develop periodontal disease after they reach the latter part of their teens.[36] Furthermore, this study showed that, among PLS patients for whom the age of onset of periodontitis in

Table 4. Median Values and Distribution of Visible Plaque Index (VPI) and Bleeding on Probing (BOP), Measured as Percentage of Present Permanent Tooth Surfaces, at Final Examination of Young Papillon-Lefèvre Syndrome Patients

Group	VPI				BOP			
	Median	Score			Median	Score		
		0	1	2		0	1	2
1 (N=13)	36%	1	9	3	10%	7	2	4
2 (N=21*)	20%	12	4	5	19%	8	4	9

All patients had been treated according to the treatment protocol (Table 1). Group 1=patients who were initially examined and had treatment started prior to the eruption of the first permanent tooth. Group 2=patients who were initially examined and had treatment started after the eruption of the first permanent tooth. VPI scores: 0=0%-24% of permanent tooth surfaces; 1=25%-49% of permanent tooth surfaces; 2=≥50% of permanent tooth surfaces. BOP scores: 0=0%-9% of permanent tooth surfaces; 1=10%-19% of permanent tooth surfaces; 2=≥20% of permanent tooth surfaces.
*One patient was excluded at the time of the final evaluation, since he was edentulous. All teeth had been extracted due to poor oral hygiene and severe periodontal disease.

Table 5. Mean Values (±SD) of Visible Plaque Index (VPI), Bleeding on Probing (BOP), and Periodontal Pockets ≥5 mm in Compliers and Noncompliers to the Preventive Program (Table 1) at Initial and Final Examination of Young Papillon-Lefèvre Syndrome Patients

Variable	Compliers (N=23)	Noncompliers (N=11*)	*P*
VPI %			
Initial exam	40±30	60±22	NS†
Final examination	21±15	58±19	*P*<.001
BOP %			
Initial exam	28±26	44±22	NS
Final examination	10±8	43±21	*P*<.001
Pockets at final examination	0.1±0.5	6.5±6.1	*P*<.001

VPI and BOP measured as percentage of present permanent tooth surfaces.
*N=11 at the final examination, since 1 patient was edentulous after extraction of all permanent teeth.
†NS=not significant.

Table 6. Cross Tabulation Vis-a-vis Presence of and Absence of Periodontal Pockets ≥5 mm at Final Follow-up in Compliers and Noncompliers in a Cohort of Young Papillon-Lefèvre Syndrome Patients

	Presence of periodontal pockets (≥5 mm)		No. of pockets		
	No	Yes	0	1-5	<5
Compliers (N=23)	21	2	21	2	0
Noncompliers (N=11*)	3	8	3	2	6

All patients had been treated in accordance with the preventive program (Table 1).
*One patient was edentulous after extraction of all permanent teeth.

their permanent dentition could be recorded (71%), all of them developed signs of periodontal disease before age 9.

It could be speculated that it was the active extraction of all severely infected primary teeth in group 1 prior to the eruption of the first permanent tooth that was the key event for the preservation of the permanent dentition. The re-evaluation of group 1 in 6 years time should provide a clearer picture of the role played by each component of the protocol.

During the follow-up period, several subjects developed early signs of periodontal inflammation in the permanent dentition. The lesions healed, provided the patients were able to obtain and maintain good oral hygiene and given supportive systemic antibiotic treatment. Earlier studies report both successful and unsuccessful systemic use of erythromycin,[37] penicillin,[38] amoxicillin and clavulanic acid,[34,39] and tetracycline.[22,40,41] Since tetracycline is not recommended for treatment in children under the age of 12, this study's treatment protocol used amoxicillin in combination with metronidazole, an antimicrobial combination with proven effectiveness against *A actinomycetemcomitans*.[42] A 7-day long course of treatment with systemic amoxicillin and metronidazole has been shown to eradicate *A actinomycetemcomitans* for up to 2 years following treatment in patients with chronic periodontitis and in one PLS patient.[29,43]

Due to geographical factors, many of this study's patients had to travel far to be examined and a time span of 4 to 6 weeks between patient visits was often necessary. Not being able to assess the presence or suppression of *A actinomycetemcomitans* with microbial testing, this study's protocol suggested use of antibiotics for 4 weeks.

The use of topical antimicrobial agents like daily chlorhexidine rinses was less successful, since few complied with recommended use. Most patients stated bad taste as the reason.

Pathological periodontal pockets were diagnosed as pockets with depths equal to or deeper than 5 mm. Since it was difficult to explore the full depth of periodontal pockets in young patients, this criteria was chosen—leading to the risk of underestimating the real depth. In a number of patients, the periodontal inflammation had led to a permanent loss of alveolar bone and, even if the inflammation subsided and the periodontal pocket regained its normal depth, the loss of attachment persisted. To avoid depicting this as a failure, the term pathological periodontal pockets was used in the present study as a diagnostic characteristic of periodontal disease in lieu of attachment loss.

Lack of adherence and compliance with the treatment protocol was a strong determinant for the presence of periodontal disease. Twenty-one of the 23 patients with acceptable compliance showed no clinical signs of ongoing periodontal disease (Table 6). The median age of this subgroup was 17 years (range=10-23), and their periodontal status was considered stable. In the past, 12 of these patients had lost several permanent teeth due to periodontal disease and, thus, the number of surfaces at risk was reduced. This was probably also the explanation for the fact that group 2 patients had less visible plaque at the final follow-up (Table 4). Five of the group 2 patients had been evaluated for or started orthodontic treatment, and another 2 others had fixed prosthetic replacements, including 1 subject with osseointegrated implants. The high number of noncomplying patients was disappointing, but it must be realized that it was perceived as quite demanding to fully cope with the program. The noncompliers suffered in most

cases from lack of support within the family and/or a low self-efficacy, and even repeated extractions did not seem to alter their motivation. It should, however, be emphasized that the clinical signs of the disease in some cases did not respond to the treatment, which tended to compromise the patients willingness to adhere to the recommendations.

The prevalence of periodontal diseases is low in healthy children. A comparison of the incidence of periodontal changes in this cohort of PLS patients and healthy children would not be useful within this study's timeframe. Future research investigating the long-term outcome on periodontal health in this treated PLS group, in comparison with an untreated group of medically healthy children, would, however, be valuable.

Conclusions

Based on this study's results, the following conclusions can be made:

1. Young Papillon-Lefèvre patients, who were treated from an early age according to a preventive treatment program, lost few permanent teeth and had few signs of periodontal disease in the permanent dentition.
2. Compliance with the treatment protocol was a significant determinant for a successful program outcome.

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