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Intraoral condition in children with juvenile idiopathic arthritis compared to controls

EVA LEKSELL[1], MALIN ERNBERG[2], BO MAGNUSSON[3] & BRITT HEDENBERG-MAGNUSSON[4]

[1]Department of Paedodontics, Blekinge Hospital, Karlskrona, Sweden, [2]Department of Clinical Oral Physiology Karolinska Institutet Stockholm, Sweden, [3]Paediatric Rheumatology Unit, Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden, and [4]Department of Oral Physiology, Eastman Dental Institute, Stockholm, Sweden

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Aims. The aims of this study were to compare the periodontal conditions in children and adolescents with juvenile idiopathic arthritis (JIA) in comparison to age-matched healthy individuals, and to describe intraoral health in relation to medical assessments.
Design. Forty-one JIA patients, 10–19 years old, were compared to 41 controls. Plaque, calculus, probing depth, bleeding on probing, clinical attachment loss, as well as mucosal lesions were registered. Marginal bone level was recorded on radiographs. A questionnaire was included. Data were analysed with chi-squared test, Fisher's exact test, and Mann–Whitney *U*-test ($P < 0.05$).
Results. The JIA patients reported pain from jaws ($P = 0.001$), hands ($P = 0.001$), and oral ulcers ($P = 0.015$) more often than controls. They avoided certain types of food because of oral ulcers ($P = 0.037$). The frequencies of sites with plaque (32% vs. 19%, $P = 0.013$), calculus (11% vs. 5%, 5 = 0.034), bleeding on probing (26% vs. 14%, $P < 0.01$), and probing depth ≥ 2 mm (32% vs. 2%, $P < 0.001$) were higher among JIA patients. No sites with attachment loss or reduced marginal bone level were observed.
Conclusions. These obtained results are probably because of joint pain, making it difficult to perform oral hygiene as well as the use of medication and general disease activity.

Introduction

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of systemic inflammatory diseases affecting one or more joints[1]. It is the most common systemic autoimmune disease in children and adolescents with an incidence of 14/100 000 in the Swedish population. The disease is taking a fluctuating course, and the outcome is generally regarded as good; one-third to half of the children have ongoing disease activity lasting into their adult years[1].

The definition of JIA in this study is based on the diagnostic criteria by the International League of Associations for Rheumatology (ILAR). The term JIA refers to persistent arthritis, episodes lasting for at least 6 weeks, and with the onset occurring before the 16th year. It is characterized by pain, swelling, and stiffness, and can lead to growth disturbances and in some cases to destruction of the joints. Other, more general impairments are pain, fatigue, and muscle weakness. Different subtypes of JIA have been defined, depending on onset and number of involved joints. The systemic type is characterized by daily fever and generalized inflammation including pericarditis, pleuritis, peritonitis, and sometimes arthritis. The oligoarthicular type is the most common subtype and characterized by four or less involved joints. It can be divided in two forms depending on the outcome, persistent and extended. The polyarthicular type is defined as arthritis in five or more joints and divided into two subcategories: the rheumatoid factor (RF) – negative and the RF positive. The RF-positive type resembles the adult form of rheumatoid arthritis (RA) and occurs in approximately 5% of JIA patients[1]. The enthesitis-related type is characterized by arthritis and/or enthesitis (inflammation of the attachment of the tendons). The psoriatic type is defined as arthritis in combination with psoriasis. Finally, there are other more uncommon forms.

Correspondence to:
Eva Leksell, Blekinge Hospital, S-371 85 Karlskrona, Sweden. E-mail: eva.leksell@ltblekinge.se

In JIA, there is a destructive inflammatory process in the border between bone and connective tissue of the joint similar to the inflammatory process of the supporting tissue around the tooth in periodontitis. For both diseases, a dysregulation of the immune–inflammatory response has been suggested[1–5]. Gingivitis is an inflammatory reaction of the tissues to microorganisms in the plaque and their products[6]. The clinical criteria for gingivitis are oedema, hypertrophy, change in texture, and change in colour towards redness and easy provoked bleeding. Previous studies on gingivitis in children with JIA have shown divergent results. Some have reported that children with JIA more often have gingivitis than controls[7–9]. Other studies have found a higher presence of attachment loss, but no differences in frequency of gingivitis[2–5]. More gingivitis or attachment loss even in the absence of increased amount of plaque is also reported[2,4,7]. Some studies[4,10] on adults with RA have shown a significant increased risk for periodontal destruction, whereas another has not[11]. Some studies have reported a higher frequency of plaque in patients with JIA compared to healthy subjects[5,8,9], whereas other authors report no differences[2–4,7].

Saliva plays a crucial role in maintaining the health of the mouth. Patients with JIA showed reduced salivary flow and altered saliva biochemistry[12]. A higher presence of caries[8,9] and more untreated caries are also reported[7,9].

The treatment of JIA is mainly symptomatic, with a multidisciplinary approach, and directed at minimizing inflammation and disability. A more effective use of disease modifying antirheumatic drugs (DMARDs) together with new types of medication during the past decades has improved disease control and even induced remission. New drugs that bind and inactivate the pro-inflammatory cytokine tumour necrosis factor alpha (TNFα) have shown excellent results in children with polyarthritis. The IL-1-inhibitor anacinra has in the same way been shown to arrest disease activity in children with the systemic onset JIA. Non-steroidal anti-inflammatory drugs (NSAIDs), however, are still the first drug of choice[1] with the DMARD, low-dose methotrexate (LDMTX) as the most common second-line agent. Systemic corticosteroids are still employed in very active disease if possible in low-dose regimes, because of side effects as growth retardation and osteoporosis. As a supplement to general administered medication, intra-articular corticosteroid injection is commonly used for children with JIA[1].

Treatment with systemic corticosteroids has been shown to cause degenerative changes in the periodontal membrane, osteoporoses of the alveolar bone, and premature tooth development. Signs of gingivitis, however, were decreased, and the gingiva was healing faster, but gingivitis was eliminated only if plaque was removed as well[13]. NSAIDs are shown to slow periodontal disease progression[14]. However, there are case reports where NSAIDs have caused formation of intraoral vesicles and fibrin-covered lesions. Side effects on the oral mucosa are also reported in connection with DMARD. Among adults with RA treated with LDMTX, up to 64% had mucosal ulcerations affecting diet leading to withdrawal from treatment in 6% of the patients[15]. Out of 17 adults with RA taking anti-TNFα, two developed candidosis, even if saliva flow improved[16]. The frequency of intraoral adverse effects because of these medications among children with JIA is not known.

Our clinical impression is that the oral mucosae of JIA patients sometimes show an intense red colour of different shades, and some patients, especially if asked, complain of oral ulcers. After considering the new medical treatment approach of JIA together with reports of attachment loss on adults with RA, we decided to examine the oral status of children with JIA. Based on our clinical findings and literature studies, we hypothesized that the oral health in children and adolescents with JIA is poorer than that of healthy controls.

The aims of this study were to compare the periodontal conditions in children and adolescents with JIA to age-matched healthy individuals, and to describe intraoral health in relation to medical assessments in the JIA patients.

Materials and methods

Study design

A cross-sectional study design surveying children with JIA and healthy controls matched for age

was used. A written, informed consent was obtained from all parents and patients before the study. No compensation was given for participation. The study was approved by the ethics committees at the Karolinska Institutet Dnr 03-796.

Subjects

Forty-seven patients (10–19 years old) with possible JIA that were referred from the Paediatric Rheumatology Unit at Astrid Lindgren Children's Hospital in Stockholm to the Eastman Institute in Stockholm as a part of their care plan participated in the study. The patients were sent a letter for an appointment, a health declaration, a questionnaire, and information about the study. All agreed to participate. Inclusion criteria were a diagnosis of JIA according to ILAR[1] together with a minimum age of 10 years at examination. Exclusion criteria were any concurrent medical condition. Six patients were afterwards excluded, one because of concurrent other condition (myelocele), and five because of uncertainty about the diagnosis (three with mixed connective tissue disease, one with reactive arthritis, and one with pain of unclear origin). The remaining 41 patients (29 girls and 12 boys) with a mean [standard deviation (SD)] age of 13.6 (2.3) years were included in the study. All of them were of Caucasian origin. The medical and oral evaluations were performed within a time-frame of on average 2 months during 2004.

Five of the patients had systemic JIA, 16 polyarthicular (two RF positive), eight oligoarthicular, three enthesitis-related HLA B27 positive, seven psoriasis arthritis, and two other JIA diagnoses. The patients were thought to reflect a population-based mix of different JIA subgroups.

Controls

Forty-one healthy children (25 girls and 16 boys) with a mean (SD) age of 13.1 (1.1) years were selected as control group. All controls were of Caucasian origin except one that was of African origin. They were selected from children attending the Public Dental Health Service in Stockholm for their regular dental check-up. Our intention was to match each JIA patient by gender and age with the controls, but we did not totally succeed with this. The controls received the same questionnaires as the JIA patients, but with modified information about the study. Children with concomitant diseases were excluded.

Questionnaire

All participants answered a questionnaire concerning frequency of subjective symptoms, medication and route of administration, food and intake of sweets, as well as toothbrushing habits.

Disease assessment and laboratory evaluation

Disease status at the time of the study included an evaluation of the disease-related parameters assessed by the patient and the rheumatologist[1]. For the patients' self-report, two visual analogue scales (VAS, 100 mm) were used, one for pain during the week preceding the visit and one for general coping in life with the disease. Disability was evaluated using a validated Swedish version for children of the Stanford HAQ disability index, Child Health Assessment Questionnaire (CHAQ, 0–3). This index measures the child's performance of 30 daily activities; the ability of the child to perform each task is scored from 0 to 3. Based on disease history, patients' self-reports, physical examination, and current laboratory results, the physician assessed the overall disease activity using outlined criteria on a VAS. Debut age, duration of the disease, as well as current medication were extracted from the medical file by the patient's physician. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), presence of antinuclear factor, and RF were registered.

Determination of salivary flow rate

Whole saliva was collected from all participants to determine the unstimulated and stimulated flow rates. Unstimulated samples were collected by the drooling method of letting saliva drool into the specimen pot for 5 min from a slightly opened mouth. Stimulated saliva was obtained

by chewing unflavoured wax (paraffin) for 5 min. At the end of each collection period, the sample volumes were measured. The patients were asked to refrain from eating, drinking, or cleaning their teeth for 2 h prior to collection. The normal average values for unstimulated and stimulated saliva were considered to be 0.3 mL/min and 1 mL/min, respectively.

Intraoral clinical assessments

The oral examination was made by a specialist in paediatric dentistry and a dental hygienist. The dental hygienist was not informed about the patient's medical status. The gingival diagnoses were recorded for the first ten patients by the dental hygienist and the specialist to assure intra-examiner agreement.

Because of the difficulties to differentiate between the different shades of red of the oral mucosa and to find oral ulcerations of small size, the oral mucosa was examined and ulcerations was defined as discontinuation of the epithelia of at least 3 mm on the lips and the oral mucosa.

Presence of plaque as well as sub- and supragingival calculus was recorded with a standard periodontal probe (UNC 15, Chicago, IL, USA). Marginal bleeding after slight touching with the probe, as well as gingival sulcus bleeding on probing (BOP), was assessed as presence or absence. Probing depth (PD) of the sulcus of more than 2 mm was recorded with the probe placed in the longitudinal axis of the tooth to the nearest millimetre. Clinical attachment level exceeding 1 mm was recorded and assessed as the distance between the cemento-enamel junction and the most apical portion the probe can reach. BOP, PD, clinical attachment loss, and marginal bleeding were measured at four sites around the first permanent molars and central incisors: the mesio-facial, disto-facial, mesio-lingual, and disto-lingual surfaces (0–32 sites)[17].

Plaque and calculus were measured on three sites: mesio-facial, disto-facial, and lingual surfaces of the first permanent molars and central incisors (0–24 sites)[17].

Only central incisors and first molars were examined because these are the only permanent teeth that are fully erupted at 10 years of age.

Radiographic assessments

Two bite-wing radiographs (Kodak Ultraspeed, Rochester, NY, USA) were taken for each patient. The distance between the cemento-enamel junctions and the alveolar crest was measured with a magnifier to the nearest 0.1 mm. Sites that were not readable as a consequence of an erupting permanent tooth next to the first molar or overlapping were excluded. The radiographs were examined again, 6 months later by the same investigator to assess agreement by the two recordings.

Caries assessment

Presence of occlusal and approximal caries visible on the bite-wing radiographs, on the first permanent molars was recorded. Caries was assessed using the decayed, missed, filled surfaces, including enamel approximal lesions (DMFS). Teeth extracted because of caries were counted as three surfaces.

Statistics

The SigmaStat software version 3.1 was used for statistical analyses. The outcome data from the medical assessment are expressed as mean and SD, as well as range based on the individual as the unit for analysis. The outcome data from the questionnaire are expressed in percent frequencies, whereas data from the intraoral examination are expressed in percent frequencies and absolute figures. Differences in proportions of individuals with regard to various characteristics were statistically tested by the use of chi-squared test (when the expected frequencies of one or more cells were greater than 5) or Fisher's exact test (when the expected frequencies of one or more cells were less than 5).

Differences between groups regarding the number of sites with plaque, BOP or PD > 2 mm were tested with the Mann–Whitney *U*-test.

Results

Disease characteristics of the JIA patients are summarized in Table 1, and medication is shown in Table 2.

Table 1. Disease characteristics of the patients in the juvenile idiopathic arthritis group.

	n	Mean (SD)	Range
Age at disease onset (years)	41	5.11 (4.2)	1–15
Disease duration (years)	41	7.4 (4)	0–15
ESR (mm/h)	33	9.5 (7.3)	2–29
CRP	33	6.4 (4.4)	4–24
CHAQ score (0–3)	37	0.5 (0.7)	0–1.9
Number of active joints	41	1.3 (3.6)	0–20
Number of joints with limited movement	39	1.7 (4)	0–77
Pain VAS by the patient	39	18 (26)	0–77
VAS for overall disease activity by the physician	37	16.5 (22)	0–72
VAS for overall disease activity by the patient	38	23 (26)	0–96

CHAQ, Child Health Assessment Questionnaire; CRP, C-reactive protein, mg/L, normal value < 10; ESR, erythrocyte sedimentation range, mm/h, normal value 2–20; VAS, 100 mm visual analogue scale.

Table 2. Anti-rheumatic drug treatment in the juvenile idiopathic arthritis group.

Type of medication	*n*
Anti-TNFα	17
LDMTX	18
NSAID	11
Systemic steroids	3
DMARD (not LDMTX)	4
Other drugs	2
No medication	8

DMARD, disease-modifying antirheumatic drug; LDMTX, low-dose methotrexate; NSAID, non-steroidal anti-inflammatory drug; TNF, tumour necrosis factor.

Questionnaire

Sixty-six per cent of the JIA children reported oral ulcerations sometimes or always compared to 37% among the controls ($P = 0.015$). Thirty-four per cent of the patients, all of them on drug therapy, and 3% of the controls reported that they avoided certain types of food always or occasionally because of the ulcerations ($P = 0.037$). Three of the JIA patients reported chewing or sucking their tablets, and seven were taking their tablets with a sweetened drink. Eight per cent of the JIA patients and 20% of the controls were consuming sweets or sweetened drinks more frequently when they did not feel well (n.s.).

Sixty-eight per cent of the JIA patients reported pain from opening of the mouth sometimes or always; none of the controls ($P < 0.001$). Seventy-six per cent of the JIA patients report pain, discomfort, or a queasy feeling at toothbrushing compared to 12% of the controls ($P = 0.001$). Forty-six per cent of the JIA patients reported pain or weakness in the hand when toothbrushing compared to 3% of the controls ($P < 0.001$). All patients in both groups reported brushing their teeth at least once a day, but 41% of the JIA patients and 49% of the controls declared that they occasionally forget toothbrushing (n.s.). Forty-six per cent of the children in both groups reported bleeding gums when toothbrushing. Thirty-five per cent of the JIA patients did not brush their teeth when they did not feel well, compared to 5% of the controls ($P = 0.002$). Two individuals in each group had sometimes help from their parents with toothbrushing. All children were using toothpaste, and 25% were taking fluoride supplements in both groups. One patient in each group reported smoking.

Oral mucosa

Five of the JIA children (12%) had oral ulcerations compared to one in the control group. Two of these patients had fissures on their lips, and three aphthous-like ulcerations on the oral mucosa. Two of them were taking LDMTX in combination with anti TNFα, one took LDMTX in combination with NSAID, one took NSAID, and one had not taken any medication for a year. The subject in the control group with oral ulceration had fissures in the lip angels, probably because of a lingering upper respiratory virus infection.

Table 3. Frequency of sites with bleeding on probing (BOP), increased probing depth (PD ≥ 2 mm), plaque, and calculus in 41 patients with juvenile idiopathic arthritis (JIA) and in a control group of 41 healthy children.

	JIA patients		Controls	
Variable	***n***	**%**	***n***	**%**
BOP 0–25%	22	55	36	88**
BOP 25–100%	18	45	5	12**
PD ≥ 2 mm 0–25%	28	68	40	98***
PD ≥ 2 mm 25–100%	13	32	1	2***
PD ≥ 4 mm	1	2	2	5
Plaque 0–50%	29	70	38	93*
Plaque 50%–100%	12	30	3	7*
Calculus 0–12.5%	22	54	34	83*
Calculus 12.5–100%	19	46	7	17*

Chi-squared test, levels of significance: ***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.
n = number of subjects, which may differ from the total ($n = 41$) because of missing data.

Salivary flow and oral hygiene

The stimulated and unstimulated salivary flow showed no lower level than normal in any case. The JIA patients had on average plaque on 32% (0–90%) of the sites compared to 19% (0–80%) of the sites in the controls ($P = 0.013$). Twelve of the JIA patients (30%) had plaque on more than 50% of the sites compared to 7% of the controls ($P = 0.019$; Table 3).

The JIA patients had on average calculus on 11% (0–25%) of the sites compared to 5% (0–33%) of the controls ($P = 0.034$). Calculus was found on the lower incisors in 19 JIA patients and seven controls except for two individuals in each group that also had calculus on upper molars (Table 3).

Gingival and periodontal conditions

The JIA children had significantly higher BOP than controls; on average 26% (0–63%) of the sites in the JIA group compared to 14% (0–69%) in the controls ($P < 0.010$). Forty-five per cent of the JIA patients and 12% of the controls had BOP on > 25% of the sites ($P < 0.002$; Table 3). Figures 1 and 2 show the gingival status of two JIA patients.

Thirty-two per cent of the JIA patients had a PD of at least 2 mm on > 25% of the sites compared to 2% of the controls ($P < 0.001$; Table 3). None of the patients or the controls had bleeding on touching of the gingival margin or clinical attachment loss ≥ 2 mm.

The alveolar bone crest registered on analogue bite-wing was readable in 232 sites on the JIA patients and 273 on the controls. The distance between the dentino-enamel junction and the alveolar bone crest was ≤ 2 mm at all sites in both patients and controls, and did not differ between groups.

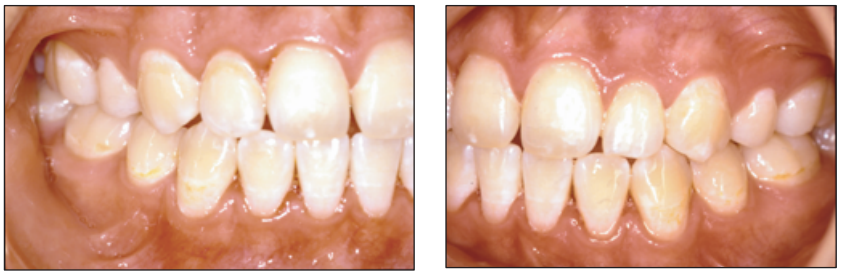

Fig. 1. Fourteen-year-old female with juvenile idiopathic arthritis since 4 years. No pharmacological therapy now. There is a high number of bleeding points and a low gingival sulcus depth.

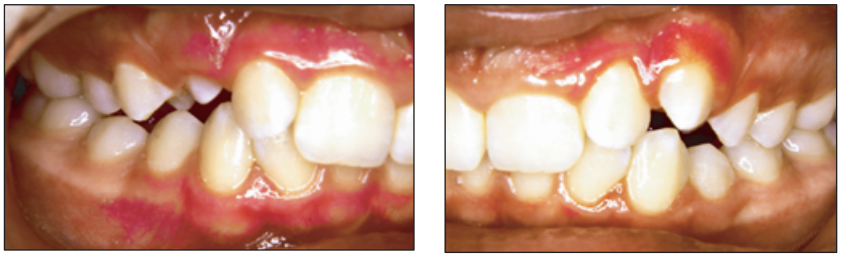

Fig. 2. Thirteen-year-old female with juvenile idiopathic arthritis since 7 years with pharmacological therapy (low-dose methotrexate). There are no bleeding points. A slight gingival hypertrophy leading to increased sulcus depth.

Caries status

The DMFS, including approximal enamel lesions assessed on radiographs, was not significantly different between the JIA patients (63 lesions) and controls (50 lesions). The number of children with two or more lesions did not differ between groups.

Three first molars in two patients in the JIA group were extracted as a consequence of caries. These teeth were extracted the first year after the onset of JIA. One JIA patient had a molar with root infection caused by caries. None of the controls had any missing molars, but one individual had a molar with root canal treatment.

Periodontal status, oral and general health, and medication in JIA

Relations between oral and general health, as well as medication and periodontal status in the JIA patients, are presented in Table 4. High frequency of plaque was associated with high frequency of BOP. High pain intensity assessed by the patient was associated with high disease activity and high CHAQ, and high CHAQ was associated with high disease activity. Use of medication was associated with high pain intensity assessed by the patient and high CHAQ.

The 17 patients taking anti-TNFα had a higher frequency of sites with increased PD and a lower frequency of sites with BOP compared to the 24 patients not taking anti-TNFα (53% vs. 33%, and 41% vs. 50%, respectively). The 18 patients taking LDMTX had a slightly higher frequency of sites with increased PD and a slightly lower frequency of BOP compared to the 23 patients not taking LDMTX (44% vs. 39%, and 33% vs. 57%, respectively). The 12 patients taking NSAID had a slightly higher frequency of sites with increased PD and a slightly lower frequency of BOP compared to the 29 patients not taking NSAID (50% vs. 38%, and 42% vs. 48%, respectively). None of the differences were significant.

The groups of patients with different subdiagnoses, increased ESR, and the CRP were considered too small for any comparison to be made.

Discussion

The main findings of this study were that patients with JIA had a higher frequency of

Table 4. Relation between periodontal staus, oral and general health, as well as medication in the juvenile idiopathic arthritis patients (*n* = 41). The patients are divided into subgroups according to their periodontal and rheumatic condition (median split).

	n	Plaque ≥ 25%	BOP ≥ 25%	PD ≥ 10%	VAS ≥ 8	Disease act ≥ 0	CHAQ ≥ 0	Duration ≥ 100 month	Medication
Plaque ≥ 25%	21		71*	33	38	48	48	57	71
Plaque < 25%	20		20	50	55	60	50	45	90
BOP ≥ 25%	19	79*		42	37	42	42	47	68
BOP < 25%	21	24		43	52	62	52	57	90
PD ≥ 10%	17	41	47		41	53	41	65	88
PD < 10%	24	58	46		50	54	54	42	75
VAS ≥ 8	19	42	37	37		89*	79*	42	100
VAS < 8	19	63	58	47		16	26	58	63
Disease activity > 0	20	50	40	35	75*		68	45	100
Disease activity = 0	17	59	53	47	18		79	59	59
CHAQ > 0	22	45	36	41	77*	75*		50	91
CHAQ 0	19	58	58	42	11	29		53	68
Duration ≥ 100 months	21	57	43	52	38	52	43		76
Duration < 100 months	20	45	50	30	55	55	55		85
Medication	33	45	39	45	58*	61	61*	48	
No medication	8	75	75	25	0	25	0	63	

BOP, bleeding on probing; CHAQ, Child Health Assessment Questionnaire; disease act, disease activity assessed by the physician; duration, duration of disease ≥ 100 months; PD, pocket depth ≥ 2 mm; %, percent of sites; VAS, pain intensity assessed by the patient; *, significant difference between subgroups ($P < 0.05$).
n = number of patients, which may differ from the total (*n* = 41) because of missing data.

sites with plaque, BOP, and PD ≥ 2 mm as compared to age-matched healthy controls.

Although the patients with JIA were more diligently everyday brushers according to the questionnaire than the healthy controls, they had a higher frequency of plaque. The localization and amount of plaque were equally distributed on the teeth, indicating that physical disability of the hand is not affecting the toothbrushing movements. The main factor to the higher amount of plaque and calculus in the JIA group is therefore probably a weaker hand force and/or pain from jaw opening[18]. This is supported by the report that the JIA patients were not brushing their teeth as often as the controls when they felt indisposed. These findings are in agreement with earlier studies that the self-efficacy regarding oral health is lower in patients with joint disease[5,8,9].

JIA patients had more sites with plaque, calculus, and BOP in comparison to the control group. Therefore, more professional help, instructions, and support with tooth cleaning are required.

BOP was significantly increased among the JIA patients. A significant relationship has previously been reported between bacteraemia and gingivitis, as well as gingival bleeding[19]. The cause of JIA is unknown, but it has been assumed that the autoimmune mechanisms could be triggered by peptides from viruses and bacterial antigens[1,20]. Therefore, it cannot be neglected that oral bacteria in some cases can be involved in this disease mechanism. There are nearly 800 different bacteria identified in the oral cavity. In this study, gingival bleeding was increased compared to healthy and correlated to a higher frequency of bacterial plaque. Also, healthy subjects inhale oral bacteria. Oral bacteria is one of the mechanisms behind respiratory infections especially if the saliva secretion is low[21]. Although in a previous report[12] quantity and quality of saliva were found different in comparison to healthy controls, our study did not reveal such a difference. The intention in this study was to find out if the saliva volume reached the lowest normal level. It was difficult to get a more exact measurement of the saliva quantity using the drooling method, on individuals at this age, on a solitary occasion. The quality of the saliva was not measured in this study.

BOP can be regarded as an early indicator of inflammation, and a higher frequency of BOP, plaque, calculus, and number of sites with increased PD in the JIA patients compared to controls could indicate an increased risk for periodontal disease in the latter group. However, there were no signs of periodontal disease, defined as attachment loss of ≥ 2 mm or increased distance between the dentinoenamel junction and the alveolar bone crest ≥ 2 mm in any group. Furthermore, BOP is reported to be only weekly associated with the development of periodontitis. In a study, the sensitivity of BOP on progression of periodontal attachment loss was only 29% compared to 6% when there was no BOP, whereas the specificity for no progression of attachment loss in the absence of plaque was 98%[22].

There were also increased values for pocket depth which can be a lower resistance of the gingival tissue against the probing force and/or the formation of pseudo pockets because of inflamed swelling of the gingiva. The high number of sites with PD ≥ 2 mm was more frequent in patients using medication or with long disease duration, but not in patients with increased BOP or plaque, although these findings should be interpreted with caution because of a limited number of patients without medication. Anyhow, this indicates that the general inflammatory response and medication affect the gingival structures, possibly in combination with local factors. Hence, this increased PD in the JIA patients might be a mild form of the gingival overgrowth that occurs as a result of certain drugs (as cyclosporin A, phenytoin, or nifedipine). Cytokine and growth factor balances are altered in these gingival tissues, but differ depending on the medication[23]. Recent studies emphasize a key inflammatory role of the endothelial cells in the disease process by an over-expression of inflammatory mediators or by proliferation of new blood vessels. Microvascular alterations are found in the gingival tissue, as well as the labial mucosa of adults with RA[24]. This might be reason to the slightly different gingival structure also in JIA patients. Other factors like individual disposition are certainly also involved.

The tendency to a lower risk of BOP in the patients on medication could be because of the anti-inflammatory effect of the medication[13–15,25]. Disease activity, duration, and combination of drugs in this study are dissimilar, but tendencies of differences between the drugs can be noted. The patients taking anti-TNFα had a slightly higher frequency of sites with increased PD and a slightly lower frequency of sites with BOP compared to the patients who were not taking anti-TNFα. This can be in agreement with a study of ligature-induced periodontitis on healthy rats given anti-TNFα, in which a clear reduction of gingival inflammation and tissue injury was reported[25].

Although the JIA patients in this study had a long disease duration and treatment for an average 7 years, we did not find any sign of attachment loss, in spite of high frequency of plaque, PD, and BOP. This is in agreement with two previous studies in JIA patients, in which no progress of attachment loss was found after treatment[3,4].

The JIA patients commonly reported jaw pain and weakness especially during chewing, jaw opening, and oral care, both professional and home care. The difficulties increased in periods when they did not feel well. They also commonly reported sore mucosal membranes making them avoid certain types of food. The latter may be related to the pharmacological therapy.

Most of the JIA patients were on medication on a regular basis. A few of them took the tablets together with sweet drinks, other sucked or chewed the tablets. These are habits that directly can course harm to the oral structures[30]. Accordingly, the JIA patients need to develop strategies in their daily life to cope with symptoms as pain, fatigue, and physical disability also from their oral area[28].

There was a big difference between the frequencies of self-reported oral ulcerations[15,16] and the presence of oral ulcerations at the clinical examination. One explanation is that this is by chance, because oral ulcerations usually heal after a few days. Another explanation can be that it is difficult to objectively investigate the oral mucosa according to different shades of red. The normal colour of healthy children can differ, and a simple upper virus infection can affect the colour of the oral mucosa to a great extent. In some patients, the oral mucosa had a generalized reddish colour, sometimes with minor areas of discontinuation of the epithelia that was associated with self-reported pain. Methotrexate mostly affects cells undergoing rapid turnover like the oral mucosa, hence mucositis is among the more common reported adverse reactions also of LDMTX. This leads to episodes of pain and discomfort that the examiner might record as a generalized reddish colour of the mucosa. The reddish colour might also be a consequence of an increased count of a microorganism as, for example, of *Candida albicans*[16], or it can be a consequence of factors that have with the general disease to do, like microvascular alterations[24].

The lesions reported in this study were apthtous lesions or lip fissures often of lingering character that the patients told they were more or less accustomed to.

The JIA patients in this study showed only a slightly and non-significant higher prevalence of caries compared to the healthy subjects in spite of a more frequent intake of sweet drinks, higher incidence of plaque, and difficulties with toothbrushing. One explanation might be that the JIA patients acquire a more regular lifestyle to cope with their disease and to obtain regularity in medication and medical check-ups[28]. This could lead to diminution of caries activity by more regular exposure of fluoride by toothbrushing with toothpaste[29]. Besides, the JIA patients never had been prescribed suger-based NSAID syrups[25], and all patients had good access to dental care and supervision through the public health care system.

Oral inflammations/infections contribute to the overall inflammatory response of the body[26]. This is one major reason to keep the oral tissues healthy. In addition, the anti-inflammatory and analgetic medication taken by JIA patients may camouflage a proceeding infection[27].

This study represents a limited number of patients, and many questions ought to be further investigated. New therapies give many JIA patients an impression of being healthy, but as long as the medical treatment is symptomatic, this study suggests that the

dental service should regard all patients with JIA as having potential risk for oral disease.

In conclusion, patients with JIA reported problems with eating, toothbrushing, and joint pain more often than controls. They also had more plaque, BOP, and an increased PD. This is probably because of joint pain, making it difficult to perform oral hygiene as well as to the use of medication and general disease activity.

What this paper adds

Children with JIA

- report more mucosal ulcers and discomfort.
- have more plaque, gingival bleeding, and slight gingival hypertrophy.
- show a need for further investigation of their gingival inflammatory response.

Why this paper is important to paediatric dentists

- It emphasizes that JIA children need support and care from dental professionals with special odontological knowledge about one of the most common systemic diseases in childhood.
- With a new medical treatment approach, it is necessary to reconsider also the odontological treatment approach.
- The results may increase our understanding of the impact of JIA, the immune defence system, and pharmacological treatments on the oral structures.

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References

1 Cassidy JT, Petty RE. *Textbook of Pediatric Rheumatology*, 5th edn. In: Cassidy JT, Petty RE, Laxer RM, Lindsley CB (ed.). *Juvenile Rheumatoid Arthritis*. New York, NY: Churchill Livingstone, 2005: 206–338.

2 Miranda LA, Fischer RG, Sztajnbok FR, Figueredo CM, Gustafsson A. Periodontal conditions in patients with juvenile idiopathic arthritis. *J Clin Periodontol* 2003; **30**: 969–974.

3 Miranda LA, Braga F, Fischer RG, Sztajnbok FR, Figueredo CM, Gustafsson A. Changes in periodontal and rheumatological conditions after 2 years in patients with juvenile idiopathic arthritis. *J Periodontol* 2006; **77**: 1695–1700.

4 Havemose-Poulsen A, Westergaard J, Stoltze K, *et al*. Periodontal and hematological characteristics associated with aggressive periodontitis, juvenile idiopathic arthritis, and rheumatoid arthritis. *J Periodontol* 2006; **77**: 280–288.

5 Reichert S, Machulla HKG, Fuchs C, John V, Schaller H-G, Stein J. Is there a relationship between juvenile idiopathic arthritis and periodontitis? *J Clin Periodontol* 2006; **33**: 317–323.

6 Matsson L. Development of gingivitis in pre-school children and young adults. A comparative experimental study. *J Clin Periodontol* 1978; **5**: 24–34.

7 Ahmed N, Bloch-Zupan A, Murray KJ, Calvert M, Roberts GJ, Lucas VS. Oral health of children with juvenile idiopathic arthritis. *J Rheumatol* 2004; **31**: 1639–1643.

8 Savioli C, Silva CA, Lin HC, Campos LM, Prado EF, Siqueira JT. Dental and facial characteristics of patients with juvenile idiopathic arthritis. *Rev Hosp Clin Fac Med Sao Paulo* 2004; **59**: 93–98.

9 Welbury RR, Thomason JM, Fitzgerald JL, Steen IN, Marshall NJ, Foster HE. Increased prevalence of dental caries and poor oral hygiene in juvenile idiopathic arthritis. *Rheumatology (Oxford)* 2003; **42**: 1445–1451.

10 Mercado FB, Marshall RI, Klestov AC, Bartold PM. Relationship between rheumatoid arthritis and periodontitis. *J Periodontol* 2001; **72**: 779–787.

11 Sjöström L, Laurell L, Hugoson A, Håkansson JP. Periodontal conditions in adults with rheumatoid arthritis. *Community Dent Oral Epidemiol* 1989; **17**: 234–236.

12 Walton AG, Welbury RR, Foster HE, Wright WG, Thomason JM. Sialochemistry in juvenile idiopathic arthritis. *Oral Dis* 2002; **8**: 287–290.

13 Markitziu A, Zafiropoulos G. Flores de Jacoby L, Pisanty S. Periodontal alterations in patients with pemphigus vulgaris taking steroids. A biannual assessment. *J Clin Periodontol* 1990; **17**: 228–232.

14 Paquette DW, Williams RC. Modulation of host inflammatory mediators as a treatment strategy for periodontal diseases. *Periodontology* 2000; **24**: 239–252. (Review)

15 Kalantzis A, Marshman Z, Falconer DT, Morgan PR, Odell EW. Oral effects of low-dose methotrexate treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005; **100**: 52–62. (Review)

16 Moen K, Kvalvik AG, Hellem S, Jonsson R, Brun JG. The long-term effect of anti TNF-alpha treatment on temporomandibular joints, oral mucosa, and salivary flow in patients with active rheumatoid arthritis: a pilot study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005; **100**: 433–440.
17 Modéer T, Barr M, Dahllöf G. Periodontal disease in children with Down's syndrome. *Scand J Dent Res* 1990; **98**: 228–234.
18 Olson L, Eckerdal O, Hallonsten AL, Helkimo M, Koch G, Gare BA. Craniomandibular function in juvenile chronic arthritis. A clinical and radiographic study. *Swed Dent J* 1991; **15**: 71–83.
19 Roberts GJ, Watts R, Longhurst P, Gardner P. Bacteremia of dental origin and antimicrobial sensitivity following oral surgical procedures in children. *Pediatr Dent* 1998; **20**: 28–36.
20 Moen K, Brun JG, Valen M. *et al*. Synovial inflammation in active rheumatoid arthritis and psoriatic arthritis facilitates trapping of a variety of oral bacterial DNAs. *Clin Exp Rheumatol* 2006; **24**: 656–663.
21 Pascual-Ramos V, Hernández-Hernández C, Soto-Rojas AE, Celis-Aguilar E, Sanchez-Guerrero J. Association between dental caries and pneumonia in patients with systemic lupus erythematosus. *J Rheumatol* 2006; **33**: 1996–2002.
22 Lang NP, Adler R, Joss A, Nyman S. Absence of bleeding on probing. An indicator of periodontal stability. *J Clin Periodontol* 1990; **17**: 714–721.
23 Trackman PC, Kantarci A. Connective tissue metabolism and gingival overgrowth. *Crit Rev Oral Biol Med* 2004; **15**: 165–175. (Review)
24 Scardina GA, Messina P. Microvascular periodontal alterations: a possible relationship between periodontitis and rheumatoid arthritis. *Clin Hemorheol Microcirc* 2007; **37**: 229–235.
25 Di Paola R, Mazzon E, Muià C, *et al*. Effects of etanercept, a tumour necrosis factor-alpha antagonist, in an experimental model of periodontitis in rats. *Br J Pharmacol* 2007; **150**: 286–297.
26 Al-Katma MK, Bissada NF, Bordeaux JM, Sue J, Askari AD. Control of periodontal infection reduces the severity of active rheumatoid arthritis. *J Clin Rheumatol* 2007; **13**: 134–137.
27 Ylijoki S, Suuronen R, Jousimies-Somer H, Meurman JH, Lindqvist C. Differences between patients with or without the need for intensive care due to severe odontogenic infections. *J Oral Maxillofac Surg* 2001; **59**: 867–872; discussion 872–873.
28 Thastum M, Herlin T, Zachariae R. Relationship of pain-coping strategies and pain-specific beliefs to pain experience in children with juvenile idiopathic arthritis. *Arthritis Rheum* 2005; **53**: 178–184.
29 Waterhouse PJ, Thomason JM, Fitzgerald JF, Foster HE, Steen IN, Welbury RR. The dental attitudes, knowledge and health practices of patients with juvenile idiopathic arthritis. *Eur J Paediatr Dent* 2005; **6**: 202–208.
30 Maguire A, Baqir W, Nunn JH. Are sugars-free medicines more erosive than sugars-containing medicines? An *in vitro* study of paediatric medicines with prolonged oral clearance used regularly and long-term by children. *Int J Paediatr Dent* 2007; **17**: 231–238.