SECTION OF OROFACIAL PAIN AND
JAW FUNCTION
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ORAL HEALTH IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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“Hon (tandläkaren) visste hur det var, att må illa på morgonen och ha svårt att kunna gapa. Hon var jättesnäll.”
Flicka, nio år.

“She (the dentist) knew how it was, that you felt sick in the morning and had difficulties to open your mouth wide. She was very kind.”
Girl, nine years old.

ABSTRACT

The overall aim of this thesis was to illuminate different aspects of oral health that can be investigated in the clinical meeting with the child diagnosed with JIA.

A cross-sectional case control study consisting of clinical examination of intraoral tissues, occlusion, facial appearance, jaw function and pain sites were designed (papers I and II). The findings were compared to controls, related to each other and to medical assessments. Patient's report of eating- and toothbrushing difficulties, the severity of pain and dysfunction and its influence on daily life was also interrelated.

Another aim was to improve our understanding and maybe gain fresh views of how children perceive their orofacial symptoms and encounter with the dental care. Therefore depth interviews were performed and analyzed in a qualitative grounded theory study (Paper III).

Furthermore, another aim was to validate clinical suspicion of arthritis by investigating its relationship to the gold standard for diagnosis of synovitis, contrast enhanced magnetic resonance imaging (MRI) (Paper IV).

Children with JIA had significantly more bleeding on gingivial probing and plaque compared to controls and need individual advice for this. Regularly check up of the gingiva concerning dental hygiene, papilla atrophy and attachment loss is to be recommended as the children might have a higher susceptibility for parodontal diseases. At examination and treatment the mucosal ulcers should be addressed as they constitute a part of the eating difficulties.

Orofacial pain and dysfunction was a substantial part of the symptoms JIA children had to cope with in daily life. They need information, coping strategies and treatments for this. To regularly perform a clinical examination of pain and jawfunction is mandatory to disclose disease activity and treatment needs. The diagnostic parameters of reduced jaw opening, reduced translation of the condyle and palpation pain of the temporomandibular joint was the most significant findings for active synovitis correlated to MRI signs. A convex profile was common but micrognathia was rare. It is important to remember in the meeting with the children that they are enduring their pain and dysfunction in silence and might need help from caregivers to put words on their problems. It is important to focus on treatment strategies of pain and maintained jaw function as well as strategies for coping, normalization and encouraging. The caregiver should be careful with pointing out diagnoses and disabilities since it was shown that to be as much as possible as a healthy child is important for the self identity and pointing out differences can be considered humiliating.

Conclusively the novel findings in this thesis were the dignity and severity of the orofacial symptoms and signs for children diagnosed with JIA, for many the symptoms influencing daily life the most. The children needs comprehensive care concerning oral health and since clinical findings of arthritis showed correlations to the general disease and to TMJ synovitis on MRI, diagnose and treatment of TMJ arthritis might be instituted on clinical grounds. Children with JIA often endure their symptoms in silence needing caregivers for coping strategies, empathy and treatments.

Key words: Juvenile Idiopathic Arthritis, oral health, mucosal ulcers, medication, gingivitis, temporomandibular joint, orofacial growth, pain, children, MRI, clinical signs, qualitative research.

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CONTENTS

1 GENERAL INTRODUCTION

Currently, there are very few scientific studies reported in the literature concerning how children diagnosed with, juvenile idiopathic arthritis (JIA) perceive symptoms related to their orofacial area. JIA is the most common inflammatory disease in childhood characterized by joint pain and dysfunction, typically involving the temporomandibular joint (TMJ). Jaw growth retardation affects facial appearance, leading to more severe pain and dysfunction later in life.

As a result, there is currently a considerable need for precise diagnostic tools and prognostic predictors for TMJ involvement. Magnetic resonance imaging (MRI) with contrast is regarded as the gold standard diagnostic tool but it is coupled to invasive elements with potential side effects and has limited availability. To detect the initial signs and consequently prevent tissue destruction is the aim of modern treatment regimes. The treatments and diagnostic possibilities are improving; nevertheless studies about patient's needs and expectations from their dental caregivers are rare. Furthermore, knowledge about the treatments effects on all oral structures and pain is required.

The focus on this thesis was therefore on what could be found in a dental treatment environment in children with JIA and what they could tell about their experiences of pain, dysfunction, coping and well-being concerning their oral area. These findings were related to general disease assessments and MRI.

To learn more about how oral clinical findings relate to disease activity and the children´s understanding, suffering and coping strategies and how this has significance for prevention of tissue destruction, pain, and the interaction with the child and its family to promote health was the overall intension of this thesis.

1.1 JUVENILE IDIOPATIC ARTHRITIS (JIA)

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of systemic inflammatory diseases that affects one or more joints. It is the most common systemic autoimmune disease in children and adolescents with an incidence of 14/100 000 in the Swedish population (1). The course of the disease fluctuates and the prognosis is generally regarded as good; one third to one half of all children with JIA have a persistent disease activity that lasts into their adult years.

1.1.1 Diagnostic criteria

The definition of JIA in this study is based on the diagnostic criteria described by the International League of Associations for Rheumatology, (ILAR) (2). The term JIA refers to persistent arthritis, where episodes last for at least six weeks, with the onset occurring before the age of sixteen. However the highest frequency of onset occurs between one and three years of age. JIA is characterized by pain, swelling, 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 joints involved. The systemic JIA is characterized by daily fever and generalized inflammation including pericarditis, pleuritis, peritonitis and sometimes arthritis. Oligoarthicular JIA is the most common subtype and characterized by the involvement of four or less joints. In addition oligoarthicular JIA can be divided into two forms depending on the outcome, persistent and extended. Polyarthicular JIA type is defined as arthritis in five or more joints and divided into two subcategories: Rheumatoid Factor (RF) - negative or RF-positive. RF-positive JIA resembles the adult form of rheumatoid arthritis (RA) and occurs in approximately 5% of JIA patients. The enthesitis-related JIA is characterized by arthritis and/or enthesitis (inflammation of the attachment of the tendons). The psoriatic JIA is defined as arthritis in combination with psoriasis. Finally, there are other more uncommon forms (2).

1.1.2 Definition and classification criteria

Due to the different classification systems for JIA, it can be difficult to compare results from different research groups. In Europe, the terminology juvenile chronic arthritis (JCA) was introduced by EULAR (European League Against Rheumatism, Wood 1978) in the 1970´s. In North American countries the disease had for long been called juvenile rheumatoid arthritis (JRA), and the classification criteria of American College of Rheumatology (ACR) excluded certain patient groups; juvenile ankylosing spondylitis, psoriatic arthritis and patients with inflammatory bowel disease (Brewer 1977). In 1995, the ILAR published their first proposal for a new set of criteria that would unify and replace JRA and JCA criteria. The name juvenile idiopathic arthritis (JIA) was introduced. However, studies are still being published using the JRA criteria.

1.1.3 The arthritic joint in JIA

The pathogenesis of JIA is complex, involving different pathways of both the innate and the acquired immune systems.

The initial changes in a joint with arthritis take place in the synovial membrane. The findings are similar to acute inflammations in other tissues, caused by an immunological reaction with edema and accumulation of plasma cells, T- and B-lymphocytes and macrophages. This leads to production of pro-inflammatory mediators, such as cytokines. The cytokines recruit and activate more inflammatory cells. As a result, the vascularity increases and is followed by exudation of fibrin into the joint space. The synovial lining cells increase in number due to hyperplasia and consequently there is an increase in the synovial layer thickness. Gradually, hyperplastic synovium changes its structure into finger-like structures, known as villous hyperplasia. The villous hyperplasia may progressively creep into the joint space, and at this stage it contains a variety of inflammatory cells and is termed pannus. The pannus continues to infiltrate and cover the articulate cartilage and isolate it from its nutritional synovial fluid. Step-by-step the pannus infiltrates and erodes the articular cartilage and adjacent bone (2).

1.1.4 Systemic treatment

The treatment of JIA is mainly symptomatic, employing a multidisciplinary approach and is directed at minimizing inflammation and disability. Over the past decades, more effective use of disease modifying antirheumatic drugs (DMARD) together with new types of medication have improved disease control and even induced remission (2).New drugs that bind and inactivate the pro-inflammatory cytokine tumour necrosis factor alpha (TNFα) have shown excellent results in children with polyarthritis. The interleukin (IL)-1-inhibitor, anacinra, has in the same way been shown to arrest disease activity in children with the systemic onset JIA. However, non-steroidal anti-inflammatory drugs (NSAIDs) are still the first drug of choice with the DMARD, low-dose Methotrexate (LDMTX) as the most common second-line agents. Systemic corticosteroids are still employed if the disease is highly active, albeit with low dose regimes because of side effects such as growth retardation and osteoporosis. As a supplement to general administered medication, intra-articular corticosteroid injections, are commonly used for children with JIA (2).

2 INTRODUCTION

2.1 ORAL HEALTH CONSIDERATIONS IN JIA

JIA is mainly an inflammatory joint disease, in most cases involving the temporomandibular joint (TMJ) and consequently often affecting the cranofacial growth, jaw function and the mucoskeletal system creating discomfort and pain. Salivary glands, gingival and parodontal tissue can be affected as well. This is caused by high synovitis activity increasing the amount of inflammatory mediators circulating and spreading to other tissues (3, 4). Also other mechanisms could be involved as the amount of and/ or nerve sensitizations, central mechanisms and/or the neuroendocrine system through complex pathways (5-7).

Medications can have adverse effects on teeth, oral mucosa and saliva. Secondary to disability, pain and discomfort there might be a risk of increased frequency of oral infections (8).

2.1.1 Saliva and oral microflora

More than 800 different bacterial species have been identified in the oral cavity and most of them in the dental plaque (9). Both healthy and pathologic bacteria, and fungi coexist in the microbial ecosystem and are influenced by the host immune system, salivary flow and composition, mouth movements, breathing and also pharmacological agents (10) such as chemotherapy, antibiotics and antimicrobiotic agents like chlorhexidine (11, 12).

Salivary glands secrete large amounts of proteins and peptides and are integrated into the neuroendocrine system. Saliva is therefore not a mirror of plasma. Saliva in children with JIA has been found to be reduced in volume and altered in its composition indicating that it can be used for measuring disease activity (13, 14). Furthermore saliva has been proposed as a diagnostic fluid for patients with chronic pain (15).

2.1.2 Rheumatic disease and periodontitis

Both Rheumatoid arthritis (RA) and JIA are characterized by a destructive inflammatory process in the border between the bone and connective tissue of the joint which is similar to the inflammatory process of the supporting tissues around the tooth in periodontitis (16). The cause has been suggested to be dysregulation of the immune–

inflammatory response as well as infectious connections to bacterial and viral agents. *Porphyrmonas gingivalis* a common bacterial agent in periodontitis is also found in synovial fluid and may trigger autoimmune responses explaining the chronicity in both diseases (17). The increase of attachment loss in JIA patients and periodontal destruction in adults with RA show improvement with anti-inflammatory medication and control of the dental plaque (18, 19).

2.1.3 Dental plaque (Oral biofilm) and gingivitis

Toothbrushing with different devices and rinsing are important to maintain an as aerobic, Gram positive environment as possible (20). Regular oral hygiene supports bacterial control and helps maintain a comparatively constant composition of healthy bacteria (21). Clinically, this bacterial control correlates with an absence of visible inflammation and pockets depths of less than three mm (22). Biofilms are bacterial communities composed of several different organisms existing in a collective state. The oral biofilm in dental plaque is characterized by large number of anaerobes, spirochetes and motile bacterial species (21). If bacterial colonization in the biofilm exceeds a threshold level, the immunological defense will react by initiating a series of events in the underlying connective tissues. Clinically, this correlates with increased clinical signs of inflammation (gingival bleeding on probing or more severe if bleeding on touching) and increased pocket depths (23). At a cellular level, this is characterized by increase of certain inflammatory parameters, cellular breakdown products, and increased crevicular fluid flow. Gingival inflammation significantly increases the prevalence of bacteraemia (24).

2.1.4 Gingivitis in JIA

Most studies have reported a higher frequency of plaque and gingivitis in patients with JIA compared to healthy subjects (8, 25). Gingival bleeding on probing decreases with NSAID medication (19).

2.1.5 Gingival crevicular fluid

Gingival crevicular fluid is a filtrate of blood, which increases its flow in response to inflammation. The exudates from the inflamed periodontal tissue, has a recognized diagnostic potential (26). It contains leukocytes, particularly polymorphonuclear (PMN) granulocytes, host derived molecules from blood, and substances from micro-

organisms of the dental plaque. The fluid may indicate systemic disease since it contains most of the humoral and cellular defense factors found in serum (27).

2.1.6 Gingival crevicular fluid and attachment loss in JIA

Adolescents with JIA, especially those clinically more affected by the rheumatic disease, have more frequently incipient attachment loss with similar plaque levels, gingivitis levels and subgingival microbiological profile compared to controls. An altered systemic inflammatory state was confirmed in JIA patients since the erythrocyte sedimentation rate (ESR), serum levels of C-reactive protein (CRP) and of two key proinflammatory cytokines IL-1β and IL-18, was significantly elevated. In gingival crevicular fluid of the JIA subgroup with attachment loss, a possible reflection of this inflammatory state, represented by a tendency of higher IL-1β and free elastase, could be observed. After two years of follow-up (with pharmacological treatments), there was a clinical and laboratory rheumatological improvement in JIA patients. Locally, the total amounts of IL-1β in the gingival crevicular fluid significantly decreased and no elevated periodontitis parameters were observed (28, 29).

2.1.7 Dental caries

Dental caries is an infectious disease, where bacteria penetrate into the highly vasculated inner parts (the pulp) of the teeth, and can spread, cause systemic infection and pain. Dental caries and more caries left untreated among children with JIA have been reported (8, 30).

2.1.8 Adverse reactions to medication

Pharmacological treatments might affect oral structures and tissues negatively through different mechanisms. This can be locally during ingestion causing erosions on teeth or mucosa or systemically by decreased saliva secretion (31), all degrees of severity of mucositis (32), affecting tooth development and/or mineralization (33), changing the microflora and/or the structure of the gingivas (10, 34). For patients with JIA there are new pharmacological therapies emerging that we do not know much about concerning the effect on the oral cavity.

2.1.9 Condylar growth in JIA

The TMJ is unique in the body in that it presents with special features compared to other joints. The articular layer is composed of dense fibrous connective tissue rather

than hyaline cartilage and the condylar growth is situated in close proximity to the articular surface and joint capsule rather than in the growth plate as in long bone. This is due to incomplete ossification such as the absence of compact bone until the third decade in life. A disc is also present for hinging and gliding movements where the two joints are connected and reciprocally dependent on each other (35).
In the arthritic TMJ, growth inhibition to varying degrees can develop depending on malfunctioning of the condylar cartilage (35). Condylar destruction can also take place(36). Studying CT and MRI images, Arvidsson et al 2009, suggest that typical condylar alterations in JIA may be caused by undergrowth secondary to growth centre damage or by overgrowth possibly related to inflammation-induced increased vascularisation and growth factor release (4, 37). The result is a deformed joint due to remodeling (37, 38). In the older JIA patients there are findings similar to arthrosis (38). However, histological studies have shown that the fibrocartilage in a child has the ability to recover and growth can proceed (35).

2.1.10 Craniofacial growth in JIA

The cranium of a newborn child is comparatively big and the jaws small. The face becomes relatively bigger and the jaws grow more in periods connected to tooth eruption. There are different types of osseous growth in the face. The sutural peak of the maxilla appears as early as 6 - 7 years of age and is almost completed at 10 years of age (Irie et al 1975), in contrast to the condyle that has ability to grow into the third decade (35).
In case condyle growth is inhibited and as a result becomes shorter during growth, the lower jaw rotates backwards in relation to the cranial base, giving a steeper mandibular plane angle and a shorter posterior facial height (39, 40). In a child compensatory growth of the dentoalveolar processes takes place and the maxilla can stop growing to adapt in size. The result is a more convex profile, retrognathia or in rare cases micrognathia. Asymmetries can emerge if the condyles are differently affected. As the dentoalveolar processes become smaller there is less space for the teeth, thereby is tooth crowding significantly more common among JIA patients (40). Arvidsson 2010 showed that 25% of the juvenile rheumatoid patients had micrognathia in a 27 years follow-up study (41). A normal profile was occasionally found, even if the jaws were severely affected at early age. This positive development was found in patients where the disease was mild or healed. Condyles that have a normal shape could still result in

an altered profile (41). Other studies have reported that structural changes seen radiographically can recover and normalize in cases with low disease activity (41, 42). The mucoskeletal system promotes function and is stabilizing the chewing system also when joint anatomy is not optimal or when edema and synovitis occurs in the TMJ. Jaw function can be almost normal in spite of a shorter or in rare cases absence of a condyle and/or ramus.

Overactivation of the mucoskeletal system e.g. oral parafunctions can lead to muscle stiffness and pain in children with JIA and might counteract normal growth. It is important to encourage relaxation and normal jaw movements to promote TMJ growth in the periods when the disease is less severe. Occlusal appliances are tailored individually to unload, for relaxation and to antagonize parafunctions and support growth (43, 44).

There are also different well documented orthodontic programs for promoting normal jaw growth, for example functional distraction splints (45).

The tongue position as a part of the mucoskeletal system is important. The tongue position might affect the occlusion by protrusion at swallowing instead of as in the normal case where the tongue position is on swallowing, at the palate. Children with an open bite often stabilize with the tongue when for example swallowing and there is a risk that the open bite will be maintained or aggravated by this parafunction.

This habit sometimes develops in children with JIA and can be very difficult to get rid of, a strong motivation and cooperation is needed and functional appliances' that can counteract are recommended.

2.1.11 Frequency and risk factors for temporomandibular joint involvement in JIA

Studies that have evaluated TMJ involvement using various imaging modalities have placed the prevalence of TMJ arthritis in children with JIA to 38% -93% (8, 37, 46-57). Children with polyarticular arthritis seem to be affected more often with TMJ problems. Oligoarthritis and enthesitis- related JIA lesser problems to a degree but not all studies agree (47, 51, 58, 59). TMJ arthritis might be present despite limited or otherwise quiescent disease and in the presence of concurrent systemic immune-modulatory therapy (60, 61).

Subjective symptoms in the literature are rare amongst children but show vast variation (48, 52, 54-57).

2.2 PAIN

Pain terminology according to the Classification of Chronic pain, by the International Association for the Study of Pain (IASP) "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."

JIA is to a great extent characterized by pain fluctuating in intensity of different character with different mechanisms behind (2). Pain is multidimensional and individuals conceptions of pain and ability to verbally communicate changes throughout life (62).

2.2.1 Classification of pain

Pain can be either acute or chronic. Acute pain is the sensory and emotional experience during the normal healing phase following an injury. This pain is also termed transient and functions in terms of protection, for example it warns of upcoming tissue damage. On the other hand, chronic pain is described as a sensation of pain, which persists past the normal healing phase usually lasting between three to six months and therefore termed persistent. This type of pain is non-protective (Merskey and Bogduk 1994). Pain conditions can be labeled by their spatial distribution, affected anatomical site, cause and underlying mechanisms. Spatially, they can be divided into localized or widespread pains. The anatomical site affected can be structures, such as viscera, head or back, while the cause can be due to for instance cancer or diabetes. It is common to classify pain by the under lying mechanisms, which can be nociseptive, neuropathic or idiopathic (63).

2.2.1.1 Nociceptive pain

Nociceptive pain occurs when a noxious stimulus activates nociceptors. This stimulus can be either injurious, causing a tissue damage or potentially injurious. Further, nociceptive pain is of acute character, like a temporary pain condition (Kidd and Urban 2001) but it can also be prolonged (Wall and Melzack 1994).

Inflammatory pain is due to a cascade of complex biochemical and cellular events caused by tissue damage, minor infections, burns or mechanical overloading. For instance, mechanical overloading in the case of stress induced bruxism, resulting in hypoxia of the muscles or impaired microcirculation. Ischemia (Monteiro and Kopp 1989) leads to the release of inflammatory mediators giving an inflammatory reaction, which is followed by pain. These mediators are released from circulating leucocytes

and platelets, vascular endothelial cells, immune cells or cells in the peripheral nervous system (Mense 1993).

2.2.1.2 Neuropathic pain

Neuropathic pain is initiated or caused by a primary lesion or dysfunction in the nervous system (Merskey and Bogduk 1994). Any disorder or process that can damage the sensory pathways can cause neuropathic pain.

2.2.1.3 Idiopathic pain

Idiopathic pain is an entity of exclusion in which pain by definition persists for a longer period than six months and has no specific physical or mental cause. Idiopathic pain can be identified in conditions, such as chronic craniofacial pain disorders and headaches (McDonald, 2007).

2.2.2 Mucoskeletal pain

Laborious work or unaccustomed exercise may provoke mucoskeletal pain, also termed myalgia. These pain conditions affect quality of life considerably although, they are not life threatening. They are further the major cause of non-odontogenic pain in the craniofacial region. Myalgia is experienced locally in the muscles as a feeling of fatigue and soreness or even overt pain (Okesson 1998). In the craniofacial region, myalgia causes a sensation of a dull steady pain overlaying the muscles in the jaw, head and neck (Lund 2001).

To date the knowledge is still limited on the peripheral and central mechanisms underlying mucoskeletal pain. The biological mechanisms that initiate and maintain chronic myalgia are still poorly understood. However, psychological factors in combination with bruxism are reported to contribute to the etiology of chronic craniofacial myalgia (Velly 2003)

Chronic mucoskeletal pain is a complex condition due to plastic changes in the nervous system. Pain transmission and modulation systems (Mense 1993, 2001, Okeson 1998) include both inflammatory and non-inflammatory components. Some inflammatory mediators are further reported to induce neuroplastic changes in the brain stem, like central sensitization, which is proposed to contribute to muscle hyperalgesia (Mense 1993).

2.2.3 General pain in children and adolescents

Twenty-five percent of children and adolescents are reported to experience chronic pain (64). Girls reported pain at multiple sites significantly more than boys, particularly in the older age groups. Headache is reported most frequently.

Ineffective handling of stress, poor self-esteem and insufficient adult contact were factors that were found to be associated with high occurrence of back pain and headaches (65, 66). Correlations between psychosomatic symptoms and pain in the neck, shoulder and low back pain were demonstrated among 12-18 years old. There is strong evidence that psychological treatments, principally relaxation and cognitive behavioral therapy, are highly effective in reducing the severity and frequency of headaches in children and adolescents (67, 68). Pain and headaches can affect identity development in young people (69). Pain may function as an excuse for young people to escape the pressures and stress of daily life. The relationship between reports of pain, feeling nervous and having difficulties in describing one´s feelings in childhood and pain reports in adulthood suggests that more attention should be given to problems of pain and ill-health in childhood (69). In children and adolescents, orofacial pain occurs about half as often as other pain complaints. However, relative to their prevalence the different pain complaints are similar regarding impairment and health care utilization (70-72).

2.2.4 Pain in children and adolescents with JIA

Pain is a primary symptom in JIA. About 25% - 30% report moderate to severe pain and most children with arthritis report at least some pain lasting from 30 minutes to 24 hours a day, with a majority (76%) reporting pain for a majority of the days (60%) (73). In rheumatic disease-related pain, nociceptive afferents in the joint are located in the joint capsule, ligaments, bone, periosteum, arthicular fat pads, and perivascular sites. They are activated by joint motion or any noxious movement or stimuli, such as inflammation or injury. The enhanced pain associated with arthritis is probably due to the response of joint afferents to mechanical and heat stimulation present during inflammation and chemical mediators of joint inflammation, such as prostaglandins, which sensitize joint afferent fibers. This inflammation induced sensitization of arthicular afferents likely contributes to hyperalgesia, an increased response to stimuli that is typically painful, and allodynia, pain due to stimuli, which do not typically provoke pain. Thereby children with JIA have a reduced pain threshold depending on

longlasting structural and functional changes due to central and peripheral sensitization, which explains why pain is not always arthritis related (2, 74-79).

2.2.5 Pain associated emotions in JIA

There is a strong correlational support for the link between negative emotions, particularly anxiety and depression, and increased pain intensity (73, 80, 81). Also daily stressful events and negative mood have been linked to increased pain, stiffness, and fatigue in children with JIA (77, 80, 82). Increased anxiety can induce muscle tension, thereby directly inducing or exacerbating mucoskeletal pain or increased pain can induce anxiety about future prognoses or interference with life activities (2).

2.2.6 Cognitive coping strategies to pain in JIA

Cognitive processing of pain can be maladaptive in at least two ways: a) people can fail to attend to information or fail to generate self-talk that might be helpful in coping with pain, or b) people can engage in dysfunctional thinking that leads to maladaptive coping and greater pain, such as wishful or catastrophic thinking. Catastrophizing may be the most "toxic" type of dysfunctional thinking related to pain. Catastrophizing is thought to include three components: 1) rumination (preoccupation with pain-related thoughts); 2) magnification (exaggeration of the threat value of pain); and 3) helplessness (adopting a helpless orientation to cope with pain).
Catastrophizing is in studies associated with a higher pain intensity, pain duration and anxiety. Cognitive refocusing (engaging in activities as a distraction from pain), and rational thinking were related to less pain intensity and emotional distress (77, 83, 84). When children are in pain, they exhibit a wide variety of pain behaviors, such as limping, grimacing, crying, resting, or asking for medication. How others respond to these pain behaviors can be adaptive or maladaptive for a child experiencing pain (2).

2.2.7 Pain and age

For children pain is multidimensional. Children have to for example to learn to understand what they feel, what pain is, localize, learn how to cope, find explanations and give words to it (62). The development for a child is to increasingly abstract and generalized definitions of pain by age. Improved understanding of objective physical explanations to pain together with the use of more words with increasing age was obvious in a study. It has also been reported that psychological aspects were better acknowledged by the older children in five to 14 year old (85). Under the stress of

illness, it was recognized that the children regress to earlier modes of thinking. For younger children studying symbolic non-verbal representations of pain, using role-playing, miming or doll play might highlight aspects of pain which cannot be expressed in an interview situation. Younger children have a tendency to report extremes of the visual analogue scale (VAS) scale, owing to a more limited cognitive capacity than older children whom can make discriminations within the VAS range (Goodenough B, Addicoat L 1997).

There is a perpetual dynamic learning curve for child experiences of what pain is and how to cope. An anxious, distressed and worried child perceive more pain, therefore an individually tailored strategy for each patient is needed (86).

2.2.8 Treatments of pain in children with JIA

Early identification and aggressive pharmacological treatment of chronic arthritis could lead to enhanced pain relief and improved function in both the short and long term, via a reduction in peripheral and central sensitization mechanisms. Adequate control of the inflammatory disease is of utmost importance in the overall approach to pain management. Adherence to effective pharmacological therapies can be less optimal, and strategies for improving and maintaining treatments need to be routinely implemented in pediatric rheumatology practice.

Cooling and resting inflamed joints, and relaxation or other psychological treatments to control pain are recommended.

Psychological interventions that reduce negative emotional states would be expected to directly or indirectly reduce pain intensity and pain interference. Helping children to manage disease-related stressors such as relaxation and problem-solving techniques, should result in concomitant reductions in negative emotions and pain. Enlisting social support and the reinforcement of family and friends should foster greater participation in social and recreational activities by patients, thereby reducing emotional distress and preoccupation with pain and suffering (2, 87, 88).

2.2.9 Cognitive-behavioral treatments for pain

Cognitive-behavioral treatments (CBT) approaches to chronic pediatric pain typically involve teaching children to use deep breathing, guided imagery, relaxation and to replace maladaptive thinking Catastrophizing, with adaptive thinking, like focusing on what can be done to control pain and encouraging oneself to engage in more effective coping. Parents are taught to encourage their children to stay as active as possible,

engage positive coping and avoid reinforcing pain behaviors, such as allowing children to avoid school or other responsibilities (2, 89-91)

2.2.10 Temporomandibular dysfunction (TMD) and pain

Temporomandibular dysfuction (TMD) represent a group of conditions characterized by pain and dysfunction in the TMJ and the surrounding tissues (92). Signs and symptoms of TMD, include joint sounds such as clicking and crepitus during mandibular motion, limited mouth opening, pain on palpation of masticatory muscles and pain on function. Besides these orofacial signs and symptoms, there is considerable evidence that TMD is characterized by increased psychological distress.

Different classification systems for TMD, based primarily on clinical findings and aimed at classifying physical pathology, have been used over the years. A widely accepted classification system is the Research Diagnostic Criteria for TMD (RCD/TMD) (92). This diagnostic system has been tested for reliability concerning clinical measurements and been found to have good reliability among adults (93) and adolescents (94, 95).

Most population-based studies of TMD prevalence use pain in the temporomandibular region as their case definition. Different questions have been used to detect persons with self-reported TMD pain, such as pain other than headache in the facial area and pain around the TMJ. Different timeframes have been used in questions about pain frequency. The timeframe, pain once a week or more, has been used in several studies and the use of a narrow timeframe seems to improve reliability of self-reported pain (96).

2.2.11 TMD in children and adolescents.

Population-based studies among adults report rates of TMD pain with ranges of 8% - 15% for women and 3% - 10% for men (leResche L 2001). It is rare in children before puberty (97). A systematic review found that self-reported TMD pain among children and adolescents varied between 0.7% and 18.6%. Most estimates center round 2% - 6%. The variance in prevalence might be related to factors like the investigated population and methodological issues. TMD symptoms fluctuate longitudinally (98). Several studies have pointed out that pain has a potential impact on daily living (64, 70, 72). List 1999, found that more than 20% of TMD subjects consumed analgesics each week and 20% were absent from school at least one day per month because of pain (99).

Early prevention of pain may be important if pain is to be prevented from developing into a more chronic condition (69, 100, 101)

2.2.12 TMD in JIA

In the literature there are vast discrepancies between reports on pain and dysfunction amongst patients with JIA. Some studies also show variation in age and disease duration. In some studies, self reported and clinical findings of pain, sounds and disabilities are not separated or definitions are diverse, which makes the results difficult to compare. Despite this both clinical findings and self-reported symptoms were increased compared to controls. Clinical findings of functional limitations as decreased mouth opening are reported to have a frequency of around 20 - 37% (52, 56, 57, 102). Other symptoms commonly reported are jaw sounds that have a frequency of 16%-19% (52, 54, 56), pain on muscle palpation 3 - 57% and pain on TMJ palpation 3-37% (52, 55, 56, 103). Patient reported symptoms as pain at jaw movements 9 - 37% (52, 55, 56, 103). Pain at rest 0 - 11% MJ sounds 12 -18% difficulties at opening 15%- 29% and headache 6% - 27% (52, 56, 103).

Patient's report of pain are increasing with age (38, 57, 104, 105).

2.3 IMAGING OF THE TEMPOROMANDIBULAR JOINT

2.3.1 The panoramic radiograph (OPG)

The panoramic radiograph (OPG) is available in most dental clinics; it is fast, technique with a relative low ionizing radiation, frequently used as a diagnostic tool for evaluating condyle alterations (54). The sensitivity is not as high as for OPG as for computed tomography (CT) or MRI.

In children, condyles are smaller, rounder and not as cylindrical as in adults. Hence the influence of the long-axis angulation of the condyle on the radiographic anatomy is less pronounced, making it easier to detect pathological condylar deformations in children (37).

2.3.2 Magnetic resonance imaging (MRI)

The overall advantage of magnetic resonance imaging MRI is its ability to visualize soft tissue, as well as bony structures, for example disc position and fluid in the TMJ can be typically diagnosed in the MRI examination. To modify the image contrast, for disclosing activity a paramagnetic agent (gadolinium-DTPA) may be added. The contrast agent has to be administrated intravenously and new pictures taken as quickly

as 30 – 90 seconds afterwards, as it rapidly passes into the interstitial spaces, although this is dependent on capillary permeability. In joints with inflammatory arthritis, capillary permeability is increased and therefore the post-contrast MRI shows increased enhancement as compared to pre-contrast MRI (106, 107). Therefore, TMJ investigation with MRI contrast medium is both highly sensitive and specific for the identification of TMJ synovitis (48, 108, 109). In a small histological study on rabbits there was a strong correlation between degree of enhancement of the synovia and pathological arthicular findings (107). Recently the specificity of MRI findings has been questioned but also the sensitivity, so further studies are wanted to increase our understanding (51).

3 AIMS

3.1.1 General aim

The overall aim of this thesis was to investigate different aspects of oral health in the clinical environment with children diagnosed with JIA, including examination of pain, intraoral structures and jaw function.

3.1.2 Specific aims

The study aimed to investigate and improve our understanding of:

- clinical intraoral and orofacial assessments by the dental caregiver, and subjective symptoms amongst children with JIA related to medical assessments and compared to controls.
- the severity of the orofacial symptoms and its influence on daily life.
- how children diagnosed with JIA perceive their oral health.
- how children diagnosed with JIA perceive their encounter with the dental professional.
- link or correlation between a child's report of pain, clinical assessments and to findings on MRI scans.

4 HYPOTHESES

The hypotheses of the studies were:

- the oral health in children and adolescents with JIA is poorer than that of healthy controls.
- patients' reports of subjective symptoms and clinical findings from the TMJ and the orofacial area are more frequent in JIA patients than among healthy children, and have a negative impact on their daily life.
- TMJ involvement can be diagnosed with the knowledge of certain specific clinical predictors.

5 MATERIALS AND METHODS

5.1 SUBJECTS

Children and adolescents diagnosed with JIA referred from Astrid Lindgrens Children's Hospital, Karolinska University Hospital to Eastman Dental Institute in Stockholm as part of their care plan. After being referred the children are regularly, according to an individual follow up schedule, visiting the orofacial pain specialist. Participants in all studies were consecutive patients coming for their check-up. For study three and four they were selected from these patients with a special purpose. Astrid Lindgrens Children's Hospital, Karolinska University Hospital belongs to the specialized care of the Public Health Service for children and Eastman Dental Institute in Stockholm is specialized for children´s dentistry and a part of the Public Dental Health Service and serve an area of nearly half a million children and adolescents aged 0 – 18 years of age .

For **studies one and two,** the same 41 patients and controls were examined at the same appointment at the Eastman Institute in Stockholm by one senior consultant (Eva Leksell) and one dental hygienist (Lisbeth Eklund) at the department for Specialized Peadiatric Dentistry and one senior consulatant at the department for Orofacial Pain and Jaw Function.

In **study three,** fifteen children, aged 6 – 16 years old, with JIA were recruited. Participants with different ages, sexes, social background and experiences of JIA were selected, as to enable a study of the multiple dimensions of the social processes of how children perceive their oral health and the encounter with the dental care. Individuals were added until theoretical saturation was reached, that is until the complete range of constructs that made up the theory was fully represented in the data. Each interview was coded before the next was conducted so that new information could be incorporated into subsequent encounters (110-112).

For **study four** children diagnosed with JIA and with clinical suspicion of TMJ arthritis were selected from the children coming for their check-up.

5.2 CONTROLS

Controls were matched from children attending the Public Dental Health Service in Stockholm for their regular dental check-ups. Our intention was to match each JIA patient by gender and age with the controls, but this was not totally possible with the sexes in study one. When writing study two, we exchanged two of the controls to be able to match also for sex, from the six controls in surplus as six of the patients were excluded. The controls received the same patient information, concent form and questionnaires as the JIA patients.

5.3 STUDY DESIGNS AND PROCEDURES

Studies one and two are cross-sectional, case – control investigations using 41 patients aged 10- 19 years old, diagnosed with JIA according to ILAR and matched controls.
Study three was a qualitative study, using the classical Grounded Theory as a method for interviewing and thereby investigating how children aged 6 – 16 years old; perceive their oral health and the encounter with dental care professionals.
Study four was a method validation study of 35 TMJ´s in 18 children. Subjective symptoms and clinical findings were compared to signs on MRI.

5.4 METHODS

5.4.1 Disease characteristics, medication and subdiagnoses

Subdiagnoses, age at diagnoses, duration of the disease, number of active joints, laboratory results, as well as current medication for each patient were extracted from the medical file by the patient's physician.
ESR, CRP, presence of antinuclear factor (ANA), and RF were registered.

5.4.2 Physisians global assessment

Disease activity by the physician according to a clinical core set parameters by Giannini et al. Based on disease history, patients self-reports, physical examination, and current laboratory results, the physician assessed the overall disease activity using the outlined criteria by a VAS.

5.4.3 Assessments of general pain and CHAQ

For the patients self-report, two VAS (100 mm) scales were used, one for pain during the week preceding the visit and one for general coping in life with the disease. Self-reported measures of pain are considered the gold standard for assessing pain intensity,

duration and location in children from three years of age. The most widely used and validated self-reported measure of pain for patients with JIA contains a 10 cm horizontal line, anchored with the descript “no pain” and “most severe pain ever”, which are also used in this study for assessment of local and general pain (Varni 1987). The patient reported VAS for present pain and for worst pain from the previous week 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 and the ability of the child to perform each task is scored from 0 to 3.

5.4.4 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.

5.4.5 Measuring saliva flow

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 (113).

5.4.6 Intraoral clinical assessments

An 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. Due to the difficulties in being able to differentiate between the various shades of red on the oral mucosa and to find oral ulcerations of small size, the oral mucosa was examined and ulcerations were 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 were 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), were assessed as presence or absence. Probing depth (PD) of the sulcus of more than 2 mm was recorded with the probe placed along the longitudinal axis of the tooth to the nearest millimeter (mm). 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 at the mesio-facial, distofacial, mesio-lingual, and disto-lingual surfaces (0–32 sites) (114). Plaque and calculus were measured on three sites: again including mesio-facial, disto-facial, and lingual surfaces of the first permanent molars and central incisors (0–24 sites).

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

5.4.6.1 Radiographic assessments of bite-wing

Two bite-wing radiographs (Kodak Ultraspeed, Rochester, NY, USA) were taken for each patient and control in study 1. 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, six months later by the same investigator to assess agreement by the two recordings.

5.4.6.2 Caries assessment

Presence of occlusal and approximal caries visible on the bite-wing radiographs on the first permanent molars were 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.

5.4.7 Patient history of orofacial pain, dysfunction and its severity

All 82 subjects were examined by a senior consultant in oral physiology according to an extended protocol that is used as part of the JIA patient's routine treatment protocol. The patients were asked to assess the current degree of spontaneous jaw pain as well as, pain of jaw movement and on chewing and to record this on a VAS with the endpoints, no pain at all and worst pain ever experienced (VAS 0 – 100 mm). The patient's experiences of TMJ sounds and occlusal discomfort were noted as yes or no.

Furthermore frequencies of headache and orofacial pain were reported with the alternatives; never, 2 times per month or more, 1- 2 times a week, more than 2 times a week or daily.
Presence of orofacial pain was registered when the patient reported pain in the jaw, temple, face and in front of the ear at rest or on jaw function. The examiner touched the patient's joint, cheek and temple area when asking the questions, to make sure that the child knew exactly what parts of the face she was referring to.
The patients were further asked for awareness of ongoing oral parafunctions.
Finally the patients were asked about the severity of their orofacial symptoms together, including headache, with the alternatives, negligible, mild, moderate, severe or unbearable, and to what extent these symptoms influenced daily life within alternatives mentioned.

5.4.8 Clinical examination of orofacial pain, jaw function and occlusion

A clinical examination including range of motion, presence of TMJ sounds, TMJ and masticatory muscle tenderness/pain upon palpation and, signs of parafunctional activity, and oral mucosa as well as occlusion, jaw relationships and facial morphology was performed (95).

5.4.8.1 Vertical and horizontal range of motion of the mandible.

Extent of maximum assisted mouth opening (mm) between incisors was measured with a ruler. A jaw opening capacity of < 40 mm was considered as restricted.

5.4.8.2 Presence of joint sounds.

TMJ clicking or crepitus was registered as yes or no. Noted with or without pain and/or locking.

5.4.8.3 TMJ and muscle palpation.

Tenderness to digital palpation of extraoral and intraoral masticatory and related muscles sites (n=20) posterior, anteriorand tendon temporalis; superficial and deep masseter; medial and lateral pterygoid; posterior digastricus; trapetzius and sternocleidomastoideus as well as the lateral and posterior portion of the TMJ (n=4 joint sites) was recorded with the alternatives: 0= pressure but no pain 1= tenderness/pain.

A pressure of 0.5-1 kg was used during palpation and the subject scored the sensation (0=pressure but no pain, 1=pain) (115, 116).

5.4.8.4 Occlusion.

Dental occlusion in the sagittal plane was classified as prenormal, neutral or postnormal. A postnormal occlusion was considered if the molar occlusion deviated by one cusp width or more on both sides, before the age of 13, and ½ a cusp width or more on both sides at the age of 13 or older, adjusted for such a deviation caused by tooth loss.

5.4.8.5 Vertical overbite and horizontal overjet

Measured between incisors with a ruler to the nearest millimetre.

5.4.8.6 Oral mucosa.

Signs of the parafunctional activities, tongue thrusting and mucosal ridging were recorded in the protocol.

5.4.9 Assessments of facial appearance

Facial profile asymmetry, indicated as straight, convex or concave profile was subjectively judged by the examiner. When chin prominence was positioned dorsally or ventrally in the midsagittal plane facial convexity or concavity respectively, was considered present.

When the midline of chin prominence deviated in the frontal plane from the facial midline, a facial asymmetry was considered present (57).

5.4.10 Criteria for bony changes of the condyle

A panoramic radiograph was analysed for deviations in TMJ structure by a specialist in oral radiology. Bony changes of the TMJ refers to those from a small abnormality of the condyle deviating slightly from the convex shape, usually flattened, with or without slightly flattened or widened fossa-eminence to a completely absent or short flat condyle and a flat fossa-eminence curvature (37, 110).

5.4.11 Interviews

All interviews took place in a quiet room and were taped. Two interviews were performed in cafés on the demand of the child (teenage boys).

A topic guide included questions about the children's perceived relations to family, peers and caregivers, facial appearance, jaw function, pain, treatments, tooth-brushing and eating. In our experience children do not provide information unless they are asked direct questions without the possibility of diverting from the subject. Therefore, questions that could be answered with yes or no were preferred. On occasions there were difficulties to find the correct words and children often touched the area in front of their ear to explain. Older children were able to express themselves using an extended vocabulary but the youngest could explain just as well, in their way with countenance and fewer words. The interviewer strived not to ask open and follow-up questions that could lead the children to respond in a particular way. After all interviews and sometimes during them, observational notes were taken to validate non verbal communication. The children in the study needed time and social support to be able to communicate their answers (77, 117-119).

5.4.12 Analysis of data the quantitative studies

Data from the inta- and extra oral examination, patient history and questionnaire were related to each other, to panoramic radiograph (OPG), MRI scans, pharmacological therapy and medical assessments. Frequencies of symptoms and patterns disclosed are reported in the studies.

5.4.13 Analysis of data from the qualitative study

The analytical phase was a process of reduction and abstraction of the material through the eyes of the researcher. A professional caregiver and a sociologist analyzed the data. It began with an open coding process. The interviews were read line by line and questions to the data were posed, for example "What is this all about?" The children's own words were used (in vivo codes) if possible. How the children handled their oral health problems was reflected over and compared to what was said during the interviews and what other children had said in their interviews. The other authors read the results and gave valuable comments.

In the transcript it was also noted when the voice was in secure and weak. Data was examined for concepts that were identified in the interviews and further condensed into a main concern and into categories. Data was thereby broken down, conceptualized and put together in new ways. Key sentences and parts of dialogues were selected as codes, what was not said, impressions and associations were found in memos. All these were compared to each other. Reflection over the meaning of what was said in the

interviews, on an abstract level, led to the identification of the main concern. The fact that the children are in a process of shaping their lives and creating an identity were identified in all the interviews. The social processes were examined for how to fulfill the main concern and simultaneously control their life situation with JIA in which the categories emerged as condensed headings. Constant comparison of all the interviews and observational notes, back and forth, relating them to each other and questioning the truth in the more abstract concepts, codes and memos gave a step-by-step the explanation of how the children handled their situation and this was condensed it into five sentences, named categories. The main category "enduring in silence" became obvious, more abstract and influencing all the categories in all interviews (110, 112).

5.5 STATISTICS

Outcome data from the assessments were expressed as mean and SD, in percent frequencies, absolute figures as well as range based on the individual, as the unit for analysis.

The presence of facial pain was dichotomized into greater than two times a week and less than two times a week before the statistical analysis. The patient's assessment of the severity of facial pain and its impact on daily life were dichotomized into severe or mild to moderate.

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 five, or Fisher's exact test, when the expected frequencies of one or more cells were less than five. Differences between groups regarding the number of sites with plaque, BOP or PD greater than two mm were tested with the Mann–Whitney U-test.

Differences in variables between patients and controls were analyzed for statistical significance with Pearson's χ_2-test or Fisher's exact test, and differences in TMJ pain intensities (VAS) were analyzed with the Mann–Whitney U-test. Correlations were analyzed with the Spearman rank correlation test.

A significance level of $p \leq 0.001$ was used and $p < 0.05$ reported as tendencies. Sigma Stat software version 3.1 and STATA version 11.0 was used for statistical analyses.

6 ETHICAL CONSIDERATIONS

Research is important and necessary for the development of both knowledge and for the society. Society and its inhabitants have the right to demand highly valid research on significant important issues. However, inhabitants also have the right to protection of their privacy and integrity. The Swedish Research Council, HSFR 1990, their ethical rules have been followed in this study with respect to the requirements for information, consent, confidentiality and utility. Verbal and written information regarding the aims and procedures in all studies were given to the subjects, and also to the parents as children were participating. Children and parents were informed that they at any time and without declaring a reason were free to withdraw from the studies. The Research Ethical Committee at Karolinska Institutet approved the study.

The risks associated with this study include the most private thoughts and feelings of the children and their parents, gleaned from the interviews, and this might result in the development of fears and/or anxiety. For this reason, a great deal of effort was invested in the preparation, diplomacy, sensitivity and the provision of back-up psychosocial personnel resources.

The approach from the researchers to the informant is a very important ethical issue. According to the Declaration of Helsinki, Article 23, research should not include individuals who are involved in a dependent relation to the researcher. In this study patients were from Stockholm area, while the interviewer was from Karlskrona, Blekinge, Sweden.

7 RESULTS AND DISCUSSION

7.1 INTRAORAL CONDITION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS COMPARED TO CONTROLS

Significant differences between JIA patients and controls were observed. Improved plaque control ($p<0.05$) was the only diagnoses on a group level that indicated the potential for a change in treatment. All JIA patients in this study received information and instruction from a dental hygienist. The children were generally positive and interested in this kind of care and received follow-up appointments.

In this group of children diagnosed with JIA or healthy, none had attachment loss or decreased marginal bone level. However, there were two children in the JIA group with papilla atrophy. There is no defined diagnosis for this condition when the gingiva does not reach the contact site between the teeth. Plaque accumulations between the teeth that cannot be reduced with tooth brushing normally recommended to children at these ages were found. This finding is in accordance to reports of an increased susceptibility to parodontal diseases (18, 19, 28). Initially this condition is not observed on bite-wing radiographs nor at gingival PD registration, and is mostly left unnoticed in the patients' regular dental care. Therefore it is of importance that dentists specialized in taking care of patients with JIA check for this.

One of the JIA patients had necroses in a permanent molar as a consequence of refusing treatment as she could not keep the mouth open long enough to restore the tooth. It is important to recognize pathological conditions since the antiinflammtory medication might camouflage symptoms (120). Furthermore it is important for caretakers to be aware of pain and functional problems in this patient group. Not only to make a clinical examination of pain and dysfunction but also to ask for if there are problems to open up the mouth wide or to keep it open as the children do not spontaneously tell.

The slight structural changes to the gingiva among JIA patients compared to healthy ($p<0.001$), include a slight enlargement, which is probably not the same as gingivitis or correlated to plaque or BOP as discussed in the article. This could be interesting to follow in another study in relation to cytokines, growth factors and microvascular alterations (34).

BOP ($p<0.01$) was increased, correlated to plaque and showed a reduction with medication, which indicated that gingival status was mirrored in the inflammatory status and its treatments, again it might be interesting to follow also this as well as crevicular fluid in relation to the disease parameters. All registrations were performed

on eight teeth, the first molars and the central incisors, on 32 sites. For caries registration the first molars was the target for registrations. If other teeth seen on the bite-wing radiograph had been registered, significance for increased caries prevalence might have been reached. Also, the control group can be questioned regarding caries activity as caries today is dependent on socioeconomic factors. To let a friend of the same age as the JIA patient be the control could have been a better option as Stockholm centre is considered to be a socioeconomically wealthy area. Furthermore, today bite-wing, is taken on children aged 6, 9, 12, 15 and 19 if they have low or no caries activity, which is the case for the majority of children in Sweden. Children in the control group were coming for check-up with bite-wing more often.

Earlier findings with high prevalence of caries in JIA could probably be explained by the addition of sugar in medicines, and less strict rules of conduct for children with JIA as a cause of the special circumstances. The findings in this study were a little bit better concerning caries frequency but otherwise in accordance with other studies on the subject with some differences in study groups and approach (8, 30, 33, 121).

There were a significantly increased number of severe problems with the oral mucosa, not related to anything specific but they influenced daily life, as for example children avoided food because of it. This has not been reported earlier. There were also significantly more eating and tooth brushing difficulties (Fig 1, 2) associated to findings of facial pain in study two (Fig 3). There are a few studies discussing these problems with a different approach (56, 84, 102, 122).

Salivary flow was equivalent to normal findings in the JIA patients; they reached the level of what is normal. But in several cases the children needed more time, concentration and training before being able to drool and spit as instructed. This was not really possible to perform on a single occasion as in this study. It would have been better to do this saliva collection in a separate appointment. More research concerning saliva flow and quality is therefore required.

Fig 1 Reported eating difficulties compared to controls, in percent frequencies (thesis).

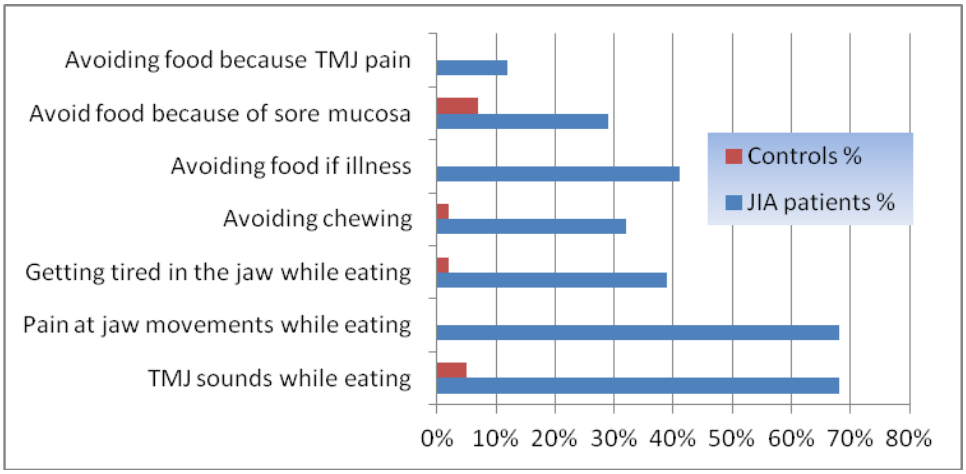


Fig 2 Reported toothbrushing difficulties compared to controls, in percent frequencies (thesis).

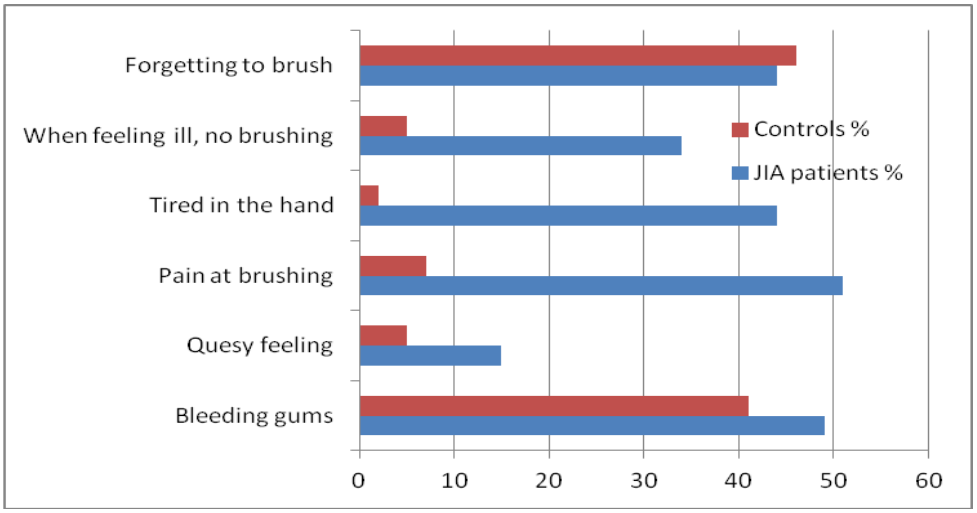
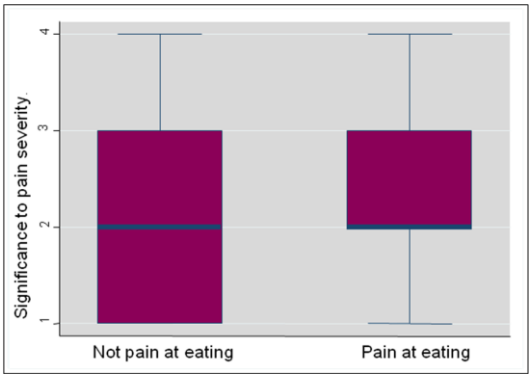


Fig 3 Facial pain is often reported as severe in JIA children with pain during eating (thesis).



7.2 OROFACIAL PAIN AND DYSFUNCTION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A CASE–CONTROL STUDY

Studies report a high frequency of orofacial symptoms compared to controls, whereas this study reported an even higher frequency and also a higher severity. The symptoms were severe for a fifth of the children, and principally all children in the JIA group experienced that the symptoms influenced daily life, mostly of a mild to moderate character but for several children it were severe. The fact that the experience of symptoms were of this dignity, affecting daily life severely was a new finding, not reported earlier.

The study group was relatively small but it still emphasizes that orofacial problems can be devastating.

For future research it would be interesting to study a non selected study group, and to follow a larger number of patients, including also younger children but with the same parameters as used in this study.

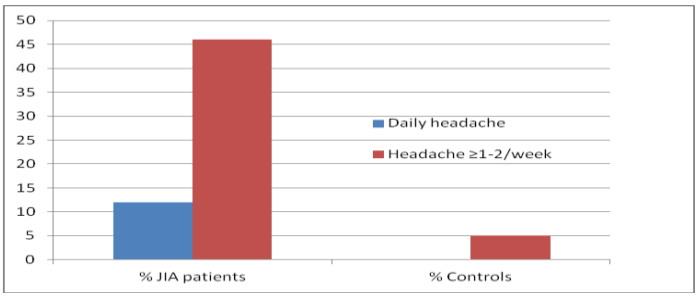
Frequent headache is significantly more common among JIA patients than among controls ($p \leq 0.001$) (thesis), and significantly associated to facial pain ($p \leq 0.001$) (Fig 4).

An examination of the temporomandibular system, used in this study took approximately 15 minutes. Most time consuming in the meeting with the patient and parents was to explain the symptoms and signs, to give coping strategies and if needed discuss a training program.

The information gathered was self-reported symptoms as the children estimated on a VAS scale the degree of pain and its influence on daily life. There was a standard protocol with questions that the majority of the JIA patients had been in touch with before. It was new to the controls and to the newly referred patients. To report symptoms from the latest week has been shown to have the best reliability (96). The questions used in the study have shown a good reliability in other studies among adolescents (94, 95). In a study self- reported orofacial pain amongst adolescents in Sweden had a prevalence of 4.2%, which was in agreement with the controls in our study. In the study group there was only one child without clinical findings and she did not report any subjective problems. However there were many JIA children who reported only mild to moderate pain in spite of many clinical manifestations of pain and dysfunction. Once again, this stresses the importance of a thorough clinical examination of children with JIA.

Pain diaries and pain drawings would have been a complement (73) and could be a subject for future research. Today there are possibilities to use electronic diaries (73).

Fig 4 Frequency of headache ≥ 1-2 times a week compared to controls, in percent frequencies (thesis).



7.3 PERCEIVED ORAL HEALTH IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

Grounded theory is a qualitative method that was chosen in preference to others with the main difference being that they emerged from different scientific disciplines. For example a qualitative method that emanated from European philosophy (phenomenology), and another that originated from linguistics and semiotics (discourse analysis) were considered (123, 124). However, to focus on the essence of a phenomenon or on analyzing the meaning of the words, how and what way language was used, was found less suitable to the research question.

Grounded theory stems from two dominant traditions in sociology and also in generating knowledge in the positivistic tradition that were used in studies one and two. The goal of grounded theory is to develop an explanatory theory of basic social processes, studied in the environments in which they take place. A model or theory is generated, explaining way of thinking and acting (112).

Theoretical sensitivity is an important concept in grounded theory and reflects the use of personal and professional experiences, as well as methodological knowledge and to think abstractly about data in the process of developing theory (125). The concern of this study was to improve the quality of this kind of understanding and knowledge concerning orofacial findings and symptoms in the child's perspective. There is a cultural dilemma in the meeting between the dentist and the patient diagnosed with JIA that has to be considered concerning trustworthiness and concordance between data and result, as well as transferability (117, 119, 126).

The first interviews were checked for credibility concerning data quality by the supervisor in qualitative methodology (Ulrika Hallberg), which contributed to the interview quality. The supervisor helped and supported the scientific framework of codes, categories and main concern, and step-by-step the first author who conducted all

interviews with the same semi structured interview protocol designed the story line. All data in the study was grounded in the interviews. In qualitative research, this so called internal validation is considerably important. Three dentists working with these issues in everyday life, one rheumatologist and one sociologist working with interviews with children and families checked and corrected the data analysis until there was congruence with their rendering of what was said in the interviews.

There are other ways for validation, for example to let the participants read, which is called triangulation. This was not done in this case, for several reasons, mainly as the participants were so young. The results have been presented at international and national research meetings, seminars and workshops with professionals. Results were found adequate, relevant, trustworthy and to elucidate experiences (119, 127, 128).

The results from this qualitative study explained why subjective symptoms are so few and diverse in studies as there were reluctance amongst JIA patients to talk about symptoms, to take treatments as it reminds them of disease, and it also makes the child feel different from others which was very important for a child's identity (82, 123, 129, 130). Another central aspect in the meeting with children diagnosed with JIA were their endeavor to keep control over their lifes and professional aid.

More research is needed, also on how parents perceive the child's orofacial symptoms and the encounter with the dental care. Other important areas for qualitative research are the collaboration between medical and dental care, and the children's need of and compliance to advanced medical and dental treatments.

7.4 ARTHRITIS OF THE TEMPOROMANDIBULAR JOINT – CLINICAL SUSPICION VS. SYNOVITIS ON MRI

There was a significant relationship between clinical findings, clinical suspicion and MRI signs. All patients in the study experienced subjective symptoms.

This study differed from other studies in several respects: a) the clear correspondence between clinical findings and MRI. b) patients were selected with clinical suspicion and had more self-reported subjective symptoms than found in any other studies, c) clinical suspicion of arthritis and MRI signs were graded 0-2.

The degree of enhancement on MRI was considered as a more important sign of current inflammation than the dimension of the synovial membrane or the joint fluid. Küseler 1998, also reported correlation to the degree of enhancement and clinical findings. She also found a few patients without clinical symptoms with enhancement on MRI (107).

The picture (Fig 5) shows contrast enhancement of significant degree of an inflammatory reaction in the joint but also in the surrounding tissue. This can be a sign of increased vascularization around the TMJ and/or inflammatory tissue. In general there is enhancement when edema is present as the capillary permeability increases. TMJ is such a small joint that the synovial layer is difficult to detect. A study of 192 TMJ in children not diagnosed with JIA, showed no abnormalities on contrast enhanced MRI (109). Kalle 2012 argued that MRI examinations revealed contrast enhancement of the soft tissue and the condyle, normally in children and adolescents, therefore subtraction analysis should be considered when defining pathological enhancement of the TMJ in children with JIA (131). In our study contrast enhanced images were acquired in the axial plane which allowed simultaneous visualization and comparison of the contrast enhancement in both joints.

Reduced condylar translation at jaw opening and palpation pain over the TMJ were outstanding findings correlated to MRI signs, graded 0 – 2. Also other authors describe prognostic significance of some clinical findings to structural changes of the condyle (103, 132).

Four authors in their prognostic studies found that reduced condylar translation and pain could improve and there were increased erosions at the follow-up occasion. It was likely that there had been a period with active synovitis affecting condylar growth (48, 103, 132-134), probably like the clinical suspicion of arthritis in our study. Palpation tenderness is validated and shown to be correlated to general disease activity in patients with RA (135).

In a case report by Larheim 1991, a patient developed condylar destruction, which could be verified by MRI during a seven month observation period.

A two years prospective study by Küseler 2005 revealed that all 15 JIA patients, except one presented with fluctuating MRI parameters such as enhancement (95%), joint fluid (23%) and that erosions (71%) increased on MRI followed with six to eight months interval (134). There were no correlations but a slight change to less clinical and subjective symptoms during this time period.

Pedersen 2008 in a two year prospective study following 15 JIA children with four MRI´s, in approximately six months intervals, reported a chronic course with increasing condylar alterations, few symptoms and inflammation on MRI detected in nearly all joints. Decreased translation was the most important correlation to condylar changes even if it not was correlated to MRI changes (103). The children in both studies were under medical treatment since a couple of years.

In a study on rabbits, enhancement of MRI in antigen-induced arthritis in the TMJ, was highly associated with inflammatory changes shown by histology (136).
A study on children with JIA routinely evaluated by MRI regardless of symptoms, 36% showed evidence of active synovitis. 62% of these children were under treatment with at least one conventional or biologic DMARD, often in combination (51). The condylar bony aberrations had a lower incidence and the authors suggested that aggressive therapy resulted in improvement at least in some patients but that the TMJ sometimes was refractory to this treatment as also active synovitis was found evidence for (51). From this the conclusion could be drawn that enhancement can be shown on MRI but that there were more factors involved that we do not know much about. A study points out pro-inflammatory cytokine tumor necrosis factor alpha TNF α control related to clinical findings in patients with RA. This might include children with JIA but more research are needed also on aspects as such (59, 137). From study four the conclusion could be drawn that the degree of enhancement and clinical findings can be related and that treatment modalities can be performed on clinical grounds. The patient's subjective symptoms and treatment needs are relevant in this context.

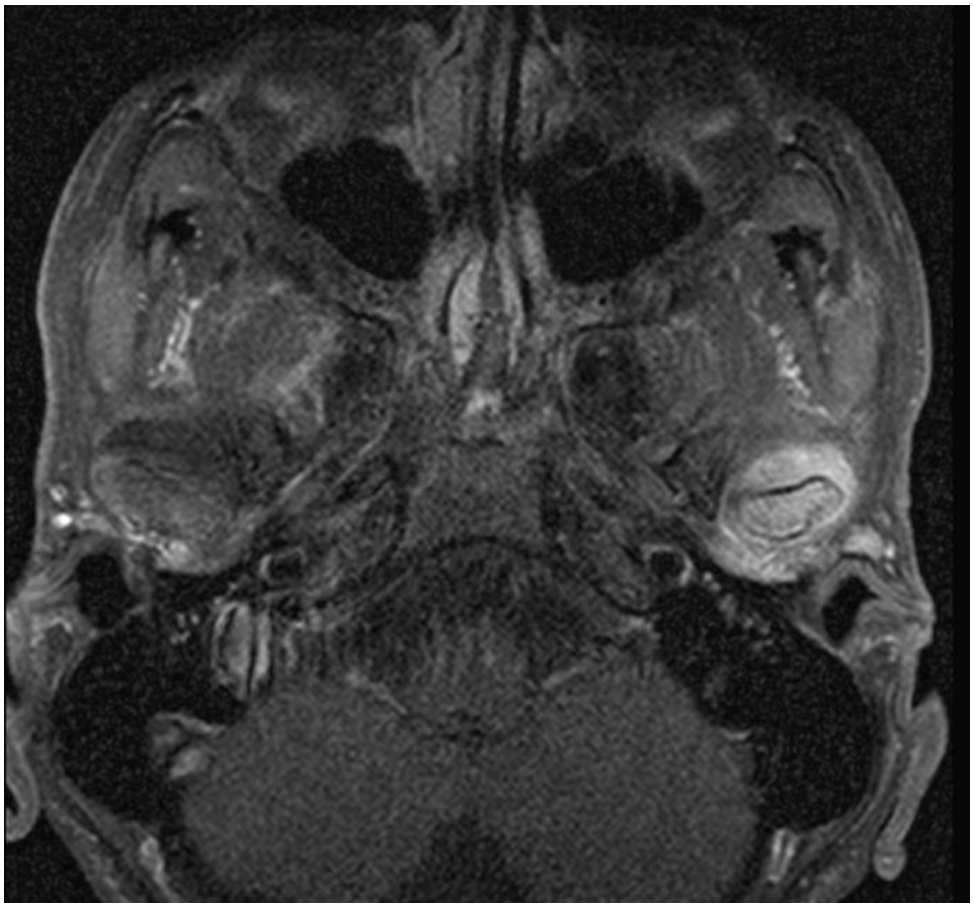


Fig 5 MRI with contrast enhancement, showing synovitis with high intense in the left TMJ of a subject diagnosed with juvenile idiopathic arthritis.

GENERAL DISCUSSION

The main findings of this thesis were the extensive numbers of symptoms from the orofacial area amongst children with JIA, mostly of mild to moderate character but for some very severe, influencing life severely.

Clinical findings of TMJ pain and dysfunction were for an experienced examiner significantly related to local disease activity according to findings on MRI as well as to the general disease activity.

Children perceived symptoms did not always relate to current disease activity but rather to mucoskeletal findings of pain, in need of coping strategies and physiotherapy.

Children needed caregivers for giving words to their problems, for localizing and for coping strategies.

Facial convexity among the JIA children were not as severe as was found some decades ago before the modern therapies. Most children with JIA had a facial appearance that did not differ or differed very little from controls. Anyhow there were vast heterogeneity and there were children with more severe convexity in need of orthodontics and some also of oral surgery.

Some children with normal profile, without bony changes on the condyles had orofacial pain, high in frequency and intensity.

Children with JIA needed a more careful dental care in more aspects, as they also were susceptible to intraoral diseases. Intraoral plaque amounts, marginal bone height, gingival papilla and oral ulcers must be checked for at the intraoral examination.

Before the intraoral examination it is necessary to ask for pain at opening the jaw wide and pain or discomfort at keeping the mouth wide open for a while as the children do not spontaneously tell. Oral ulcers can also be difficult to detect without asking.

These are important findings since this is a big patient group for which a lot can be done with increased knowledge and modern treatment strategies.

In the general dental practice, at the regular check-up of oral health, to give the young patient questions about orofacial pain, headache and examination of the chewing system should be included with the same dignity as the intraoral examination. Orofacial pain and headache is common among adolescents and keeping in mind that children and adolescents mostly do not tell unless an adult helps them with that makes this information a part of education in selfcare. The most important treatment for this kind of pain disorder is information, relaxation and to learn coping strategies. This order could also help to detect children with TMJ arthritis earlier (138).

For children with known JIA diagnoses, an adequate examination and treatment program of the temporomandibular system as well as of the intraoral structures can be regulated and thereby avoiding insecurity both in the medical and dental service.
The study group in this thesis was well taken care of. They were under medical supervision and called to regular controls at the specialized dental care, given information, coping strategies, occlusal appliances, orthodontic treatments and corticoidsteroid injections when TMJ arthritis was suspected, all this in close collaboration with their medical caregivers (60).
The heterogeneity of this patient group was not disclosed, which is a weakness in studies like this. There were a few cases with more severe problems but these disappear in a cohort where most patients are without. Anyhow these few children might take more resources and time in the clinical practice than all the others together. There are also children that do not have the family support as the children in these studies or they have other problems so that they do not have the same possibility to receive complete treatment and support.
In study two, jaw opening capacity was significantly related to findings of structural changes on the panoramic radiograph and in study four to the intensity of enhancements on MRI scans. This emphasizes the importance of regular measurement of jaw opening capacity which other authors agree with (51, 52, 132). It has been reported that jaw opening capacity increased after a more adequate general pharmacological therapy or after corticosteroid injections locally (60).
To see these children regularly was emphasized also by other authors not only to provide pain relief but also to find signs of early TMJ arthritis and growth aberrations. This will not only prevent suffering but also reduce costs for longstanding pain and/or complicated treatments with surgery (122, 139).
This was a small study with relatively few children included; more studies have to be performed.
A study on adults with RA in North America, revealed that they have symptoms for which they see the dentist and occlusal appliances were used by around half of the patients (140). That children also may need this kind of care is more and more recognized also outside the Scandinavian countries. Keeping in mind that children are enduring in silence unless an adult gives them what they need stresses the importance for them to see a dentist specialized in the care for this group of children.

8 LIST OF ABBREVIATIONS

JIA	Juvenile idiopathic arthritis
RA	Rheumatoid arthritis
BOP	Bleeding on probing
PD	Probing depth
TMJ	Temporomandibular joint
TMD	Temporomandibular dysfunction
DMFS	Decayed missed filled surfaces
OPG	Panoramic radiograph
VAS	Visual analogue scale
MRI	Magnetic resonance imaging
CHAQ	Child Health Assessment Questionnaire
ILAR	International League of Associations for Rheumatology
NSAID	non-steroidal anti-inflammatory drugs
DMARD	disease modifying antirheumatic drugs
TNFα	pro-inflammatory cytokine tumour necrosis factor alpha

DEFINITIONS

Pain terminology according to the Classification of Chronic pain, Second Edition by the International Association for the Study of Pain (IASP) (Merskey and Bogduk, 1994).

Pain	An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.
Hyperalgesia	An increased response to stimulus which is normally painful.
Pain threshold	The least experience of pain which a subject can recognize.

9 POPULÄRVETENSKAPLIG SAMMANFATTNING

Ledsjukdom hos barn (JIA) är den vanligast förekommande inflammatoriska sjukdomen hos barn och drabbar cirka14/100 000 varav cirka hälften har kvarstående sjukdom som vuxna. Förbättrade behandlingsmetoder under senare decennier, med nya biologiska läkemedel och effektivare användning av gamla metoder har medfört att barnen idag oftast ser friska ut.

Vetenskapliga studier har visat hög förekomst av käkledsartriter samt försämrad munhälsa hos barn med JIA. Käkledspåverkan kan leda till smärta, inskränkt funktion och försämrad käktillväxt vilket påverkar utseende och ger funktionsstörningar senare i livet. Trots att JIA karaktäriseras av smärta och hög förekomst av till synes asymptomatiska käkledsartriter finns få studier som berör smärta, munhälsa samt barnens egen upplevelse av symtom från tuggapparaten och vilken hjälp de behöver av tandvården. Att tidigt upptäcka tecken på käkledsartrit hos barn med JIA skulle öka möjligheterna att förhindra och förebygga smärta och funktionsnedsättning.

Det övergripande syftet med avhandlingen var att belysa olika aspekter av den orala hälsan i det kliniska mötet med barnet. En fall-kontroll studie designades där tänder, tandkött, munslemhinna, bett, käkfunktion, smärta och käktillväxt registrerades och relaterades till varandra samt till allmänmedicinska data. Grad av smärta, ät- och tandborstningssvårigheter, funktionsstörning och dessa parametrars inverkan på det dagliga livet registrerades också (Studie I-II).

Ett annat syfte var att förbättra vår förståelse för hur barnen upplever sina symtom och mötet med tandvården vilket föranledde en kvalitativ studie med djupintervjuer av barnen (Studie III).

Ytterligare ett annat syfte var att jämföra kliniska fynd av käkledssjukdom med tecken på synovit på magnetkamerabilden (MRI, magnetkamera med kontrast anses vara det objektiva mätinstrumentet för synovit).

Barnen med JIA visade sig ha ökad förekomst av ät- och tuggsvårigheter liksom svårigheter med tandborstning. Som vårdgivare inom tandvården är det högst västenligt att fråga barnen om de har gapsvårigheter och kanske smärta om de måste gapa längre stunder. Det är viktigt att hålla i minnet att barnen sällan berättar detta spontant.

Kliniskt hade de signifikant ökad blödning vid tandköttssondering och mer plaque än kontroller. Dessa barn behöver regelbunden kontroll hos tandvården för att tidigt upptäcka papillatrofi och fästeförlust då det kan föreligga en ökad risk för parodontal sjukdom. Tandvården bör också erbjuda individuellt utformade munhygien

instruktioner. Då det förelåg en ökad förekomst av munsår bör barnet tillfrågas om munsår eftersom det är en av orsakerna till ätsvårigheter och erbjudas behandlingsstrategier för dessa.

Ansiktssmärta och käkfunktionsstörningar visade sig utgöra en viktig del av vardagliga symtom hos barn med JIA. Barnen behöver därför information om hur besvären ska hanteras och ibland behandling.

Att regelbundet undersöka smärta och käkfunktion är nödvändigt för att tidigt upptäcka tecken på käkledsartrit och behandlingsbehov. Diagnostiska parametrar som minskad gapförmåga, nedsatt glidrörelse av kondylen och smärta vid palpation av käkleden var de mest signifikanta kliniska fynden för aktiv synovit i relation till MRI fynd.

En konvex ansiktsprofil var vanlig jämfört med kontroller men grav tillväxtstörning var däremot ovanligt.

I mötet med barnen är det angeläget att komma ihåg att de ofta uthärdar i tysthet vad gäller smärta och funktionsnedsättning, därför kan de behöva hjälp av en vuxen att sätta ord på symtomen. Som vårdgivare är det viktigt att förutom individuellt anpassade behandlingsstrategier för minskad inflammation, smärta och god funktion, lyssna på barnet med fokus på empati, uppmuntran och normalisering av symtomen. En vårdgivade bör också vara försiktig med att peka ut diagnoser och funktionsnedsättningar eftersom de är viktiga för barnets identitet och kan upplevas kränkande.

Sammanfattningsvis; ny kunskap i denna avhandling är omfattningen av orofaciala symptom och kliniska fynd hos barn diagnostiserade med JIA, samt hur dessa påverkar barnet. För många var dessa symtom de som påverkade vardagen mest. Barn uthärdar sina käkledsymtom i tysthet och behöver vuxna och vårdgivare för empati, strategier, uppmuntran och behandling. Kliniska fynd visade korrelation med synovitfynd på MRI varför diagnos av käkledsartrit i vissa fall bör kunna ställas på klinisk grund.

10 THESIS SUMMARY

Orofacial pain and dysfunction was a substantial part of the symptoms JIA children had to cope with in daily life.
Most children had experienced eating and toothbrushing difficulties.

Convex profile was common but micrognathia was rare.

To regularly perform a clinical orofacial examination of pain and jaw function was mandatory to disclose disease activity and treatment needs.

Regular check up of the gingiva concerning dental hygiene, papilla atrophy and attachment loss is to be recommended as the children might have a higher susceptibility for parodontal diseases.

At examination and treatment the mucosal ulcers should be addressed as they constitute a part of the eating difficulties.

Clinical suspicion of arthritis showed correlation to intensity of enhancement on MRI scans.

The diagnostic parameters of reduced jaw opening, reduced palpated translation of the condyle and palpation pain over the temporomandibular joint were the most significant findings correlated to MRI signs of active synovitis.

JIA children often endured their pain and dysfunction in silence.

Children needed adults and caregivers to give words to their problems, information, coping strategies and sometimes treatments. Children also needed caregivers for normalizing and encouragement to keep their jaw mobility.

The caregivers approach to the child was very important. Diagnoses and disabilities were shown to be central for the self identity and pointing out differences from healthy children could be considered humiliating.

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