Chapter 10

General discussion
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In absence of clear knowledge of the exact pathophysiology and risk factors for arthralgia of the temporomandibular joint (TMJ), treatment is usually focused on pain relieve and regaining mandibular function. However, treatment duration and outcome are usually hard to predict. The general aim of this thesis was to investigate the clinical and cost effectiveness of arthrocentesis as initial treatment and explore the applicability in the TMJ of a related therapeutic treatment modality that proved to be successful in treating arthralgia of the knee joint, i.e. viscosupplementation.

In this chapter the results of this thesis are discussed and placed into a broader clinical and economical perspective. Furthermore, future research directions are considered, especially with regard to intra-articular fluid analysis and the role of minimally invasive procedures in the treatment strategy of arthralgia of the TMJ.

Arthrocentesis as initial treatment modality

The effectiveness of arthrocentesis as treatment modality for TMJ arthropathy has been extensively described in the literature. Success rates up to 91% have been reported for the use of arthrocentesis in anterior disc displacement without reduction. Although evidence is still inconclusive, it seems that arthrocentesis has indeed a beneficial effect on pain and impairment of mandibular motion. Al-Belasy and Dolwick concluded that arthrocentesis is a highly efficient procedure with low morbidity. The results of the systematic review described in chapter 2 indicate that lavage of the TMJ is slightly more effective than non-surgical treatment with regard to pain reduction. However, the available evidence does not substantially support superiority of TMJ lavage, especially with regard to improvement of mandibular movement.

Currently, treatment of TMJ arthralgia usually starts with non-invasive treatment. Only when the result of this treatment is not satisfactory invasive treatment modalities are considered. This order seems to be mainly based on the non-invasive and supposed reversible nature of conventional therapy and does not seem to be substantiated by scientific evidence. Arthrocentesis (often supplemented with injection of anti-inflammatory substances, such as corticosteroids) and arthroscopic surgical procedures have shown to be effective even when conventional therapy is not satisfactory. Arthrocentesis is considered to be a highly efficient procedure with low morbidity. Therefore, it seems reasonable to reconsider the role of arthrocentesis in the treatment strategy of TMJ arthropathy.

The results of the randomized controlled trial described in chapter 3 indicate that it is the lavage of the joint space that mainly accounts for the effectiveness of the treatment, regardless the addition of dexamethasone. Although dexamethasone modifies the vascular response during the inflammatory process and inhibits destructive enzymes and the actions of inflammatory cells, this study suggests that the possible effect of additional dexamethasone was not clinically relevant. In the study design, arthrocentesis...
was applied as initial treatment. Under this experimental condition, in both groups the TMJ pain declined, maximum interincisal opening (MIO) improved, and the Mandibular Function Impairment Questionnaire (MFIQ) score decreased. However, this study was not designed to investigate the effectiveness of arthrocentesis as initial treatment. Moreover, the sample size was too small to be able to allow firm conclusions in this regard. Therefore, based on the promising results of this study, an additional randomized controlled trial was conducted to investigate the effectiveness of arthrocentesis as initial treatment compared to the conventional treatment approach, which was referred to as ‘care as usual’ (CAU). This study is reported in detail in chapter 4. In particular, TMJ pain seemed to decrease more rapidly after arthrocentesis as compared to CAU. Furthermore, when considered in economical perspective as is described in chapter 5, the results suggest that arthrocentesis as compared to CAU is the best initial therapy for the treatment of TMJ arthralgia. Arthrocentesis seems to be associated with better health outcomes and lower costs than CAU.

Although additional studies are indicated to allow more definitive conclusions, based on these four chapters, it is doubtful whether conventional care should still be preferred as initial therapy, since its indication is probably mainly based on its non-invasive character and is lacking scientific evidence. Therefore, the treatment order for TMJ arthralgia, in which conventional treatment is offered first, as is suggested in currently available guidelines (AAOP guidelines for orofacial pain, ASTMJS guidelines, RCDSO guidelines for diagnosis and treatment of TMD) should be reconsidered.

Pathophysiology of TMJ arthropathy

In order to develop effective treatment modalities or strategies, it is important to understand the pathophysiological mechanisms involved. Therefore, many studies have been conducted to investigate different parts of the pathophysiological mechanisms involved in TMJ arthralgia. However, still most of the current understanding of the pathophysiology of arthropathies, e.g. articular cartilage maintenance and degradation, is derived from large joints, in particular the knee joint. One of the most prominent theories in this context is the ‘hypoxia-reperfusion injury’ theory, which is stated in many textbooks on this subject. However, the few studies that could be included in the systematic review described in chapter 6 did not provide any evidence to support or reject the hypothesis that hypoxia-reperfusion plays a (major) role in TMJ osteoarthritis. Positive but weak evidence supports the hypothesis that hypoxia-reperfusion injury occurs in osteoarthritis in the knee.

An important difference between the TMJ and the knee joint is the type of cartilage that forms the articular lining. In the TMJ the fibrocartilage lining predominantly contains collagen type I, whereas hyaline cartilage in the knee joint mainly consists of collagen type II. However, the results of the study that was described in chapter 7 indicate that the relative concentrations of specific markers for type I and II collagen degradation, CTX-I and II respectively, did not significantly differ between the two joints. The inflammatory
component was more distinct in osteoarthritis of the TMJ as compared to the knee joint. According to these findings, the type of collagen seems to be of minor importance when comparing TMJ and knee joint osteoarthritis. However, the more prominent role of the inflammation marker, i.e. PGE₂, suggests differences in pathophysiology between the TMJ and the knee joint. Therefore, results obtained from research in the knee joint should not be applied to the TMJ indiscriminately.

The same markers were investigated in chapter 8, where a comparison was made between TMJ osteoarthritis and healthy symptom-free joints. Assumed changes in synovial fluid concentrations of CTX-I, CTX-II, cartilage oligomeric matrix protein (COMP) and PGE₂ seem to occur proportionally, indicating that more distinct inflammation is accompanied by more cartilage degradation. These findings are consistent with findings in knee joint osteoarthritis. Furthermore, an unexpected large contribution of CTX-II in TMJ osteoarthritis was found, both in chapters 7 and 8. Although the fibrocartilage lining in the TMJ mainly consists of type I collagen, the superficial layer of the articular fibrocartilage may contain more collagen type II than the inner part, especially with regard to the articular disc. Therefore, CTX-II may be useful to quantify the activity of cartilage degradation in TMJ OA.

**Viscosupplementation**

In order to sufficiently investigate the effectiveness of treatment options for TMJ arthralgia it is essential, according to the current standards, to obtain evidence using a randomized, double blind, placebo controlled trial research design. However, for therapeutic options that consist of the intra-articular application of therapeutic agents, such a research design has still not been reported. In chapter 9 a technique is described that may allow a double blind, placebo controlled design. Although the technique was described in a case report, its feasibility seems promising. Furthermore, the application scheme, that was derived from investigations in the knee joint, seems to have a beneficial effect on the health outcome as well, although the reported case was a severe of chronic TMJ pain.

**Conclusions**

Based on evidence available in the literature and the results described in this thesis, a more prominent place for arthrocentesis in the treatment TMJ arthralgia appears to be justified. The indication of arthrocentesis as initial treatment results in better health outcomes, especially with regard to pain reduction, and also may contribute to the reduction of healthcare costs. However, since the clinical effectiveness of arthrocentesis and CAU as initial treatment did not differ significantly over time, this new treatment strategy is not likely to decrease the number of cases that remain symptomatic. Therefore, modification of existing treatment modalities or development of novel therapeutic options is necessary to increase the clinical effectiveness. Hereby treatment options that have been
tested in larger synovial joints may serve as a starting point. However, thoroughly testing of these treatment modalities in the TMJ itself remains needed, because differences in pathophysiology between the TMJ and other joints may influence the clinical results.

Future perspectives

In general, and parallel to clinical effectiveness, cost effectiveness is becoming an important focus in medicine. This also applies to the treatment of TMJ disorders. Causal therapy is not yet within reach, because the pathophysiology is still not clear. Therefore, exploration and testing of hypotheses with regard to pathologic mechanisms that may be involved in TMJ diseases still remains essential in order to develop more targeted treatment modalities. Meanwhile, modification of the treatment strategy may result in improvement of clinical effectiveness as well as in cost reduction. Investigating the influence of applying arthrocentesis as initial therapy was a first step towards a more cost effective approach in the management of TMJ arthralgia. An international multicentre randomized controlled trial investigating the clinical and cost effectiveness of arthrocentesis as initial treatment may allow more definite conclusions to substantiate reconsideration of the international guidelines for the treatment of arthralgia and may facilitate implementation if guidelines are revised.

Based on the results of research performed in the knee joint, a possible additional step may be to test the effectiveness of viscosupplementation in TMJ arthralgia in a double blind, placebo controlled trial. Subsequently, when viscosupplementation would appear to be effective in the TMJ as well, its role has to be determined in order to further improve cost effectiveness in the management of TMJ arthralgia.
References


