Pain Patterns and a novel way of evaluation of therapy outcome in myogenous temporomandibular disorders

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SUMMARY

Temporomandibular Disorders (TMD) is a collective term embracing a number of clinical problems including conditions of the masticatory musculature, the temporomandibular joint and/or associated structures. These disorders are characterized by chronic pain and restricted jaw movements. Muscle disorders alone occur in one third of the patients, corresponding to the myofascial subtypes Ia and Ib of the Research Diagnostic Criteria of TMD (RDC/TMD), further denoted as myogenous TMD. Although the RDC/TMD does not differentiate between patients with and without pronounced occlusal interferences, we have made such a differentiation in a search for an optimal therapy strategy for myogenous TMD.

Regarding patients without pronounced occlusal interferences, a therapy with an occlusal appliance (splint therapy) is commonly used in dental practice. In the absence of somatic factors in the dentition as well as in the temporomandibular joint, mainly myogenous and psychobiological, or psychosocial factors are involved in the aetiology of myogenous TMD. Hence, physiotherapy which includes, apart from massage, aspects of cognitive-behavioural therapy, might be a basic therapy for myogenous TMD. It is therefore of interest to compare treatment outcome between physiotherapy and splint therapy. 'Simple' myogenous TMD patients have been selected, i.e. patients without possibly confounding influences from the Temporomandibular joint, dentition, major psycho-social factors, or factors related to general health. The effect of physiotherapy or splint therapy on signs and symptoms will then be mostly related to myogenous and psychobiological factors.

Furthermore, we have selected myogenous TMD patients with the same profile of psycho-social factors and general health, but with pronounced occlusal interferences. These interferences were mainly of iatrogenic origin, i.e. related to restorative dental work (fillings and/or crowns). For this reason alone, Occlusal Adjustment (OA) could be indicated, and carried out while hardly, if at all, affecting healthy enamel of teeth. In order to examine a possible influence of pronounced occlusal interferences on signs and symptoms of myogenous TMD, the effectiveness as treatment in this respect has been compared between solely OA therapy and a combination of occlusal splint therapy and OA treatment (Sp-OA). The rationale for choosing Sp-OA as a control therapy was to ensure that the combination therapy included a component (splint therapy) of known effectiveness for TMD. If as a null hypothesis, solely OA therapy were entirely unsuccessful to diminish signs and symptoms of myogenous TMD, the effectiveness of solely OA would be much smaller than that of Sp-OA.

A novel way of therapy evaluation has been introduced in this thesis, which is applicable for chronic pain patients in general. The effect of, for example, splint therapy has

previously been compared with other therapies or conditions using a traditional Randomized Controlled Trial (RCT), in which evaluation has occurred after a constant duration of treatment of 6 weeks to 3 months. However, the duration of treatment varies in clinical care as it depends on the type of therapy as well as on a patient's speed of recovery. Allowing variation of treatment duration in RCTs complies with clinical care and enables a realistic comparison of the therapeutic potential of different therapies. Such RCTs also address all three features of treatment outcome that are of interest for a complete costs-effectiveness-analysis, i.e. (1) the time and number of visits needed to come to the decision whether a patient's treatment is either successful or unsuccessful, (2) success rate, i.e. the percentage of patients whose treatment is successful, and (3) therapy effectiveness which is based on the magnitude of an outcome variable averaged across patients.

In order to examine features (1) and (2), it is necessary to measure change in the various outcome variables from individual patients, which is due to treatment rather than to chance fluctuations. Traditionally, the raw change in scores has been considered to determine the effect of treatment. A statistically Reliable Change (*RC*) in scores from two measurements should exceed the change caused by chance fluctuations, denoted as the Smallest Detectable Difference (*SDD*; thus *RC* > *SDD*). Regarding *RC* and *SDD*, a change in a score value should not only exceed the measurement error of the instrument. Additionally, a change should occur in the long-term that exceeds fluctuations of the biological origin within the entire interval of repeated clinical examinations. The *SDD* of pain scores is determined using repeated scores. Data on *SDD* of pain intensity from the literature were related to short measurement intervals, i.e. from a couple of hours up to 1 week. In order to gain information on natural fluctuations of pain intensity during a longer period, this intensity was recorded at 4 daily moments using a 2-week pain diary (**Chapters 2 and 3**).

The aims of **Chapter 2** were: (1) to characterize pain related to myogenous TMD, during 2 weeks and in terms of intensity, frequency, duration, and behaviour; (2) to identify main intraday pain patterns and to examine whether subgroups of patients in this respect differed in clinical, demographic, pain and sleep variables, in psychosocial factors, and in the use of medication; and (3) to investigate some possible inter-day trends of pain intensity. Patients with myogenous TMD formed two subgroups regarding daily pattern of pain intensity (79%: maximal pain late in the day, PM patients; 21%: early in the day, AM patients), which might be related to differences in processes that influence pain sensitivity and jaw muscle activation. Daily mean pain intensity was constant for the various diary days. This

finding suggests that a possible effect of counselling at the intake was stabilized as counselling occurred, on average, 2.4 weeks before the start of the pain diary.

The first aim of **Chapter 3** was to determine *SDDs* for scores of pain intensity from a 100 mm Visual Analogue Scale (VAS), for relatively long test–retest intervals. Apart from a 2-week pain diary, VAS-scores were also obtained from a cold-pressor-test with an interval of several months. A regression analysis on duplicate VAS-scores was used to examine whether *SDD* is invariant to the baseline scores (second aim). The third aim was to examine the extent to which *RC* (inter-patient change > *SDD*) detects clinically important difference (*CID*). *CID* is the difference in mean scores of pain intensity in a questionnaire, obtained before and after a therapy of known effectiveness. *CID* is a measure of the potential of a therapy. The long-term *SDD* was 49 mm for pain intensity and *CID* was 24 mm. *SDD* was largely invariant to the baseline scores. Because *RC* (> 49 mm) exceeds *CID*, *RC* might serve as an indicator of a patient's change in pain intensity which is clinically important and probably also important for a patient's perception of treatment effect. However, *RC* could be detected in only 17% of the patients, mainly because the baseline of pain intensity is smaller than the long-term *SDD* in 67% of the patients.

The aim of **Chapter 4** was to determine *SDD* for scoring pain behaviour on a 0-5 point adjectival scale in the pain diary and to examine whether this *SDD* is similar to that for pain intensity from a VAS, using normalization with respect to scale range. Furthermore, **t**he relationship was explored between these *SDDs* (inter-patient change) with *CID* and Cohen's effect size of therapy (*ES*; the ratio between *CID* and the baseline SD). The normalized *SDD*, *CID* and *ES* values were similar for both types of scores on different scales, i.e. in the long-term 48.8 – 54.5 scale-% (*SDD*), 24.2 – 22.6 scale-% (*CID*) and 1.09 – 1.38 (*ES*).

Previously, Routine Outcome Monitoring (ROM) has been introduced to help a clinician to end a patient's treatment in an objective way, thus to control treatment duration and the number of visits needed. ROM uses multi-dimensional questionnaires as measuring instruments to limit the *SDD* of an overall score. ROM considers raw changes in overall score and normative levels to define *RC* and functional status. A patient's functional status corresponds to a score level that is related to a sufficiently low severity of signs and symptoms. The criterion for a 'successful' treatment in ROM is that both *RC* has occurred and the overall score level becomes lower than the Upper Limit of Functional Status (*ULFS*).

In order to be clinically relevant, a change in raw scores should not only comply with statistical criteria but a patient should also consider the change beneficial. A patient with a high level of signs and symptoms must show a larger improvement in raw score level to pass

ULFS, than a patient with a lower level. A large improvement is likely concomitant with a patient's perception of a large effect of treatment. In contrast, a patient whose score level at baseline is located just above *ULFS* (at a distance of *SDD*), and whose score level passes just below *ULFS* with *RC* (attaining statistically a 'successful' treatment), likely perceives a smaller effect of treatment. This perceived smaller effect may be unsatisfactory for a chronic pain patient because the expectation of treatment effect is high (60%) for such patients. In order to avoid a possible discrepancy between a statistical treatment outcome and a patient's perception of treatment effect, a novel procedure has been introduced in **Chapter 5** which uses relative change rather than raw change in score levels. A patient with the largest baseline scores of signs and symptoms in a sample requires a particular relative decrease with a treatment factor *T*, just to pass *ULFS*. It has been shown mathematically that any patient with smaller baselines will attain the zone of functional status (hence a successful treatment) with the same relative decrease in score values (same factor *T*). Because the end levels of patients with smaller baselines will be lower with respect to *ULFS* than with a traditional ROM, such patients will perceive more treatment effect by using relative change. Furthermore, it is known that any chronic pain patient, regardless of baseline, will perceive a similar treatment effect following a particular relative decrease in pain intensity. This perceived effect will be related to a patient's assessment of 'much improved' or better, if functional status (achieved through factor *T*) corresponds to residual levels of signs and symptoms which occasionally occur in a healthy population.

Relative change is concomitant with large chance fluctuations ('noise') when the basic score values of items are small. Items with significantly large basic score values were therefore selected for monitoring relative change by using short-term *SDDs* from single variables as a threshold. Thus relative change was tested adaptively only for items which were related to significantly pronounced signs and symptoms. Relative changes from such items have been summarized in the index 'Treatment Duration Control' (*TDC*; **Chapter 5**). A cut-off point of *TDC*, which is related to a global relative change required for any patient to pass *ULFS* ('factor *T*'), indicates a clinician when to end treatment. TDC based on the data from a blinded assessor, serves to determine treatment outcome in an RCT.

In **Chapter 6**, physiotherapy was compared with occlusal splint therapy in an RCT in which *TDC* was used, thus enabling variation in treatment duration. Both types of therapy included preceding counselling on TMD. Number of visits needed, treatment duration, success rate and *TDC*-values following treatment and a one-year follow-up (measure of effectiveness) were determined as treatment outcomes. Cohen's *d* (measure of effect size of a

therapy) was determined for pain intensity. Using a theoretical model, the overall success rate was assessed for stepped-care, and the effect of therapy sequence on this success rate was examined (stepped-care: a second of the two studied therapies was applied if the first treatment was unsuccessful). Success rate and effectiveness were similar for physiotherapy and splint therapy (long-term success rate: 51.3-60.0%; *TDC*: -0.512 – -0.575). Cohen's *d* was large (> 0.80), i.e. 0.86 (physiotherapy) and 1.39 (splint therapy). Treatment duration was shorter for physiotherapy (on average 10.4 weeks less). However, splint therapy needed 7.1 less visits. Physiotherapy may be preferred as initial therapy over occlusal splint therapy in stepped-care of myogenous TMD. With a similar success rate and effectiveness, physiotherapy has a shorter duration. Thus patients whose initial physiotherapy is unsuccessful can continue earlier with subsequent treatment. The stepped-care model reinforces the conclusion on therapy preference as the overall success rate hardly depends on therapy sequence.

Analogous to Chapter 6, OA therapy was compared with Sp-OA therapy in **Chapter 7**. Success rate and effectiveness were similar for OA therapy and Sp-OA therapy (long-term success rate: 52.2-60.9%; *TDC*: -0.490 – -0.585). Cohen's *d* was large (> 0.80), i.e. 0.91 (OA) and 1.04 (Sp-OA). Treatment duration was, on average 15.5 weeks shorter for OA therapy than for Sp-OA therapy, and OA needed 1.8 less visits. Because of the large similarity in effectiveness between OA and Sp-OA therapy, the null hypothesis can be rejected, *i.e.* that solely OA therapy would be entirely unsuccessful to diminish signs and symptoms of myogenous TMD. In contrast, our study shows that a combination therapy of occlusal splint therapy with OA has no added value.

Hence, if pronounced occlusal interferences are mainly of iatrogenic origin (in itself a sufficient reason to apply OA), and these interferences occur concomitantly with signs and symptoms of myogenous TMD, Occlusal-Adjustment-therapy is then the therapy of preference for myogenous TMD. Like physiotherapy as preferred therapy for patients without pronounced occlusal interferences, the duration of OA is similarly short (mean 13.8 weeks). Moreover, OA needs the smallest number of visits (mean 3.6) of all therapies tested. The recommendations on OA refer to a protocol which includes (1) counselling on TMD, (2) a check on feasibility of OA using dental casts in an articulator, and (3) three occasions for possible OA with an inter-visit interval of 3 weeks..

The end conclusion in Chapter 8 is that for patients with basic myogenous TMD, and without pronounced occlusal interferences, an optimal therapy strategy includes physiotherapy as initial therapy, which if unsuccessful is succeeded by splint therapy. For

patients with pronounced occlusal interferences for which occlusal adjustment is feasible, an optimal strategy is solely OA as initial therapy, which if unsuccessful is succeeded by physiotherapy.

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