TREATMENT POSSIBILITIES FOR TEMPOROMANDIBULAR DISORDERS

Ph.D. Thesis Booklet

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1. INTRODUCTION

1.1. Overview of the topic

1.1.1. What is the topic?

Our primary focus is on evaluating conservative and semi-conservative treatment options for temporomandibular disorders, including both myogenic and arthrogenic cases.

1.1.2. What is the problem to solve?

There is no universal agreement on the best treatment strategy for temporomandibular disorders and the scientific evidence supporting the therapeutic possibilities is often limited and controversial.

1.1.3. What is the importance of the topic?

TMD is the third most common stomatological disorder which affects the masticatory system including the muscles and joints. The main symptom of the disorder is pain, which has a prominent impact on patients' quality of life. Besides this symptom, the limited functions are also crucial inferences, that can lead to several challenges for patients. The unknown background and the lack of prompt etiology make healthcare workers face many obstacles in treatment possibilities.

1.1.4. What would be the impact of our research results?

Through a consistent assessment of different treatment possibilities for TMDs, including myogenic and arthrogenic disorders, the effectiveness of these modalities can be evaluated which have a prominent effect on patients' lifestyles, incorporating functional and psychological improvements. Using objective disease monitoring and diagnostic

systems allows healthcare workers to personalize the treatment possibilities for patients.

2. OBJECTIVES

2.1. Study I. – Additional splint therapy has no superiority in myogenic temporomandibular disorders

Even though previous systematic reviews and meta-analyses compared reversible treatment possibilities, the limitations were the high heterogeneity and the lack of high-quality evidence, making it difficult to observe consistent outcomes. Additionally, no meta-analysis has yet explored the most common combination therapies for myogenic TMD. Our review aims to narrow the intervention group to achieve more homogeneous results, comparing combination therapy (splint therapy along with physiotherapy, manual therapy, and counseling) and physiotherapy, manual therapy, and counseling in adults with myogenic TMD.

2.2. Study II. Efficacy of different intraarticular injection materials in the arthrocentesis of arthrogenic temporomandibular disorders

Despite a prior network meta-analysis conducted in this topic, which evaluated not only the conservative, minimally invasive but also the surgical treatment possibilities for arthrogenic TMD, the stage of the disorder was not mentioned, thus a high heterogeneity was observed in the diagnostic method and in the results.

This systematic review and network meta-analysis aimed to summarize the treatment outcomes of recent intraarticular devices developed for the management of arthrogenic TMD in a homogenous population, focusing on different follow-up periods.

3. METHODS

Study I:

The eligibility criteria for Study I were based on our PICO (patient characteristics, type of intervention, control, and outcome) format. Two-armed interventional randomized controlled trials were included. The population was adult patients diagnosed with myogenic temporomandibular disorders; the intervention was combined therapy (splint + physiotherapy), the comparator was physiotherapy, manual therapy, and counseling, while the main outcomes were the extent of mouth opening and pain perception. Only English randomized controlled trials were monitored.

Patients with a history of head trauma, congenital abnormalities and mental, physical problems were excluded.

Two kinds of meta-analysis were conducted, a „self-control" one, where the control and the treatment groups were compared to the baseline values, to conclude a statistically significant effect. In the second kind of meta-analysis the treatment and the control groups were compared to each other. A random effect model was used to pool the effect sizes. The standard deviation (SD) of the change from baseline was calculated by adding the baseline and follow-up time. Each follow-up time were evaulated separately. For Between-study heterogeneity the Cochrane Q test and Higgins and Thompson's I^2 statistics were used. Forest plots were used to graphically summarize the results.

Study II:

The PICO format was used, which included patient characteristics, type of intervention, control, and outcome. Based on our protocol, we included RCTs investigating (P) adults (>18 years) with arthrogenic, Wilkes stage II-V TMD. As a network meta-analysis was conducted on all the medical devices that can be used for arthrocentesis. As outcomes: the extent of maximum mouth opening (MMO), protrusion, joint sound, and pain perception were measured. Only studies that provided baseline and follow-up data were included. Moreover, only English articles were encompassed in the review.

The mean differences (MD) and the standard deviations were evaulated according to the Cochrane Handbook. A network plot was created to check if the networks were fully connected. Pairwise Bayesian NMAs were performed. Random-effects models were used to calculate the pooled MD with a pre-specified 95% confidence interval (CI). A node-splitting analysis was performed to assess consistency. The surface under the cumulative ranking (SUCRA) curve values were calculated based on their posterior probabilities to rank different treatments.

Both of the conducted MAs adhered to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) 2020 recommendations. The Cochrane Handbook (https://training.cochrane.org/handbook) was used to conduct the reviews.

The studies were registered with Prospero (https://www.crd.york.ac.uk/prospero/) under the registration number Study I: CRD42021284777 Study II: CRD42022331212.

4. RESULTS

4.1. Study I.

4.1.1.Maximum mouth opening

The outcome was measured in mm using a caliper or a ruler. An analysis was conducted on the baseline and 1-month follow-up changes between the intervention and the control group using 2 articles. In this analysis, a 0.07 mm difference was detected, which is statistically insignificant and clinically irrelevant. The effect size in the intervention group was 3.69 (95% CI: -0.34;7.72) in mm, while in the comparator group it was 3.62 (95% CI: -3.43;10.67) in mm.

Another analysis was performed at 1-month follow-up, comparing two articles. The effect size was -1.11 (95% CI: -2.83;0.61) with low heterogeneity(I2=0%). The results showed a modest decrease in the intervention group. The overall effect was statistically insignificant and clinically not relevant.

4.1.2. Pain perception

Pain perception was measured using the visual analog scale (VAS) or the numerical rating scale (NRS). As the pain perception is highly influenced by many factors, it is considered as a secondary outcome.

The baseline and 1-month follow-up results of the intervention and control groups were analyzed in five articles. In the intervention group, the effect size was -2.54 (95% CI: -3.38; -1.70), while in the comparator group it was -2.33 (95% CI: -4.06; -0.61). There is a slight difference between the two groups which is clinically not relevant and statistically not significant.

Furthermore, the 1-month results were reported from four articles.The effect size was -0.03 (95% CI: -0.64;0.58), which is neither clinically nor statistically relevant.

4.2. Study II.

4.2.1. Maximum mouth opening

This outcome was measured in 3 different follow-up periods: 1,3,12 months. For the short-term:1-month-6 articles were included in the analysis. The different treatments were ranked by calculating the surface under the cumulative ranking (SUCRA) curve values based on their posterior probability, with the highest ranking of saline-PRP (94.8%), where the effect size was: 4.48 mm (95% CI: –0.77, 9.87). The result is clinically relevant, as it shows a 4.48 mm increase in MMO.

7 studies were included for the 3-month follow-up, where the effects of saline-steroid and saline-PRP were MD=3.36 mm (CI: –4.70, 10.46) and MD=3.49 mm (CI: –4.23, 10.81). The effects are clinically relevant, as they show a 3.36- and 3.49-mm increase in MMO. The treatments included were saline-PRP, saline-steroid, saline-hyaluronic acid and saline.

4 studies were included for the analysis of 12-month, the saline-HA with glucoseamin ranked as the highest with the effect size of 3.07 mm (95% CI: –2.06, 8.41). The saline-streoid had the same effect with 3.07 (CI: –4.34, 10.24) in MD.

4.2.2. Pain perception

This outcome was also measured in 3 different time points on the numeric rating scale, scoring from 0 to 10. As the outcome is mainly dependent on the patient's subjective opinion, it was considered as a secondary outcome. For the 1-month follow-up 5 studies were included, saline-PRP reached a clincally relevant result with the effect size of -2.89 (95% CI:

–6.17, 0.57) in MD. It means that the pain perception reduced with 2.89 in patients who got the saline-PRP treatment. The other treatments did not reach a clinically relevant level, as saline-HA resulted in -0.72 (95% CI: -2.35; 0.93). For the medium-term follow-up 3 months, still the saline-PRP reached the best ranking with the effect of MD=–2.72 (95% CI: –5.80, 0.35), with 78%. The second ranking was very similar to the 1-month follow-up result, as saline- HA reached a decrease with 1.01 (95% CI: -2.63;0.70) on the NRS. For the 1-year follow-up 4 studies were included, the saline-PRP resulted in (MD=–1.86, 95% CI: –5.72, 2.18), with the highest ranking of 73.5%. The saline usage decreased the pain perception with 1.44 (95% CI: –5.72, 2.18), while the saline-steroid resulted in a decrease with 1.14 (95% CI: -9.45; 7.24).

5. CONCLUSION

5.1. Study I.

For the conservative treatment of temporomandibular disorders combination therapy and physiotherapy can be used, however, a slight difference was observed between the two groups, thus the usage of additional splint therapy can be questioned. Moreover, regarding the results a multidisciplinary team should be emphasized, especially drawing attention to physiotherapy more.

5.2. Study II.

Relating to the treatment of arthrogenic temporomandibular disorders, the intraarticular joint lavage showed promising outcomes, particularly the PRP-saline combination therapy yielded a remarkable increase both in mouth opening and pain reduction.Saline-steroid combination therapy showed a prominent enhancement for both outcomes, however the side effects of the treatment must be considered.

6. BIBLIOGRAPHY OF THE CANDIDATE'S PUBLICATIONS

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