On the treatment of tennis elbow. Effectiveness and prognostics of braces and physical therapy
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Chapter VIII

General discussion
General discussion

Since more than a century, tennis elbow is known as a highly prevalent and sometimes disabling complaint. It is a complaint that limits patients in daily activities, in some patients causing problems in work and even absenteeism. Both loss of unpaid and paid labour makes it a complaint with not only implications for the patients, but also with economical implications. The more important it is to know and provide optimal medical care, looking at both the effectiveness and costs of treatment strategies. Up to now, there is insufficient evidence in the medical literature to allow drawing definitive conclusions concerning effectiveness of widely used approaches, like the use of a brace or physical therapy treatment. In this thesis, the effectiveness of brace-only treatment, physical therapy treatment and the combination of both strategies was evaluated in a large-scale randomised clinical trial.

The known literature on effectiveness of brace treatment, more broadly described as orthotic devices, for tennis elbow complaints was described in a systematic review. The first step in developing a systematic review is to search medical literature for comparative trials on a specific topic. Extensive search of the literature resulted in only five small-scale randomised clinical trials comparing this type of treatment with others for tennis elbow. These trials were then assessed on quality using a criteria list. This assessment initially resulted in the five trials being judged as “inadequate” concerning methodological quality. When the authors were contacted and requested for additional information on the quality items that were initially inadequately described in their trials, all authors came up with additional and trustworthy information. This information resulted in a new assessment with a more positive view on quality. Based on this experience we can conclude that all authors had major flaws in the initial presentation of their trial. Trials turned out to be adequately performed, but not adequately described in their published manuscripts. This finding implicates that the presentation of a trial should be of utmost attention to the trialists. The major problem with the five included trials was that the trials were heterogeneous on interventions, outcome measures and duration of follow-up. Thence, it was not possible to draw definitive conclusion concerning effectiveness of braces for tennis elbow. These conclusions made it even more important to perform a high-quality, sufficiently powered trial comparing braces with other therapeutic modalities for tennis elbow complaints.

The ELO trial

A large randomised prospective trail, the ELO-trial (Epicondylitis Lateralis Onderzoek in Dutch, Lateral Epicondylitis Study in English), was started in January 1999. The sample size calculation indicated that a total of 180 patients would be adequate to draw definitive conclusions on effectiveness of braces and physical therapy for tennis elbow.
Outcome Measures

A total of nine outcome measures was used. These were hierarchically ranked in advance. Both objective and subjective patient-oriented outcome measures as well as non-patient-oriented outcome measures were used. A comparable set of outcome measures will be used in future trial on tennis elbow complaints. Continuity of assessors is a recommendable approach, limiting potential bias. We realise, however, that this is often difficult to achieve.

Patients were referred to the outpatient clinic of the Department of Orthopaedic Surgery of the Academic Medical Center in Amsterdam by both general practitioners and primary care physical therapists. Patients were included based on a set of in- and exclusion criteria applied by a research physician.

Recruitment

We were able to recruit the required 180 patients within 16 months. A strategy to maintain inflow of patients was the continuous newsletter, which was sent to all participating practices approximately every 6 weeks. In this newsletter, facts about the study were combined with things worth knowing. The response from the participating practices was very positive and this might have acted as a continuous stimulating factor to send in patients to our referral centre. However, the inflow of patients from physical therapists and general practitioners fluctuated over time. In response to a decreasing inflow, different measures were taken, for instance telephone calls and visits to practices. The last strategy worked very well, whilst the contact between referring practice and the referral centre became closer and more personal. Another method to keep contact with the practices was by sending a comprehensive feedback letter after a patient’s visit describing findings and conclusions. Furthermore, one researcher was continuously available for additional information on inclusion or to answer any questions that came up in the practices during the study. By means of a pager, he was constantly present during working hours. Thus, by both passive and active feedback, the enthusiasm of the referring practices was tried to be optimised. The inclusion of patients was, however, not completed within the planned schedule, which was one year. This schedule was based on estimations of practices on how many patients they thought to be able to refer. The one year schedule even was a careful estimation. Point is, that the longer the trial lasts, the more the enthusiasm is reduced. It is therefore advisable, to complete inclusion of requested patients as quickly as possible. In our trial, after 4 months, only 41% of the practices had send in one or more patients, meaning 59% of the practices had send in none. The number of practices was limited to 80, because otherwise we thought we could not handle the patients inflow and would thus create a waiting list. This was never the case. In a new trial, we would therefore create a larger group of referring practices.
The referral procedure worked very well. Referring therapists or GPs contacted the researcher and he made an appointment. This was always realised within 1 week, so the patients did not have to wait long.

**Protocol Violations**
A total of seventeen patients violated the treatment protocol and were excluded for the per-protocol analysis. Main reason was the number of treatment sessions being less than seven or more than 11. Despite the fact that in our trial the per-protocol did not provide different results than our main analysis it is recommended that in a future trial, it should be more clear for physical therapists that the number of treatment sessions is very important and non-adherence is a main protocol violation. In retrospect we realise that some physical therapists were not enough aware of the necessity of restricting the treatment to the standardised protocol as much as possible. A future trial should deal with this difficulty and perhaps uncertainty.

**Losses to Follow-up**
Not many patients were lost to follow-up. Follow-up percentages were 98% at six weeks, 96% at 26 weeks and 94% at 52 weeks. All possible efforts were made to try to persuade patients to return to follow-up. Some patients, however, did not provide their correct telephone number and did not respond to letters. This is difficult to prevent in the future, because all patients were prepared to return at the moment of randomisation. Preventive measures were proper information on the trial, the sending of the newsletter, reimbursement of travel expenses which were made, and providing a telephone number for questions or complaints.

**Potential Biases**
**Selection Bias**
Selection bias occurs when the outcomes of a trial are affected by systematic differences in the way in which individuals are accepted or rejected for a trial, or in the way in which the interventions are assigned to individuals once they have been accepted into a trial.\(^3\) There is empirical evidence that effects of new interventions can be exaggerated if randomisation is not concealed at the time of obtaining consent from trial participants, by as much as 40% on average.\(^5,7\) In our trial, this was prevented by using a strict list of in- and exclusion criteria and a randomisation computer program using minimisation strategy. Neither participants, nor investigators could influence group allocation. In addition, patients were excluded if they had received any intervention for their current episode of tennis elbow complaints. These measures thus guaranteed concealment of allocation and true randomisation and reduction of selection bias.
Ascertaintment Bias

Ascertaintment bias occurs when the results or conclusions of a trial are systematically distorted by knowledge of which intervention each participant is receiving. This was prevented by blinding of the outcome assessor. We instructed the patients not to speak about the treatment they would or had received to the outcome assessor. A slight unforeseen problem occurred during summertime, when in some patients it was visible that they had been wearing a brace due to tanning of the surrounding skin. Luckily, the sun did not shine that much in the summer of 1999! The blinded assessor was asked to guess the allocation of the 176 patients at six weeks follow-up, and was correct for 73 (41%) patients ($k=0.12$) and was never certain of his guess. Thus, assessor blinding seemed adequate in the ELO trial. However, participants and administers of the intervention (physical therapists), were clearly aware of the allocated treatment. Blinding for these persons could therefore not be implemented, and some ascertainment bias may have been introduced. In the analysis, this type of bias was tried to be reduced by describing the complete analyses, including all time-points, types of outcome measures and strategy of statistical testing in the trial protocol. However, the analyst was aware of the type of treatment during the analysis, and this might also have introduced a form of bias.

Bias by inappropriate handling of withdrawals, drop-outs and protocol violations

Ideally, all participants would have completed the study, followed the protocol, and provided all necessary data. However, that is Utopia, and adequate handling of missing data should be applied. Using an intention-to-treat analysis and Last-Measurement-Carried-Forward principle, this type of distortion can be dealt with, guaranteeing no overestimation of the treatment effects.

Results

On the different outcome measures representing different dimensions of the ailment (pain, disability, satisfaction, costs) conflicting results were found. We found a beneficial effect of physical therapy on pain, disability and satisfaction, however, only on the short-term. In contrast, brace-only treatment showed to prevent inconvenience during daily activities. No other outcomes showed statistically significant differences. The hypothesised working mechanism of the brace is that it reduces the forces on the common extensor tendon and will therefore decrease the patient’s pain during activities in which the extensor muscles contract. This was supported by the outcome measure “inconvenience during daily activities”. The brace-only group showed superior on this outcome measure when compared to physical therapy. The combination group showed a similar trend, but the difference was not statistically significant. This outcome shows a potential major advantage for use of the brace, with implications for daily practice and patient education.
On success-rate, no significant differences were seen. On short-term follow-up, success percentages in the physical therapy group, the brace-only group and the combination group were 50%, 40% and 45% respectively. Over the intermediate-term these percentages were 70%, 72% and 75% and over the long-term 89%, 85% and 88%. Thus no significant differences in global improvement as assessed by the patients were identified.

Combination treatment showed no superior effectiveness when compared to physical therapy treatment only. It did, however, show superior on various outcomes when compared to brace-only treatment over the short-term. Thence, physical therapy seems to have additional beneficial effects compared to brace-only treatment. However, the question remains whether this surplus in effectiveness outweighs the extra costs of the physical therapy. The number needed to treat was 9 (95% CI 3 to 15). This was a statistical significant difference, though to our opinion not clinically relevant in regard of our pre-trial assumptions in which a difference of 25% was regarded clinically significant.

On effectiveness of physical therapy for tennis elbow, Labelle et al. concluded very limited evidence was present to draw definitive conclusions on effectiveness of physical therapy strategies for tennis elbow complaints. Recently, a new systematic review was undertaken which had similar conclusions.

Over intermediate-term and long-term it showed to be indifferent which approach a patient received since no differences were present at those time-points. Also, no statistically significant differences were present between groups on additional treatment. This may partially be caused by the quite favourable natural course of tennis elbow.

Thence, for selected purpose, knowing support of daily activities, brace treatment might be useful as initial therapy, since it is a relatively cheap intervention that helps awaiting the natural course.

This therapeutic implication is supported by the results of the extensor grip test. Results show that by using the extensor grip test one is able to discriminate between patients expecting to have a successful outcome and patients expected to have a non-successful outcome after brace-only treatment. On success-rate, decrease in pain for the patient's most important complaint and satisfaction over the short-term, patients with a positive test show statistically significant superior results. This test is thus capable of implicating direction of treatment. The success-rates on short-term in the test-positive brace-only group (47%) are comparable with results on effectiveness of physical therapy (50%) and the combination therapy (44%). Thence, in case of a positive test, a brace could be started as initial treatment strategy for the patient with sub-acute and chronic tennis elbow complaints. For patients with a negative test, application of a
brace as single initial treatment is not indicated, since it will result in a success-rate at six weeks in a success-rate of only 23% of the patients, which is significantly lower when compared to success rates in the physical therapy and combination groups.

Thence, brace-only treatment is indicated for patients with a positive extensor grip test. The test can be easily applied in general practice. When the test is positive, patients will directly feel that the brace aids in limiting the pain they experience. The patients, and also the general practitioner, will feel comfortable with the brace as initial treatment and will help awaiting the natural course of tennis elbow complaints. It is therefore recommendable that general practitioners apply the test in daily practice. The predictive value of the extensor grip test thus seems confirmed.

This in contrast to the diagnostic and predictive value of ultrasound. The identified ultrasound entities showed to be of no value for predicting effectiveness of braces, physical therapy or the combination for treating tennis elbow. However, the study was of limited size and the different subgroups might have been too small to identify differences. The fact that the final evaluation was based on printed images and not real-time screen images is an important limitation of our study. Since ultrasound is a dynamic diagnostic tool, real-time evaluation may have lead to a different interpretation of the ultrasound findings. In addition, the ultrasound equipment used may have been limited its diagnostic abilities. Using more advanced ultrasound equipment with a higher resolution and better contrast, abnormal findings might be found in a higher number of patients, allowing more reliable conclusions concerning prognostic and diagnostic value of ultrasound in tennis elbow. The scanning was performed by 5 different persons. This may also have introduced some variation in the results and should ideally be prevented in a future study. The total number of patients, however, was too small to perform inter-performer analyses. A new study therefore might be useful and should incorporate this advanced equipment and real-time evaluation of the imaging by one imager.

Since the outcomes of our ELO-trial revealed no clear advantage for any of the interventions, the costs of the interventions can be a decisive factor in choosing the optimal treatment approach. Physical therapy treatment showed considerably lower costs compared to brace-only treatment, near statistical significance. As a previous cost-effectiveness study showed that compared with an expectantly awaiting policy, physical therapy as an initial treatment of tennis elbow is not cost-effective, there seems no place for physical therapy (our most cost-effective approach), brace-only or combination treatment either, in patients with tennis elbow in primary care. We feel, however, that brace-only treatment for patients with a positive extensor grip test may be an option. Due to the limited number of patients in this subgroup, no definitive conclusions on this subject can be drawn yet.
Whilst natural course is relatively mild, a treatment strategy that significantly reduces duration of an episode would be more than welcome. From recent literature it is clear that none of the current available, most frequently used, strategies are able to accomplish this. On short-term, corticosteroid injections do reduce complaints, but a recurrence of complaints is seen in approximately 50% of the patients.\textsuperscript{12} Thence, it is alluring to treat the complaint with an expectant policy or, to diminish the patient's limitations, application of a brace. An alternative strategy might be manipulation of the wrist. This treatment strategy has not yet been described as a treatment strategy for tennis elbow complaints. Personal experience with this strategy persuaded us to compare results of this treatment with more commonly applied treatment strategies. The results of our small-sized randomised clinical trial, comparing this strategy with a physical therapy regimen, are promising. On 6 weeks, in the manipulation group an 85% success-rate was found, compared to 67% in the physical therapy group. The success rates for physical therapy in this study were higher compared to the success rates in the ELO trial (67% compared to 50%). This might be due to differences in baseline characteristics between both trial or a higher provider-enthusiasm. On the other hand, the small size and resulting low power of the trial might enhance differences due to chance. On 6 months follow-up, success-rate was 100% in the manipulation group. The manipulation treatment is directed at the wrist as location of the problem, in contrast to current treatment, aiming at the lateral epicondyle of the humerus. The promising results of the small-sized trial need replication in a large-scale randomised clinical trial, which is sufficiently powered. This train of thought might be the start a new era in the treatment of tennis elbow.

**Recommendations**

Regarding the question of optimal treatment for tennis elbow complaints, it seems that neither physical therapy nor brace-only treatment nor the combination of both is superior as initial treatment for tennis elbow patients in primary care. Brace is superior for limitations in daily activities, physical therapy for pain, disability and patient satisfaction, all over the short-term. Combination treatment has no advantage over physical therapy only. Based on the comparison with a study with a similar design \textsuperscript{12}, it seems that an expectantly awaiting policy should be considered as initial approach in this population. Within this expectantly approach, a brace might, however, be successfully applied in patients with a positive extensor grip test. Since this is a test which can easily be applied in general practice, it is recommendable for general practitioners to do so.

It is definitely recommended to replicate the results from the manipulation treatment in a large-scale RCT. For future trialists it is advisable to follow CONSORT guidelines when submitting a RCT to a journal.\textsuperscript{13} This in order to ensure adequate reporting of trials, helping physicians and policy-makers in interpreting clinical data.
Reference List

5. Jadad. Randomised Controlled Trials