Critical Review: Effectiveness of trismus treatment in irradiated patients with head and neck cancer

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The purpose of this critical review is to evaluation the effectiveness of treatment protocols available for the treatment of trismus resulting from radiotherapy in adult patients with head and neck cancer. Included in this review are the following study designs: randomized controlled trials, a retrospective cohort study, and a case report. Overall, research suggests that treatment of trismus is possible and can be effective. Suggestions for future studies in this area are discussed. In addition, clinical recommendations for speech-language pathology services are listed.

Introduction

Radiotherapy is one of the possible treatment options in the management of head and neck cancer. It can be used on its own, or in addition to surgery. In some instances, chemotherapy is also being used concurrently. Clinical side effects following radiotherapy can include mucositis, hyposalivation, loss of taste, osteoradionecrosis, radiation caries, and trismus (Vissink, 2003).

Trismus, occurring in 5%-38% of head and neck cancer patients (Steelman, 1986 & Thomas, 1988), can be defined as a "severely restricted mouth opening" (Dijkstra, 2006). Mouth opening or maximal insical opening (MIO) is commonly measured as the distance (in millimetres) between the maxillary and mandibular incisors. Dijkstra et al. (2006) determined that a mouth opening of less than 35mm is a functional cut-off point for head and neck cancer patients suffering from trismus.

In irradiated patients, trismus results from fibrosis and subsequent scar contracture in the muscles of mastication (temporalis, masseter, medial pterygoid and the lateral pterygoid) (Ichimura & Tanaka, 1993). Wang et al.'s (2005) study that looked at the degree of trismus and its progress over time in patients with nasopharyngeal cancer treated with radiotherapy revealed that there was no significant change in mouth opening during the course of treatment. However, between months one and nine following the completion of radiotherapy, mouth opening decreased rapidly at a rate of 2.4%, and then became slower and protracted over later years. At four years post-treatment, patients had a mean decrease in mouth opening of 32% (Wang et al. 2005).

The impact of trismus on a person's quality of life can be dramatic, and the following areas can be affected:

- Oral Hygiene
- Swallowing
- Speech
- Eating
- Nutrition
- Follow-up examinations
- Intubation

As the majority of these impacted areas fall within the scope of practice of a speech-language pathologist (S-LP) it is therefore critical that an S-LP be aware of the best method of treatment for the irradiated patient who suffers from trismus.

Objectives

The objective of this review is twofold: (1) to evaluate existing literature detailing treatment protocols for trismus in adults with head and neck cancer following radiotherapy, and (2) to provide evidence-based practice recommendations for treatment of trismus in this population.

Method

Search Strategy

Computerized databases, including PubMed, CINAHL, Web of Science, and Cochrane Library, were searched using the following key words: ((trismus) OR (jaw hypomobility)) AND ((treatment) OR (exercise therapy) OR (physiotherapy)). The search was limited to articles written between 1987 and 2007.

Selection Criteria

Only studies evaluating a treatment protocol for trismus in head and neck cancer were included in this review. Studies were limited to those whose participants were (1) adults, and (2) had received radiotherapy either as their primary treatment or as a post-operative measure.

Data Collection

Following the search parameters and the selection criteria, the following types of articles were

retrieved: randomized controlled trial (2), retrospective cohort study (1), prospective series: pre-test and post-test (1), and a case report (1).

Results

Mobilization Regimens: A Comparison

Buchbinder et al. (1993) used a randomized controlled trial to evaluate and compare two trismus appliances: (1) the Therabite Jaw Motion Rehabilitation System, and (2) tongue blades. Twenty-one participants (16 men and 5 women) were sequentially chosen from patients referred to the Oral and Maxillofacial Surgery Clinic (Mount Sinai, New York, NY) for treatment of jaw hypomobility secondary to radiotherapy. Participants were randomly assigned to one of three groups: (1) five patients performed unassisted exercises (control group), (2) seven patients performed unassisted exercises combined with mandibular mobilization using stacked tongue depressors, and (3) nine patients performed unassisted exercises combined with mandibular mobilization using the Therabite System. In groups 2 and 3, the stretch using either the tongue depressors or the Therabite was held for 30 seconds, and was performed five times per session. In all groups, the stretching activities were repeated 6 to 10 times per day. The unassisted exercises involved opening the mouth to maximum interincisal distance, closing, and then moving maximally to the left, right, and protrusively. MIO was measured pre-treatment, and subsequently thereafter in 2-week increments for a duration of 10 weeks. In addition, all patients were asked to subjectively rate pain, range of motion, well being, as well as compliance. An analysis of variance as well as a Student's *t*-test revealed no significant difference ($p < .05$) in MIO increase for groups 1 (4.4mm, SD; 2.1mm) and 2 (6.0mm, SD: 18.mm) at 6 weeks. However, at this same time marker, the net increase in MIO for group 3 was statistically significant (13.6mm, SD: 1.6mm), and the rate of improvement was 2.6 times faster than the other two groups. The rate of gain for groups 1 and 2 levelled off at 4 weeks. In addition, participants in group 3 reported being less fearful of self-injury and being more in control of their treatment.

This study presents with a number of methodological strengths. First, authors clearly established their criteria for trismus, limiting participants to those who had an MIO of less than 30mm (pre-treatment). Additionally, the authors excluded patients whose radiotherapy was more than 5 years prior to the study. Secondly, mobilization regimens were described in detail, which increases the likelihood of successful reproducibility. Furthermore, data was collected in two-week intervals which allows for a clear visualisation of change over time. Finally, statistical measures (analysis of variance and the Student *t*-test) were appropriate considering the nature of the data (continuous data on a ratio scale) and the small sample size.

Although this study clearly demonstrated differences among therapy groups, and recommended the use of the Therabite over tongue blades, some methodological weaknesses must be considered. The greatest limitation of this study is in relation to the participants and their selection. Sample size was very small, which limits the power of the study; there were 3.2 times more male subjects than female subjects; the span of the age range was large (31-77 years of age); and it was not indicated whether any of the patients had additional treatment to manage their cancer (e.g., surgery, chemotherapy, etc.). While participants were randomly assigned to their treatment groups, they were not equally distributed among them. This, in turn, could have skewed the results, especially considering the limited number of subjects. The authors did not report their reasoning behind this decision. Although compliance was subjectively measured, the results were not given. Finally, it is not possible to determine whether researcher bias was controlled for as the authors did not state who measured MIO and whether they were blinded to the various groupings. In considering these strengths and weaknesses, the level of evidence for this study is moderate to strong.

A similar study by Grandi et al. (2007) used a randomized controlled trial to compare the effectiveness of two physiotherapy exercise regimens: (1) Buchbinder's (1993) unassisted exercise regimen, and (2) Santos' (2003) regimen which included unassisted exercises similar to those described by Buchbinder, in addition to chewing two gum tablets for 15 minutes following the exercises. A third group was included as a control, where no exercises were completed. Participants were selected from the Radiotherapy Service at Santa Rita Hospital in Proto Alegre, Brazil. They were stratified according to the Helkimo Masticatory Dysfunction Index[1] (as described by Goldstein, 1999) and then

[1] This index helps to classify patients according to the following parameters: mandibular mobility, temporomandibular joint function, presence of pain during opening (both laterally and protrusively), presence of pain during palpation in on or more masticatory muscles, and the presence of pain in the temporomandibular joint using digital pressure.

"systematically distributed" into one of the three treatment groups, with 18 patients per group. Two MIO measurements were taken, one on the day before radiotherapy began, and the other on the final day of this cancer treatment. The data was analysed using the following parametric tests: Pearson test of co-relation, Student *t*-test, analysis of variance with repeated measures, multiple linear regression, Fisher's exact test, and ANOVA. These tests revealed no significant differences among groups. Authors did notice trends indicating a greater presence of trismus in the control group, and a better increase in MIO in the Santos' regimen group.

Various methodological strengths were noted in this study. For example, only patients who had had radiotherapy (specifically affecting one of the masticatory muscles) as the sole treatment protocol were selected. Unlike Buchbinder's (1993) study, the control group in this study did not follow any specific therapeutic course which allowed for direct comparison between those who received treatment and those who did not. Finally, the same examiner measured MIO in all patients (although the authors did not state whether that person was blinded).

Despite these strengths, the results should be interpreted with caution as a number of serious methodological flaws were found. In terms of participants, it is not clear how many patients were included. It is stated that there were 18 patients in each of the three groups; however, this number does not match the percentage values given to indicate the gender breakdown. In addition, the age range is wide at 15-80 years. As far as data collection and interpretation is concerned, several limitations were noted. The authors did not clinically define trismus. In other words, they did not set any exclusion criteria based on participants' pre-treatment MIO. Researchers did not indicate the duration of radiotherapy, and therefore, it was impossible to determine the length of the trismus treatment course. Also, in limiting the final MIO measures to the last day of radiotherapy treatment, the authors failed to account for changes in mouth opening beyond this point. There is concern over the statistical tests chosen as little explanation is given to justify the use of such a large battery of tests. This study could have been simplified and more powerful had they avoided the initial stratification and looked only at continuous data and parametric tests. Lastly, very little measurement data was included and this made the interpretation of the results difficult to assess. Overall, the level of evidence of this study is low.

Mechanical Stretching Device

Cohen et al. (2005) used a prospective case series with a pre-test and post-test to evaluate the use of the Therabite System. Seven participants were instructed on the use of the Therabite (holding the mouth open for 6 seconds, with 6 repetitions per session, and 6 times daily) and began exercise sessions within 6 weeks of surgery (composite resection with a radial forearm free flap). Four patients began post-operative radiation following the initiation of the exercises. MIO was measured at the onset of treatment and at the most recent follow-up visit which ranged from 12-48 weeks post-op. Additionally, five of the seven patients completed a self-assessment telephone survey after the completion of the study. Data was analyzed using a paired *t*-test. Average gain in MIO was 10mm (range 1-21 mm). No complications were reported in association with the use of the Therabite.

Although this study provides important information regarding the effectiveness of the Therabite System, the results should be interpreted with caution considering the methodological limitations. First, the sample size was very small and not all patients received radiotherapy. Additionally, two of the seven patients had an initial MIO greater than 35mm (which is commonly used as a cut-off for trismus). The length of treatment (between 12-48 weeks) was quite variable and no measurements were taken during this therapeutic course; therefore, it is difficult to assess progress over time. Compliance was subjectively recorded but results were not provided. Finally, no control group was included in order to measure the treatment effect. Taken as a whole, this study represents a moderate to low level of evidence.

Exercise Therapy

Dijkstra et al. (2006) used a retrospective cohort study to (1) assess the effects of various exercise therapy programs on trismus relating to head and neck cancer, and (2) compare these affects to patients with trismus unrelated to head and neck. For the purposes of this review, only aspects relating to the first objective will be reviewed. Researchers reviewed a total of 27 patient/physical therapy files for participants who were seen for treatment of trismus relating to head and neck cancer between 1997 and 2005. The following information was collected: age at the time of referral, gender, whether trismus was related to head and neck cancer or not, interval between cancer treatment and start of physical therapy, types of intervention, number of treatments, and mouth opening before and after therapy. Data within the head and neck cancer group

was analyzed using a paired sample *t*-test. Effect size was also calculated in order to compare the obtained data to results from previous studies. Research found that (1) the mean increase in mouth opening of 5.5mm (SD: 6.0mm) was significant ($p < .05$), (2) effect size was calculated as 0.74, (3) 21 of the 27 participants still had an MIO of 35mm or less following an average of 7.7 treatment sessions (SD: 9), and (4) tumour recurrence did not have a significant impact on MIO measures. In comparing this effect size with those calculated for Buchbinder (1993) and Cohen (2005) for patients treated using the Therabite System, the authors concluded that the Therabite was more effective in increasing mouth opening, compared to those treated using one or a combination of the following treatments: active range of motion exercises, hold relax techniques, manual stretching (using one or a combination of rubber plugs, tongue depressors, dynamic bite opener, Therabite), and joint distraction.

The results from this study are clinically relevant; however, certain limitations should be addressed. Aside from radiotherapy, the authors did not mention if any other cancer treatments were completed by patients. Due to the nature of the study, the overall effect of specific types of trismus treatments and their impact on MIO over the course of therapy could not be assessed. Lastly, the variation in the number of treatment sessions was great, and this could have had an impact on the results. The patient selection and statistical analysis were appropriate in this study. The level of evidence of this study is moderate.

Unconventional Approach

Abdel-Galil et al. (2007) presented a case report of a 63 year-old male who devised a unique treatment course to manage his worsening trismus following radiotherapy to the head and neck. At the completion of his radiotherapy treatments, the patient's mouth opening was 20mm. This patient was prescribed a number a treatment options including jaw opening exercises, stacked tongue depressors, an Archimedes screw, and a Ferguson's mouth gag. When no gain in mouth opening was noted, the patient then began suspending a 14lb sledgehammer, tied to a necktie, from his lower jaw (2 minutes/2X/day/1 month). Mouth opening improved to 38mm.

As the authors stated, they do not recommend this type of treatment for those suffering from trismus. However, this case does help to inform clinicians about the gains that can be made when a client is motivated by the changes observed. Details regarding the measurement of the mouth opening (i.e., how it was measured and by whom) would have been beneficial in the interpretation of the results. This study does not present any significant evidence.

Conclusions

Based on the research presented in this review, it is clear that incorporating trismus rehabilitation into a speech-language pathology program is both important and effective. Overall, evidence from the above studies appears to support the use of passive motion exercises in addition to stretching. This recommendation is also supported by the Oral Cancer Foundation (2001-2007) which states that:

> The primary factor in limiting jaw motion in the irradiated patient or surgery patient is the rapid formation of collagen secondary to radiation damage or surgery. In planning treatment, it is important to recall that immobile joints also suffer degenerative changes. Thus, while the initial cause of limited motion lies with the connective tissue, degradation of the joint can compound the problem. Joints which are immobilized show very rapid degeneration changes which can make remobilization difficult. Treatment that incorporates motion of the joint in addition to simple stretching has been shown to be more efficacious than other treatment that simply stretches connective tissue.

A number of limitations existed across all studies which should be addressed in future studies. In terms of participant selection, the sample size needs to be larger, researchers should include (if possible) more females, and age limits should be set. Methodologically speaking, participants should be observed while completing the exercises in order to ensure that each participant is completing the exercises in the same way and an equal amount of times throughout the day. Additionally, follow-up data should be collected to assess the participants' residual increase in MIO over time. Lastly, the use of prophylactic treatment for trismus should be investigated.

Final recommendations for S-LPs include:

1. Although no studies have been completed to assess prophylactic trismus treatment, some authors recommend that exercise therapy begin as early as possible (Vissink, 2003).
2. Clinicians should include exercises that encourage both passive motion and stretching. The Therabite system which addresses both types of exercises has been shown to be more

effective than tongue depressors; however, its accessibility and cost may factor into the treatment plan.

3. Exercise schedules and tracking sheets should be implemented in order to help the client visualize their daily routine and any progress made over time. This may serve to further motivate the client.

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