



Review

Prevention and treatment of trismus in head and neck cancer: A case report and a systematic review of the literature

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ABSTRACT

Introduction: Trismus, or limited mouth opening, is a well-known complication of head and neck cancer and its treatment. It may be caused by tumour infiltration into the masticatory muscles or by treatment like surgery and radiotherapy. A limited mouth opening may have a negative effect on nutrition, phonation, dental hygiene and treatment, and quality of life. The severity of this complication depends on the location of the tumour, the type of reconstruction, the total radiation dose, fractionation, and treatment techniques. If there is no intervention, these changes may be progressive and persist for life. There are no specific treatments for trismus. Current strategies emphasize prevention and, in instances of existing trismus, collaboration between health care professionals to establish pain control, prevent the progression of trismus, and restore function. The prevalence of trismus in head and neck cancer patients ranges from 5% to 38%. Despite numerous studies, reliable data on the aetiology of trismus and appropriate treatment for it are scarce.

Case report: We describe a patient with squamous cell carcinoma of the oropharynx who developed trismus after surgery and radiotherapy. A multidisciplinary treatment strategy including analgesics, regional blocks, hyperbaric oxygenation therapy, external dynamic bite opener and physiotherapy, increased the mouth opening from 5 mm to 22 mm, however, the patient still suffered from xerostomia and had problems with intake of solid food.

Material and methods: A systematic literature search (starting January 1., 1980, and ending June 1., 2009) was performed to identify evidence-based interventions for the treatment of trismus in head and neck cancer patients. A total of 244 articles were identified from the databases. Of these, eight were excluded because of the absence of an English abstract and 214 were excluded because they were of marginal relevance to the inclusion criteria. The remaining 22 articles were evaluated independently by two experts using the Scottish Inter-collegiate Guidelines Network criteria for quality and evidence.

Results: There were few studies of good methodological quality on this topic. Two systematic reviews and two RCTs were identified. The other reports involved cohorts, case series, and expert opinions.

Discussion: Evidence in the form of clinical studies on therapeutic interventions is scarce. Numerous pharmacological treatment modalities have been described, but few are supported by the results of comparative trials involving control groups. Few studies have documented therapeutic effects for longer than a year. Better evidence was found for non-pharmacological methods, especially for physical therapy with passive and active stretching exercises, an important first-line strategy. The interincisal distance criterion for trismus varies between authors from 15 to 40 mm, which renders comparison between studies difficult. The absence of a standardized assessment protocol may also have contributed to variation between studies. An interincisal distance of 35 mm has been proposed as a definition of trismus. Explicit and precise treatment algorithms could not be established based on the available literature. However, a coordinated multidisciplinary approach in order to estimate and understand patient dysfunction is recommended; a systematic treatment plan should result in good symptom control and patient care. Prevention of trismus is more desirable than treatment for trismus.

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1. Introduction

Trismus, or limited mouth opening, is a well-known complication of head and neck cancer and its treatment [1]. It may be caused by tumour infiltration into the masticatory muscles, viz., the masseter, temporalis or pterygoid muscles, or the temporomandibular joint (TMJ). Surgery and radiotherapy are common treatment modalities for head and neck cancer. Scar formation resulting from surgery may reduce the mouth opening because of contraction and fibrosis [2]. Radiotherapy induces fibrosis not only in the masticatory muscles, but also in the soft tissues and salivary glands included in the radiation field. Muscle dysfunction and reduced oral mucosal lubrication resulting from radiation-induced hyposalivation may cause oral pain and promote the development of trismus.

Inflammation of the pterygomasseteric sling and soft tissues is often the first sign of trismus. A limited mouth opening may have a negative effect on nutrition, phonation, dental hygiene and treatment, and quality of life [3]. The severity of this complication depends on the location of the tumour, the type of reconstruction, the total radiation dose, fractionation, and treatment techniques [4,5]. If there is no intervention, these changes may progress and become permanent. There are no specific treatments for trismus. Current strategies emphasize prevention and, in instances of existing trismus, collaboration between health care professionals to establish pain control, prevent the progression of trismus, and restore function [1].

The prevalence of trismus in head and neck cancer patients ranges from 5% to 38% [1,6]. The variation in the prevalence of trismus may be explained by the absence of uniform criteria for defining trismus. An interincisal gap of less than 35 mm has been proposed as a cut-off point for trismus [7]. Despite numerous studies, reliable data on the aetiology of trismus and appropriate treatment for it are scarce.

2. Case report

A 47-year-old woman suffering from a T2N0M0 squamous cell carcinoma of the oropharynx involving the left lateral border of the tongue and soft palate underwent a tumour resection at another institution. Postoperative radiotherapy was not conducted (according to our institution's guidelines, the patient should normally have received postoperative radiotherapy, 50 Gy if free margins, otherwise 66 Gy against the tumour bed). After six months, she gradually developed trismus and was admitted for examination. MRI showed degeneration of the TMJ cartilage and a detached intra-articular fragment. She was unable to eat solid food. Clinical examination revealed a maximum interincisal gap of 5 mm (Fig. 1). Intra-oral examination was not possible, even with a flexible scope. CT (computed tomography) showed osteoarthritis of the left TMJ with an intra-articular fragment as observed on MRI, but tumour recurrence could not be confirmed.

Two months later, she was examined under general anaesthesia. A distinct foetor ex ore and oral ulceration were observed. The results of a biopsy confirmed that tumour recurrence had occurred.

The tumour mass was located anterior to the tonsillar region and had infiltrated the floor of the mouth, the base of the tongue, and the medial pterygoid muscle.

Radiotherapy was administered to the tonsillar (70 Gy) and neck (46 Gy) regions (2 Gy per fraction).

The average doses to the masticator space, the TMJ, the medial pterygoid muscle, and the lateral pterygoid muscle were 42, 14, 59, and 32 Gy, respectively. The maximum mouth opening increased during radiotherapy despite the absence of physiotherapy and exercise. The patient did not experience a subsequent recurrence of the cancer.

A few months after completion of radiotherapy, the patient developed severe trismus; the maximum mouth opening was only 2 mm. She lost weight and reported intense pain in the left mandible up to the external auditory meatus and in the oral cavity. Fibrosis of the pterygoid muscles was detected using MRI. Intake of fluids caused allodynia and she experienced severe xerostomia.

Pain control using conventional analgesic therapy (paracetamol, amitriptylin, and gabapentin) was unsatisfactory. She received an escalating dose of morphine before being admitted to a pain clinic.

After assessment of the source of the pain and her previous treatment history, the trigeminal nerve and the medial pterygoid muscle were blocked using 6 mL of lidocain solution (10 mg/mL) under CT guidance. The blocks resulted in pain relief for several hours, but the trismus did not improve. An external dynamic bite opener, the



Fig. 1. A few months after radiotherapy was completed, the patient developed severe trismus in which the maximum mouth opening was 2 mm.



Fig. 2. The forced interincisal distance was 22 mm 4.5 years after radiotherapy.

Therabite, was used in addition to psychomotor physiotherapy and a splint device, which was used at night. Carbamazepine (300 mg/d) was administered and intensive physical exercises consisting of passive and active jaw movements were conducted. Her mouth opening gradually increased to 20 mm and the intensity of pain decreased. She was weaned off all analgesic drugs during the following three months but still suffered from severe xerostomia. She then underwent hyperbaric oxygenation therapy, which relieved the xerostomia, but her mouth opening remained at 20 mm. At a follow-up 4.5 years after radiotherapy, passive and forced interincisal distances were 20 mm and 22 mm, respectively (Fig. 2) and she was still unable to eat solid food. According to the patient, xerostomia was the most annoying late complication of her cancer treatment and interfered with her daily activities.

3. Materials and methods

A systematic literature search (starting January 1, 1980 and ending June 1, 2009) was performed to identify evidence-based interventions for the treatment of trismus in head and neck cancer patients as follows:

1. Electronic databases (MEDLINE-OVID, EMBASE, HTA, CINAHL, and Current Contents) were used to identify primary studies.
 - A. The MEDLINE-OVID database returned 1267 articles in response to a search for “trismus”. Only two restrictions were applied: the first was publication from 1980 to 2009 and the second was the term “humans”. No limitation was applied regarding the language of the publication.
 - B. The combination of “trismus” and “head and neck neoplasms” resulted in 244 references.
 - C. The combination of “trismus and evidence-based medicine” and “trismus and randomized controlled trials” resulted in no references.
 - D. Similar searches were made using EMBASE and CINAHL. The Cochrane database is a part of MEDLINE.
2. The Index Medicus, MeSH, and Thesaurus were used to standardize and improve accuracy of the search.
3. Reference lists from relevant articles were scrutinized.
4. The keyword “trismus” was applied to textbooks on oncology [8], palliative medicine [9], and pain treatment [10], but no results were returned.
5. A search of Norwegian and international guidelines via www.helsebibliotek.no, which is linked to the National Institute for Health and Clinical Excellence, the Scottish Inter-collegiate Guidelines Network, and the Guidelines International Network, was conducted without positive results. A search for “consensus”

and “standards/recommendations” did not produce any results either.

Inclusion criteria:

1. *Target population:* all patients with head and neck cancer and trismus caused by a tumour or antineoplastic treatment.
2. *Trismus intervention:* medical or non-pharmacologic management (i.e., exercises and use of devices).
3. *Primary endpoint:* A. 30% improvement of the maximum mouth opening after treatment; B. preservation of the maximum mouth opening but with potential tissue damage caused by radiotherapy. An interincisal reduction of less than 30% was considered successful.
4. *Secondary endpoint:* side-effects of preventive and anti-trismus treatment.
5. *Study design (according to quality and evidence grade):* (a) systematic reviews and meta-analyses, (b) RCTs, (c) cohorts, (d) case-control trials, and (e) guidelines and non-systematic reviews.

Additional criteria: (a) English abstracts and Norwegian, Danish, and Swedish articles published between 1980 and 2009; (b) the following Keywords: were used separately or in combination: trismus; limited mouth opening; head and neck cancer; radiation therapy; evidence-based medicine; and randomized controlled trials.

4. Results

A total of 244 articles were identified from the databases (the references are available from the corresponding author). Of these, eight were excluded because of the absence of an English abstract and 214 were excluded because they were of marginal relevance to the inclusion criteria. The remaining 22 articles (Table 1) were evaluated independently by two experts using the Scottish Inter-collegiate Guidelines Network criteria for quality and evidence. There were few studies of good methodological quality on this topic. Two systematic reviews [1,11] and two RCTs were identified [12,4]. The other reports involved cohorts, case series, and expert opinions (Fig. 3).

5. Discussion

Heterogeneous pathogenic factors such as tumour infiltration, postoperative tissue-adhesion, radiotherapy-induced fibrosis, and the neurotoxic and myotoxic effects of chemotherapy can cause trismus. Anatomical differences in the causes of complications (e.g., intracapsular vs. extra-capsular) necessitate individual approaches to treatment. The predominant cause of a persistent mobility dysfunction should be identified before a decision is made regarding treatment modality [13].

Evidence in the form of clinical studies on therapeutic interventions is scarce [11]. Trials conducted with small numbers of subjects can be misleading [12,14,15]. Some reports are contradictory, e.g., those on the preventive role of physiotherapy [7,16]. Various reports claim to be comparative but detailed randomization criteria are lacking and some of the most recent publications used historical controls. Comparison of heterogeneous groups can result in conclusion bias. Limited jaw opening is usually investigated as a secondary outcome variable [17].

The interincisal distance criterion for trismus varies between authors from 15 to 40 mm [18,19], which renders comparison between studies difficult. The absence of a standardized assessment protocol (vertical vs. diagonal measurement of interincisal

Table 1

Characteristics of controlled and uncontrolled trials on the prevention and treatment of trismus in cancer patients.

Author	Study type	Design	Quality and validity	Level of evidence	Recommendation grade
Dijkstra (2004)	Systematic review	2	++	2++	B
Van der Molen (2009)	Systematic review	2	+	2++	B
Teo (2000)	RCT	1	++	1+	A
Buchbinder (1993)	RCT	1	+	1+	B
Grandi (2007)	Cohort	2	+	2++	C
Levendag (2004)	Cohort	2	+	2+	C
Karakoyun-Celik (2005)	Cohort	2	+	2+	C
Dijkstra (2007)	Cohort	2	+	2+	C
Goldstein (1999)	Case series	3	+	3++	C
Bhrany (2007)	Cohort	3	+	3++	D
Wang (2005)	Case series	3	–	3+	D
Duke (2005)	Case series	3	–	3+	D
Cohen (2005)	Case series	3	–	3+	D
Chua (2001)	Case series	3	–	3+	D
Yeh (2005)	Case series	3	–	3+	D
Kielbassa (2006)	Narrative review	4	–	4	D
Sciubba (2006)	Narrative review	4	–	4	D
Harrison (2002)	Narrative review	4	–	4	D
Vissink (2003)	Narrative review	4	–	4	D
Nguyen (1992)	Narrative review	4	–	4	D
Marien (1997)	Narrative review	4	–	4	D
Fischer (2008)	Narrative review	4	–	4	D

Hierarchy of study types/design: (1) systematic review and meta-analysis of randomized controlled trials, (2) randomized controlled trial, (3) non-randomized intervention study, (4) observational study, (5) non-experimental study, (6) expert opinion. Quality and validity ratings were performed according to [20]; scores ranged from ++ to –, where ++ represents the highest quality and validity and – represents the lowest quality and validity. The level of evidence was determined according to [21]; scores ranged from 1+ to 4. The recommendation grade was determined according to [21]; scores ranged from A to D, where A represents the highest recommendation and D the lowest.

distance) may also have contributed to variation between studies. An interincisal distance of 35 mm has been proposed as a definition of trismus [1].

Numerous pharmacological treatment modalities have been described, but few are supported by the results of comparative trials involving control groups. A report of a pilot study concluded that pentoxifylline had promising effects [22], but this study was not followed by randomized controlled trials. A prospective study involving base-line assessment of trismus is lacking. Few studies have documented therapeutic effects for longer than a year.

Better evidence was found for non-pharmacological methods, especially for physical therapy with passive and active stretching exercises, an important first-line strategy. Current treatment methods include dynamic bite-openers, rubber plugs, and tongue blades. Many studies have found that the Therabite is a harmless and effective device [12,14,19,7,16]. The Dynasplint has been recommended for patients with severe established trismus [23].

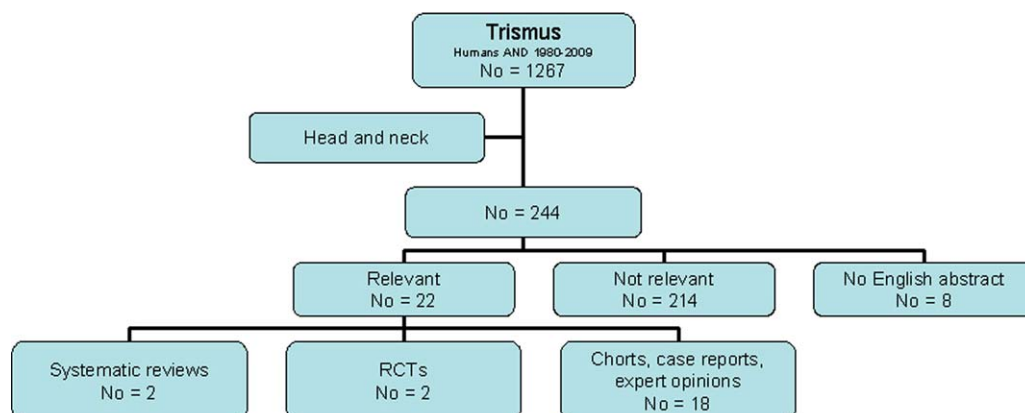
A recent prospective case series [24] concluded that coronoidectomy is an effective option for trismus that is refractory to traditional treatment modalities such as physical therapy, but aggressive postoperative stretching, which is sometimes applied

in conjunction with this treatment, could affect the efficacy of coronoidectomy. Randomized controlled studies are required to validate this treatment modality.

Methodical and structured estimation of jaw function before, during, and after radiotherapy is essential. If early reduction of the mouth opening occurs, the patient may benefit from follow-up by a multidisciplinary team to optimize treatment and symptom control.

The European Society for Therapeutic Radiology and Oncology and the European Committee for Hyperbaric Medicine organised a consensus conference in 2001, and the results were published in 2004 [25]. Guidelines were difficult to draw due to the limited documentation. They concluded that hyperbaric oxygen therapy (HBOT) may be indicated for the treatment of mandibular osteoradionecrosis after dental extraction and possibly for haemorrhagic cystitis resistant to conventional treatment. Despite lack of definitive documentation, our patient received HBOT, with no effect on trismus, but with a possible improvement of her xerostomia.

Trismus may be accompanied by intense pain, particularly if trigeminal nerve branches are included in the radiotherapy portal.

**Fig. 3.** A flow diagram of systematic literature search to identify evidence-based interventions for the treatment of trismus.

Therefore, treatment for neuropathic pain may be required. Carbamazepine was found to have an NNT (number-needed-to-treat) of 2.6 for trigeminal neuralgia, whereas the NNT for gabapentin ranges from 3.2 to 3.8 for chronic neuropathic pain states [17]. Although our patient did not present with typical trigeminal neuralgia, initial treatment with carbamazepin resulted in a definite improvement. Pain control enabled the patient to begin physiotherapy, and she gradually increased her mouth opening. If this anticonvulsant had not resulted in improved pain relief, we would have started with second-line therapy with alternative drugs like voltage dependent sodium channel blockers such as oxcarbazepine or lamotrigine.

Surgery, radiotherapy and chemotherapy are the most important treatment modalities in oncology but can lead to devastating complications. Surgical intervention can cause critical nerve damage with neuropathic pain as a clinical symptom. Side effects of radiotherapy are dose-dependent. Inflammation and following fibrosis in the affected area compress nerves and provokes paroxysmal pain. It is well documented that risk of chronic, neuropathic pain increases considerably after combination of surgery and radiotherapy in patients with breast cancer [26,27].

Risk factors for the development of soft tissue fibrosis and its prophylaxis have been documented. The most important risk factor is probably the inclusion of the medial pterygoid muscle in the radiation portal [28,8,16]. 3D treatment planning, intensity-modulated radiotherapy, and brachytherapy have been proposed as preventive measures [29,3].

We believe that a coordinated, multidisciplinary approach for estimating and understanding patient dysfunction would make optimal symptom control easier, although there is insufficient evidence for this practice [13,31].

6. Conclusions

1. Interincisal distance should be measured before radiotherapy is commenced, and should be monitored frequently thereafter. Systematic dental control is necessary [32,33].
2. Protection of sensitive anatomical structures such as the medial pterygoid muscle and the TMJ, which may trigger trismus, are recommended during radiotherapy [2,19].
3. Patients at risk of trismus should receive instructions in home exercise with devices such as tongue depressors and rubber stops to maintain their mouth opening and jaw mobility [12,34,19].
4. If trismus develops, the exercise program should be intensified and combined with physiotherapy and dynamic bite-openers such as the Therabite, which is effective and safe [13,14,19,7,16].
5. Detailed analysis of the pathogenesis of trismus is essential, as the efficacy of treatment depends on the cause of the trismus. Therapy should be individualized [13,7].

Explicit and precise treatment algorithms could not be established based on the available literature. However, a coordinated multidisciplinary approach in order to estimate and understand patient dysfunction is recommended; a systematic treatment plan should result in good symptom control and patient care. Prevention of trismus is more desirable than treatment for trismus.

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