Trismus in head and neck cancer patients

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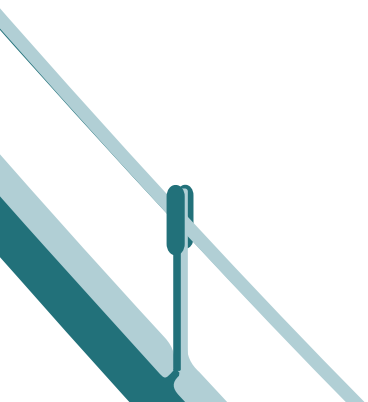
General introduction



Head and neck cancer

Head and neck cancer includes lip, oral cavity, salivary glands, nose (sinuses), oropharynx, nasopharynx, hypopharynx, larynx and complex skin tumours in the head and neck region. In the Netherlands, around 3100 people developed head and neck cancer in 2016.[1] Most of the tumours were located in the oral cavity, oropharynx, and the larynx (crude rate: 5.13, 4.08, and 4.13 per 100.000 person years at risk respectively).

Head and neck cancer treatment side-effects

Side- effects may occur after head and neck cancer treatment (consisting mainly of surgery, radiotherapy, and/or chemotherapy), such as mucositis, hyposalivation, taste change or taste loss, osteoradionecrosis, radiation caries, dysphagia and trismus.[2,3] Trismus, hyposalivation and restricted tongue mobility are the most frequently occurring and most burdensome late side-effects of treatment reported by head and neck cancer patients.[4]

Criterion for trismus

The prevalence of trismus ranges between 5% and 65%.[5-10] This range might be the result of different cut-off points for trismus.[6-8] Cut-off points for trismus are, for instance, based on dental status (such as 35 mm for dentate patients and 40 mm for edentulous patients)[7], or based on the severity of the restriction (such as 35 mm for moderate trismus and 20 to 25 mm for severe trismus).[6,8] Hence, the risk factors for and the effectiveness of treating trismus cannot be analysed in a uniform manner and the research results cannot be interpreted easily.

Factors associated with trismus

The prevalence range of trismus could also be affected by the narrow inclusion criteria, consisting of specific patient, tumour and treatment characteristics, such as a particular tumour localization[5,9,10] or a particular treatment modality[5-7,9-11]. Trismus is more likely when the masticatory structures (the temporomandibular joint[6,13,14], the masseter muscle[6,14,15], the lateral pterygoid muscle[6,13-16], the medial pterygoid muscle[6,13-15], and the temporal muscle[6,14,15]) are affected, either by tumour infiltration or tumour treatment. Regarding treatment modality, trismus is more likely to develop after radiotherapy and chemoradiotherapy, than after surgery alone.[9,17] Multivariate analyses are necessary, in order to identify the patients at risk of developing trismus.

Therapy for trismus

Once trismus develops, it is difficult to treat. Several therapies have been described for trismus, such as tissue condition enhancing[18,19], pain reducing[20], surgical[21], and physiotherapeutic options[22]. Tissue condition enhancing options, such as microcurrent therapy and pentoxifylline had a minor positive effect on mouth opening (effect size 0.3 and 0.3, respectively).[18,19] Pain reducing options, such as botulinum toxin injections, are effective in reducing pain scores and jaw spasms, but did not improve mouth opening.[20] Surgical treatments, such as a coronoidectomy increases mouth opening directly post-operatively, but it decreases slightly in the six months thereafter.[21,23] Coronoidectomy should only be considered when other therapies have no effect, mouth opening restriction is severe (<20 mm), and the cause of trismus is probably related to restrictions in the temporomandibular area. Surgical trismus release in combination with a free flap reconstruction led to a significant increase in mouth opening directly afterwards (mean gain 31.0 mm, SD 7.0), but had decreased by 71% at the follow-up (mean loss 22.1 mm, SD 7.3).[24] This procedure has been found to be particularly effective in head and neck cancer patients who consume betel nut (mean increase: 17.4 mm, SD 6.1) compared to patients who do not (mean increase 10.5 mm, SD 5.8). It has been suggested that trismus among the patients who consume betel nut is related to the presence of superficially located oral submucous fibrosis, whereas trismus among other patients who didn't consumed betel nut is related to fibrosis of the deeper muscular structures.[24] Physiotherapeutic options including stretching and mobilization, using tongue depressors, rubber plugs, manual stretches or stretching devices, seem promising, but mouth opening measurements smaller than 35 mm are still found at the end of the stretching regimen.[22] It has been suggested that early, preventive stretching regimen for trismus had greater effects on the increase of mouth opening.[25] However, still no exercise technique was superior to another, neither regarding early or late stretching regimen.[22]

AIMS OF THE THESIS

The general aims of this thesis, with respect to trismus in head and neck cancer patients, are to determine the criterion for trismus, to identify the factors associated with trismus and to assess the effectiveness of stretching regimens as a therapy for trismus.

Criterion for trismus

In order to identify which factors are associated with the development of trismus and to analyse which treatment is effective in treating trismus, one should determine first at which point patients experience trismus. A cut-off point for trismus was determined in a large study population (n= 671) based on multiple maximal mouth opening measurements and patients' perception of difficulties opening the mouth (**chapter 2**).

Factors associated with trismus

Factors associated with the development of trismus were identified in large study populations with a variety of patient and tumour characteristics, that were predominantly treated with surgery (n=730) (**chapter 3a and 3b**) or were predominantly treated with radiotherapy (n=641) (**chapter 4**).

To get an overview of the factors influencing trismus in head and neck cancer patients, a systematic review was performed (**chapter 5**). This systematic review aimed to identify the prognostic factors for trismus (objectively measured and subjectively assessed) from patients treated for head and neck cancer. A wide range of patient, tumour and treatment characteristics were included.

Exercise therapy for trismus

Of the studied physiotherapeutic options to prevent or treat trismus, stretching devices seem promising, including: the TheraBite® Jaw Motion Rehabilitation System™ (Atos Medical, Sweden) and the Dynasplint Trismus System® (Dynasplint Systems, Inc., Maryland, the United States of America). No comparison has been made yet to establish which stretching device is most effective in treating trismus. In order to compare the effectiveness of these two stretching devices on increasing maximal mouth opening, a randomized controlled trial was performed (**chapter 6**).

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