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Therapeutic exercises for affecting post-treatment swallowing in people treated for advanced-stage head and neck cancers (Protocol)

Perry A, Cotton S, Kennedy C

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[Intervention Protocol]

Therapeutic exercises for affecting post-treatment swallowing in people treated for advanced-stage head and neck cancers

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

The primary objective of this review is to determine the effects of therapeutic exercises on oral swallowing, aspiration and adverse events, in people treated curatively for an advanced-stage (stage III, stage IV) squamous cell carcinoma of the head and neck.

BACKGROUND

Description of the condition

Cancers that are known collectively as 'head and neck cancers' include squamous cell carcinomas of the head and neck. Over 80% originate in the squamous cells that line the moist, mucosal surfaces of the head and neck (inside the mouth, the nose and the throat).

Head and neck cancers are a heterogeneous group, consisting of cancers of the mouth (base of tongue, other tongue, gum, floor of mouth, palate and other mouth), salivary glands, pharynx (tonsil, oropharynx, nasopharynx, pyriform fossa, hypopharynx, other mouth/pharynx), nasal cavity, middle ear, sinuses and larynx. Over the past decade, there has been a rise in the incidence of oropharyngeal squamous cell cancer (specifically of the lingual and palatine tonsils) in white men, younger than 50 years of age, who have no recorded history of alcohol or tobacco use; this is associated with human papillomavirus (HPV) infection rather than tobacco and alcohol usage (Marur 2010; Ragin 2007).

Overall, head and neck cancer accounts for more than 550,000 cases annually worldwide. Males are affected significantly more than females with a ratio ranging from 2:1 to 4:1. The incidence rate in males exceeds 20 per 100,000 in regions of France, Hong Kong, the Indian subcontinent, central and eastern Europe, Spain, Italy, Brazil and among African Americans in the Unites States. Mouth and tongue cancers are more common in the Indian subcontinent, nasopharyngeal cancer is more common in Hong Kong, and pharyngeal and/or laryngeal cancers are more common in other populations (Jemal 2011).

Although the incidence is relatively low, survival remains poor as people (who are mainly men) often present late to treatment. Five-

year relative survival from head and neck cancer in Europe ranges from 20% in Slovakia to 51% in the Netherlands, with the figure for Ireland (37%) being close to the average (www.ncri.ie).

Most head and neck cancers develop in the upper aerodigestive epithelium after exposure to carcinogens such as tobacco and alcohol, although human papillomavirus (HPV) has also been strongly implicated as a causative agent in a subset of these cancers (Argiris 2008). The goals of treatment are to improve survival outcomes but also to preserve organ form/function.

Treatments for advanced head and neck cancer include: surgery and radiation therapy; surgery and chemoradiotherapy; or chemoradiotherapy without surgery. The benefits of concurrent chemotherapy and radiation therapy on survival were confirmed by Pignon et al in 2009 in a meta-analysis of 84 trials (Pignon 2009). However, such improvements have resulted in an increased prevalence of dysphagia (difficulty in swallowing) in survivors.

Description of the problem

Although survival rates from head and neck cancer have improved overall, this has been due to more aggressive treatment so morbidity has correspondingly increased. Morbidity includes dysphagia, which may be due to the cancer itself or may occur as a result of modern aggressive treatment(s), or both. Dysphagia ranges from a temporary problem in swallowing (due to mucositis or xerostomia during treatment) through to a more long-term or even permanent problem (due to fibrosis or a stricture), which results in non-oral tube feeding being needed, using a nasogastric tube or a percutaneous endoscopic gastrostomy.

The consequences of dysphagia are not only a reduction of food/fluid intake, but often a reduction in people's activity and social participation (ICF 2001), with corresponding negative changes to their quality of life. In countries where much socialisation revolves around preparing and eating food together, psychological well-being can be negatively affected by dysphagia (Rappoport 2003).

Description of the intervention

Dysphagia therapy is recognised internationally as the provision of services to patients with a difficulty in swallowing, usually by a speech and language therapist (also known as a speech pathologist or speech therapist). Therapy may occur through using behavioural management procedures, principally divided into compensatory strategies and direct techniques (Logemann 1999). *Direct techniques* are the focus of this review.

Direct techniques (also known as therapeutic exercises) consist of either *swallowing* or *neuromuscular* exercises. *Swallowing exercises* are designed to change the swallow physiology by improving sensory motor integration or by gaining voluntary control over the timing or the co-ordination of selected oropharyngeal movements during swallowing (Logemann 1999).

Neuromuscular exercises target tongue strength, endurance and/or power. Strength is achieved by exercises that use high levels of resistance (isometric) exercises. Endurance is achieved through repeated performance of exercises involving low levels of resistance. Power is achieved by using exercises that focus on the speed of muscle contraction (Clark 2003).

How the intervention might work

Swallowing exercises are designed to improve swallowing safety (i.e. to reduce penetration, in which a bolus (a ball of food, fluid) enters the larynx at/above the vocal folds, or to reduce aspiration, in which a bolus enters below the vocal folds into the trachea/upper airway). Other swallowing exercises are designed to improve efficiency (i.e. to increase the speed or amount of a bolus swallowed, or both) (Logemann 1999).

Neuromuscular exercises are designed to increase tongue range of motion and/or strength, thus indirectly improving oral bolus transit (speed and bolus clearance) as tongue force/strength is a key component of a safe swallow. Exercises to increase tongue range of motion are used to keep the tongue mobile during/after head and neck cancer treatment and to mitigate against the stiffening and fibrosis that can result from radiotherapy and/or from surgery (Appleton 1994).

Why it is important to do this review

Changes to head and neck cancer treatment mean that patient survival has improved over the last decade, but this has been at the expense of increased morbidity (speech, swallowing function).

Treatment nowadays promotes 'organ preservation', which is appealing, but preservation of structure does not always mean preservation of function and, unfortunately, some head and neck cancer treatment regimens have profound and long-lasting negative side effects. Indeed, all head and neck cancer treatments have side effects, but these are compounded when multi-modal treatments are used, as in modern protocols.

A swallowing problem (dysphagia) is now widely accepted as both an acute and a late toxicity after radiotherapy treatment and it has been stated that, "the problem of swallowing dysfunction is probably becoming one of the most important and clinically relevant side effects after curative radiotherapy or chemo-radiation." (Langendijk 2007).

Given the need to prevent and/or reduce treatment-related morbidity in order to reduce the survivorship burden for patients and families, as well as the cost to healthcare systems, a review of the usefulness of therapeutic exercises for affecting post-treatment swallowing in patients treated for advanced squamous cell carcinoma of the head and neck using Cochrane methodology is warranted.

OBJECTIVES

The primary objective of this review is to determine the effects of therapeutic exercises on oral swallowing, aspiration and adverse events, in people treated curatively for an advanced-stage (stage III, stage IV) squamous cell carcinoma of the head and neck.

METHODS

Criteria for considering studies for this review

Types of studies

We will only include blinded and unblinded randomised controlled trials (RCTs) of patients with advanced (stage III, stage IV) head and neck cancer.

Types of participants

Adults who are treated with surgery and radiation therapy, surgery and chemoradiotherapy, or chemoradiotherapy without surgery for large (stage III, stage IV) squamous cell carcinoma of the head and neck, who are at risk of, or are presenting with, dysphagia (swallowing impairment). We will include people at all levels of dysphagia severity and will set no age limits.

We will look separately at patients presenting with dysphagia and at patients receiving interventions designed to prevent swallowing problems when they undergo cancer treatment.

Types of interventions

We will include direct therapeutic techniques involving *swallowing* and/or *neuromuscular exercises*.

Therapy programmes may be delivered pre- peri- or post-head and neck cancer treatment, but they must last for more than one session. Interventions may be provided by one or more health disciplines (for example, we will include studies involving only speech and language therapists).

Types of outcome measures

Primary outcomes

- Safety and efficiency of oral swallowing, as measured by:
  - reduced/no aspiration;
  - adverse events, such as chest infections, aspiration pneumonia, profound weight loss;
  - oropharyngeal swallowing efficiency (OPSE) measures, taken from videofluoroscopy swallowing studies.

Secondary outcomes

- Time to return to function (swallowing).
- Self reported changes to quality of life.
- Changes to psychological well-being: depression, anxiety and stress (DAS).
- Patient satisfaction with the intervention.
- Patient compliance with the intervention.
- Cost-effectiveness of the intervention.

Search methods for identification of studies

We will conduct systematic searches for randomised controlled trials. There will be no language, publication year or publication status restrictions. We may contact original authors for clarification and further data if trial reports are unclear and we will arrange translations of papers where necessary.

Electronic searches

We will identify published, unpublished and ongoing studies by searching the following databases from their inception: the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL, current issue); Ovid MEDLINE; Ovid MEDLINE In-Process & Other Non-Indexed Citations; PubMed (as a top up to searches in Ovid MEDLINE); EMBASE; CINAHL; LILACS; KoreaMed; IndMed; PakMediNet; CAB Abstracts; Web of Science; ISRCTN; ClinicalTrials.gov; ICTRP; speechBITE (Australian speech and language therapy database); Google Scholar and Google.

We will model subject strategies for databases on the search strategy designed for CENTRAL (Appendix 1).

Searching other resources

We will scan the reference lists of identified publications for additional trials and contact trial authors if necessary. We will search dissertation abstracts and contact key researchers in the area and international head and neck cancer organisations to request information about any unpublished or ongoing studies. In addition, we will search PubMed, TRIPdatabase, *The Cochrane Library* and Google to retrieve existing systematic reviews relevant to this systematic review, so that we can scan their reference lists for additional trials. We will search for conference abstracts using the Cochrane Ear, Nose and Throat Disorders Group Trials Register and EMBASE.

Data collection and analysis

Selection of studies

Two review authors (AP and SC) will independently review the titles and abstracts of the records identified from electronic searches and exclude immediately irrelevant studies. We will obtain the full text of the remaining studies and two review authors (AP and CK) will select studies based on the inclusion criteria of the review. If these authors are unsure, then the third review author (SC) will make a final decision. We will contact trial authors for further details when required. We will document the reasons for exclusion.

Data extraction and management

Two review authors (AP and CK) will independently extract study data and record information on a data extraction form. We will resolve discrepancies through discussion. We will extract the following from each study:

1. Citation details: title, authors, source and year of publication.
2. Participant inclusion and exclusion criteria.
3. Participant details: age, gender, location/size of tumour, time since diagnosis, level of swallowing ability, setting.
4. Recruitment details: number of people screened, eligible, recruited and randomised, withdrawals.
5. Methodological quality details (by use of The Cochrane Collaboration's tool for assessing risk of bias).
6. Intervention details: description of intervention/exercises, personnel involved, training of personnel, duration, dosage, comparison intervention.
7. Outcome measures: measures chosen, by whom and when they were administered, how they were administered (in person, via other communication technologies or by mail).
8. Study results (positive, negative, equivocal results, withdrawal).

Where required, we will contact trial authors for missing information. We will resolve differences by discussion or by referral to a third review author, if needed.

Assessment of risk of bias in included studies

Two review authors (AP and CK) will undertake assessment of the risk of bias of the included trials independently, with the following taken into consideration, as guided by the*Cochrane Handbook for Systematic Reviews of Interventions* (Handbook 2011):

- sequence generation;
- allocation concealment;
- blinding;
- incomplete outcome data;
- selective outcome reporting; and
- other sources of bias.

We will use the Cochrane 'Risk of bias' tool in RevMan 5.2 (RevMan 2012), which involves describing each of these domains as reported in the trial and then assigning a judgement about the adequacy of each entry as: 'low', 'high' or 'unclear' risk of bias.

Measures of treatment effect

Two review authors (AP and CK) will independently assign outcome measures to the domain assessed (oral swallowing; aspiration; adverse events; time to return to oral swallowing; quality of life; psychological well-being; patient satisfaction; patient compliance; cost-effectiveness of intervention).

If more than one outcome measure is used for the same domain from the same study, we will include the measure most frequently used across included studies.

If possible, we will conduct separate analyses for short-term (three months or less) and long-term (more than three months) outcomes.

We will calculate risk ratios (RR) and 95% confidence intervals (CI) for dichotomous outcomes and mean differences (MD) or standardised mean differences (SMD) and 95% CI for continuous outcomes, as appropriate.

Unit of analysis issues

The unit of randomisation in these trials will be the individual patient.

Dealing with missing data

We will contact trial authors for missing data. We will convert available data where possible (for example, when data are reported as standard error) using the procedures detailed in the *Cochrane Handbook for Systematic Reviews of Interventions* (Handbook 2011). Where possible, as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions*, we will conduct intention-to-treat analyses. Where drop-outs are clearly identified, we will use the denominator of participants contributing data at the relevant outcome assessment.

Assessment of heterogeneity

We will pool results to present an overall estimate of the treatment effect, using a random-effects model. We will assess heterogeneity by visual inspection of the forest plot along with consideration of the Chi^2 test for heterogeneity and the I^2 statistic (Handbook 2011).

Data synthesis

We will conduct a meta-analysis using a random-effects model with 95% CI using RevMan 5.2 (RevMan 2012). We will explore heterogeneity as detailed above.

Subgroup analysis and investigation of heterogeneity

If there are sufficient number of comparable studies (four or more), we will perform subgroup analyses to determine whether outcomes vary according to:

- type of therapeutic exercise (swallowing and/or neuromuscular);
- when therapeutic exercises were initiated (pre-, peri- or post-cancer treatment);
- frequency of therapeutic exercise;
- intensity of therapeutic exercise (dosage - number of hours of intervention);
- intervention approach (for example, retraining with a speech and language therapist or self directed);
- mode of delivery (face to face versus use of a brochure/DVD);
- whether the intervention is provided by a healthcare professional or not;
- cancer treatment modality (surgery and radiation therapy; surgery and chemoradiotherapy; chemoradiotherapy treatment without surgery);
- site of tumour;
- size of tumour;
- HPV status.

REFERENCES

Additional references

Appleton 1994
Appleton J, Machin J. *Working with Oral Cancer*. Oxon, UK: Winslow Press, 1994.

Argiris 2008
Argiris A, Karamouzis MA, Raben D, Ferris RL. Head and neck cancer. *Lancet* 2008;**1371**(9625):1695–709.

Clark 2003
Clark HM. Neuromuscular treatments for speech and swallowing: a tutorial. *American Journal of Speech-Language Pathology* 2003;**12**:400–15.

Handbook 2011
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

ICF 2001
WHO. *International Classification of Functioning, Disability and Health: ICF Short Version*. Geneva: World Health Organization, 2001.

Jemal 2011
Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA: A Cancer Journal for Clinicians* 2011;**61**:69-90. [DOI: 10.3322/caac.20107]

Langendijk 2007
Langendijk JA. New developments in radiotherapy of head and neck cancer: higher precision with less patient discomfort?. *Radiotherapy and Oncology* 2007;**85**:1–6.

Logemann 1999
Logemann JA. Behavioural management for oropharyngeal dysphagia. *Folia Phoniatrica et Logopaedica* 1999;**51**(4-5): 199–212.

Marur 2010
Marur S, D'Souza G, Westra WH, Forestiere AA. HPV-associated head and neck cancer: a virus-related cancer epidemic. *The Lancet Oncology* 2010;**11**(8):781-9.

Pignon 2009
Pignon JP, le Maître A, Maillard E, Bourhis J, MACH-NC Collaborative Group. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. *Radiotherapy and Oncology* 2009;**92**:4-14.

Ragin 2007
Ragin CC, Modugno F, Gollin SM. The epidemiology and risk factors of head and neck cancer: a focus on human papilloma virus. *Journal of Dental Research* 2007;**86**(2): 104–14.

Rappoport 2003
Rappoport L. *How We Eat*. Ontario, Canada: ECW Press, 2003.

RevMan 2012 [Computer program]
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

www.ncri.ie
The Irish Cancer Society. Cancer Trends No 10. National Cancer Registry, 2011. Cancers of the head and neck. www.ncri.ie (accessed March 2013).

* *Indicates the major publication for the study*

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Oropharyngeal Neoplasms] explode all trees
#2 MeSH descriptor: [Head and Neck Neoplasms] this term only
#3 MeSH descriptor: [Pharyngeal Neoplasms] this term only
#4 MeSH descriptor: [Otorhinolaryngologic Neoplasms] this term only
#5 MeSH descriptor: [Neoplasms] explode all trees
#6 cancer* or carcinoma* or neoplas* or tumor* or tumour* or malignan* or SCC
#7 #5 or #6
#8 MeSH descriptor: [Oropharynx] explode all trees
#9 oropharyn* or mesopharyn* or tonsil* or (head near/3 neck) or "tongue base"
#10 #8 or #9
#11 #7 and #10
#12 HNSCC or SCCHN or OP-SCC or OPSCC
#13 #1 or #2 or #3 or #4 or #11 or #12
#14 MeSH descriptor: [Deglutition] explode all trees
#15 MeSH descriptor: [Deglutition Disorders] this term only
#16 swallow* or deglutit* or dysphag*
#17 #14 or #15 or #16
#18 MeSH descriptor: [Exercise Therapy] explode all trees
#19 MeSH descriptor: [Isometric Contraction] explode all trees
#20 MeSH descriptor: [Behavior Therapy] explode all trees
#21 (swallow* or deglutit* or dysphag* or neuromuscular or mendelsohn or masako or "neuro muscular") near/3 (exercis* or maneuver* or manoeuvre* or manoeuver* or technique* or treatment* or strateg* or rehab* or therap*)
#22 isometric or IOPI or "iowa oral pressure instrument*" or pharyngocise
#23 nmt or "lingual exercis*" or "effortful swallow*" or "supraglottic swallow" or "super glottic swallow*" or "supra glottic swallow*"
#24 (tongue or BOT) near/3 ("range of motion" or ROM or resistance or strength* or holding)
#25 (voluntary near/3 (control or maneuver* or manoeuvre* or manoeuver*)) or "bearing down" or "progressive resistance" or "behav* management" or (exercis* near/3 (therap* or regime)) or "therapeutic techniq*" or "behav* therap*" or "larygeal elevat*"
#26 #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25
#27 #26 and #17
#28 MeSH descriptor: [Deglutition Disorders] explode all trees and with qualifiers: [Prevention & control - PC, Rehabilitation - RH, Therapy - TH]
#29 #27 or #28
#30 #13 and #29

CONTRIBUTIONS OF AUTHORS

Alison Perry is the guarantor of the review. The protocol was written with contributions from Catriona Kennedy.

All authors (Perry, Kennedy and Cotton) will be involved in searching for trials, extracting data, interpreting the analyses and drafting the final review. Specifically, Alison Perry and Sue Cotton will independently review the titles and abstracts of the records identified from electronic searches and exclude immediately irrelevant studies. Alison Perry and Catriona Kennedy will select suitable studies based on the inclusion criteria for the review. If these authors are unsure, Sue Cotton will make a final decision.

Alison Perry and Catriona Kennedy will independently extract study data and record information on a data extraction form, with Sue Cotton acting as arbitrator.

DECLARATIONS OF INTEREST

Alison Perry: none known.

Sue Cotton: none known.

Catriona Kennedy: none known.

SOURCES OF SUPPORT

Internal sources

- None, Other.

External sources

- None, Other.