Systematic or Meta-analysis Studies

The effects of swallowing disorders, dysgeusia, oral mucositis and xerostomia on nutritional status, oral intake and weight loss in head and neck cancer patients: A systematic review

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ABSTRACT

Background: Combined-modality treatment of head and neck cancer is becoming more common, driven by the idea that organ(s) preservation should maintain patient appearance and the function of organ(s) involved. Even if treatments have improved, they can still be associated with acute and late adverse effects. The aim of this systematic review was to retrieve current data on how swallowing disorders, dysgeusia, oral mucositis, and xerostomia affect nutritional status, oral intake and weight loss in head and neck cancer (HNC) patients.
Methods: A systematic literature search covered four relevant electronic databases from January 2005 to May 2015. Retrieved papers were categorised and evaluated considering their methodological quality. Two independent reviewers reviewed manuscripts and abstracted data using a standardised form. Quality assessment of the included studies was performed using the Edwards Method Score.
Results: Of the 1459 abstracts reviewed, a total of 25 studies were included. The most studied symptom was dysphagia, even if symptoms were interconnected and affected one other. In most of the selected studies the level of evidence was between 2 and 3, and their quality level was from medium to low.
Conclusions: There are limited data about dysgeusia, oral mucositis and xerostomia outcomes available for HNC patients. There is a lack of well-designed clinical trials and multicenter-prospective cohort studies, therefore further research is needed to ascertain which aspects of these symptoms should be measured.

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Background

Head and neck cancer (HNC) is common in several countries around the world, with an estimated number of 30,0400 new cases and 14,5400 deaths from oral cavity and lip cancer occurred in 2012 [1]. Oral cavity cancers, as well as larynx and pharynx cancer, represent about 10% of all malignancies in men and 4% in women [2]. Some studies [3,4] show that, unfortunately, many HNC patients are diagnosed when the disease is already at an advanced stage (Stage III/IV) and patients suffer conditions of nutritional vulnerability, with a high risk of malnutrition [5–7]. HNC, due to their site, directly impact on patients' oral intake, taste, and appetite,

and intensify the effects of treatments increasing the risk of severe malnutrition [7,8], hardness, persistence of symptoms, and weight loss [9,10]. Even if antineoplastic treatments, like radiotherapy (RT) and chemotherapy (CT) or a combination of these (CRT), contribute to local disease control and patient survival, they may also cause multiple symptoms that compromise oral intake [7]. Some acute therapy effects may persist, becoming permanent or late effects of the treatments, while some late effects may develop 90 days after the end of the treatment [11], or develop within the first 3 years after the various treatments, and some may appear or progress even after this period [12].

Acute symptoms that have an impact on oral intake, on weight loss and on dehydration during and immediately after CRT are mainly mucositis, swallowing disorders, xerostomia, and distortion of taste and smell [13,14]. Late effects are dysphagia, pain, xerostomia, mucosal sensitivity, taste alterations, trismus,

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osteoradionecrosis, and dental disease [14–18]. Such effects are common and influence the patient's ability to eat and drink [11], and for these reasons, patients being treated with RT frequently require various nutritional support methods, through oral, enteral (via tube), and parenteral nutrition [19]. The use of tube feeding is indicated in patients undergoing surgery, and it may be started before, during, or after RT and CRT [7]. However, enteral nutrition is not routinely indicated in all HNC patients during their treatment, especially in the early stage [20,21]. Besides, even if acute treatment toxicities like mucositis, pain, and nausea decrease oral nourishment ability [22], many patients maintain their oral food intake before, during and after treatment. Dysphagia is one of the most studied and cited nutritional impact symptoms (NIS) in HNC patients [7], but it is not the only one that influences nutritional status in these patients. Indeed, symptoms like dysgeusia, xerostomia and oral mucositis all seem to impact on patients' appetite [23,24]. Even HNC literature has grown significantly over the past decade, the relationship between NIS and reduced oral intake or weight loss is still unclear.

In this systematic review, the principle aim was to retrieve current data on how swallowing disorders, dysgeusia, oral mucositis, and xerostomia affect nutritional status, oral intake, and weight loss in HNC patients. The secondary aim was to analyse the quality and level of evidence (LoE) of selected studies, highlighting the implications for clinical practise and future research.

Material and methods

Literature search strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [25,26] and the Centre for Reviews and Dissemination Papers [27]. The selected studies were categorised and assessed considering their methodological quality and their LoE. The search strategy was designed with the support of a trained librarian to identify which studies met the inclusion criteria of this review [28] and to use a suitable search strategy for each database. The best terms to be used in the final sources were identified through preliminary trials.

Study inclusion and exclusion criteria

We selected articles that dealt primarily with the effect of xerostomia, swallowing disorders, oral mucositis, and dysgeusia on nutritional status, oral intake, and weight loss in HNC. Studies that evaluated adult patients undergoing RT and/or CT and compared them with those receiving no treatment or surgery treatment for HNC were considered. The study design included randomized and non-randomized clinical trials, cohort studies, and case-control studies published in English, Spanish, and Italian, with abstracts.

Studies were excluded for the following reasons: (1) different target conditions, such as patient treated with parenteral nutrition or enteral feeding; and (2) qualitative research. Grey literature like reviews, letters, editorials, dissertations, and conference abstracts were analysed [29] but not included in the review.

Information sources and search strategy

A systematic literature search was performed using: PubMed, CINAHL, Scopus, and the Cochrane Library, and limited to the period between January 2005 and April 2015 to ensure that the studies included were up-to-date. It was conducted using various combinations of relevant keywords, such as *xerostomia,* *hyposalivation, dry mouth, dysgeusia, taste disorders, taste perception, dysphagia, swallowing disorders, swallowing difficulties, mucositis, stomatitis, head and neck cancer, weighs loss, nutritional status.* The MeSH terms were exploded and modified as necessary and if possible in the databases. Manual searches through the references in the chosen studies were also carried out. The title and abstract of all potentially relevant studies were identified for their contents before retrieving the full articles. Full articles were retrieved and analysed if the title and abstract were unclear. The reference list was checked at the end of the search after removing the duplicates.

Study selection

The study selection was performed in two phases. In the first, two authors (VB and SS) independently reviewed the titles, keywords, and abstracts of all the references. They selected articles having abstracts that met the inclusion criteria. In the second phase, the same authors independently carried out a second selection, by reading the full texts of all the selected articles and excluding those that were not considered appropriate. Any discrepancy was resolved through comparison and mutual agreement between the two authors. If there was no consensus between the two, a third author (MB, AB, LS) was involved to resolve the disagreement.

Quality assessment

To appraise the methodological quality of all the selected studies, we used the Edwards Method Score (EMS) [30] and the criteria suggested by van Loon et al. [31]. EMS uses scores between 0 and 2; higher scores correspond to a higher quality and the total maximum score is 22 for experimental studies or 16 for observational studies [30]. Before the assessment, three reviewers (VB, SS, MB) discussed and analysed the tools and after that, they independently checked and evaluated the quality of the included studies. Eventually, the reviewers compared their evaluations. The definitions of Wasserman et al. [32], following the standards supported by the Oxford Centre of Evidence-based Medicine [33] and adapted to otolaryngology, were used to grade the LoE of the analysed studies. The articles were categorised with a 'high', a 'low', or a 'moderate' LoE, according to the analysis of each study, while the evidence level ranged from 1 (highest LoE) to 5 (lowest LoE). A third reviewer resolved any disagreement between the evaluations of the two reviewers.

Data extraction

Data extraction was conducted by VB using a worksheet developed for this review and pre-piloted to ensure that the reviewer collected appropriate data [29]. A second reviewer (SS) checked the extracted data for accuracy and completeness [29]. Extracted data included: the type of design and aim of the study, sample characteristics (mean age, gender, tumour location), outcome measures, methodology, measurement tools, and results (Tables 1–3).

Synthesis of results

Studies that met the inclusion criteria included in this review were synthetized using a narrative approach, because they were heterogeneous, had different aims and interventions, and used dissimilar outcome measurement tools [27,34,35].