



Oral toxicity management in head and neck cancer patients treated with chemotherapy and radiation: Dental pathologies and osteoradionecrosis (Part 1) literature review and consensus statement

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ABSTRACT

Radiotherapy alone or in combination with chemotherapy and/or surgery is the typical treatment for head and neck cancer patients. Acute side effects (such as oral mucositis, dermatitis, salivary changes, taste alterations, etc.), and late toxicities in particular (such as osteo-radionecrosis, hypo-salivation and xerostomia, trismus, radiation caries etc.), are often debilitating. These effects tend to be underestimated and insufficiently addressed in the medical community.

A multidisciplinary group of head and neck cancer specialists met in Milan with the aim of reaching a consensus on clinical definitions and management of these toxicities.

The Delphi Appropriateness method was used for developing the consensus, and external experts evaluated the conclusions. This paper contains 10 clusters of statements about the clinical definitions and management of head and neck cancer treatment sequels (dental pathologies and osteo-radionecroses) that reached consensus, and offers a review of the literature about these topics.

The review was split into two parts: the first part dealt with dental pathologies and osteo-radionecroses (10 clusters of statements), whereas this second part deals with trismus and xerostomia.

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1. Introduction

Radiotherapy (RT) with/without chemotherapy (CT) and/or surgery is the most common form of treatment or palliation of head and neck cancer patients (HNCPS). In recent years, advances in RT helped achieve better loco-regional disease control and higher survival rates (Parliament et al., 2005; Dirix and Nuyts, 2010; Retel et al., 2011; Vissink et al., 2003). RT delivery has also improved with decreased radiation exposure of normal tissues by use of intensity modulated radiation therapy (IMRT), which targets the tumor but partially spares the surrounding healthy tissues. Nevertheless, acute and late adverse events (AEs) continue to be an important concern in HNCPS treatment. Acute AEs may be intense and debilitating but usually resolve over time. Conversely, late AEs might be more problematic because they may be lifelong in cancer survivors. As a consequence, osteoradionecrosis (ORN), xerostomia, trismus, dysphagia, radiation caries, neuropathic pain, and chronic drainage can leave patients physically and emotionally disabled.

In the last few years, the awareness of functional RT sequels has grown, and efforts have been made to limit RT exposure of structures essential for functions such as swallowing, mastication and salivation. Thus, studies aimed at identification of the dysphagia/aspiration-related structures (DARSs) (Eisbruch et al., 2004) (e.g., the pharyngeal constrictors, tongue base, and larynx), altered-mastication-related structures or (AMRSs) (Teguh et al., 2008; Johnson et al., 2010; Van der Molen et al., 2011, 2013) (e.g., the masseter and pterygoid muscles, the temporo-mandibular joints, and the oral cavity), and xerostomia-related structures or XRSs (Van de Water et al., 2009; Jellema et al., 2005) (e.g., the major and minor salivary glands) have been undertaken in recent years.

As a consequence, RT techniques sparing the above-mentioned structures have been employed and they seem to improve patients' health-related quality of life (HRQoL) (Pow et al., 2006; Nutting et al., 2011; Bhide et al., 2009), even when RT is combined with CT (Hancock et al., 2003; Roe et al., 2010; Van der Laan et al., 2012). Yet, few studies report the exact dose-volume correlation for each individual DARS, AMRS and XRS (Nutting et al., 2011; Caudell et al., 2010; Eisbruch et al., 2011; Jensen et al., 2007; Levendag et al., 2007; Li et al., 2009; Bhide et al., 2012), and the majority of these are retrospective. However, recently published reviews (Van der Laan et al., 2012; Nutting, 2012; Wang et al., 2011; Goldstein et al., 1999) concluded that a number of the structures' dosimetric constraints might reduce the negative impact of RT on swallowing. Moreover, Cartmill et al. (Cartmill et al., 2012) suggested that future studies examining the predictive power of dosimetric factors should include pre-treatment functional data, and more standardized, validated measurement protocols.

Considering all the above-mentioned issues, a task force of radiation oncologists (ROs), oncology physicians (OPs), oral care physicians (OCPs), radiologists (Rs), and nurses (Ns) met in Milan with the aim of reaching consensus on the supportive management of HNCPS' oral problems through careful review of the available data.

Consensus discussions were focused particularly on those statements with limited evidence available.

The results of the literature review and the discussions that reached consensus are reported in this paper.

2. Material and methods

We used the Delphi rating method for consensus development (Loblaw et al., 2012).

The panel consisted of a group of 37 multidisciplinary experts (ROs, MOs, ENTs, OCPs, Rs, Ns) who met in Milan on February 17–18, 2013 and appointed a facilitator board of 13 experts from different clinical disciplines (6 ROs, 4 OCPs, 2 MO, 1 R). The facilitator board performed a systematic review of the literature on stomatological problems in Chemo/RT-treated HNCPS.

The MEDLINE database was searched for English-language studies published from 1992 to March 2013 containing the terms head and neck cancer, osteo-radionecrosis, periodontal problems, radiation caries, CT, and RT.

In addition, potentially relevant abstracts presented at annual meetings of the American Society of Clinical Oncology and the European Society of Medical Oncology were examined. The study selection included the following:

(a) Observational and prospective studies about assessment and treatment; (b) randomized, double-blind, placebo-controlled, or uncontrolled studies; (c) retrospective and uncontrolled studies; (d) systematic reviews and meta-analyses; (e) consensus guidelines. Furthermore, the electronic search results were supplemented by manual examination of reference lists from selected articles and were periodically updated to April 2014 (before the second meeting).

Based on this literature review, the facilitators identified a number of key statements.

All experts rated these statements through a two-round process. A 4-level scale was used, where 1 was defined as "high consensus", 2 as "low consensus", 3 as "no consensus", and 4 when panelists were "unable to form an opinion".

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