(e) ISSN Online: 2321-9599

(p) ISSN Print: 2348-6805

ORIGINAL ARTICLE

A study on Pain management in patients undergoing radiation therapy for head and neck cancer

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ABSTRACT:

Introduction: The harmful effects of radiation therapy (RT) and chemotherapy can cause inflammation of the oral and oropharyngeal mucous membranes, which is known as oral mucositis. These therapies can be used singly or in combination. They might cause excruciating symptomatology. This article addresses the treatment of somatic pain brought on by radiation therapy (RT). **Materials and Methods:** Recruitment of patients for the study was based on referred patients from the oncology clinic to the PRC prior to RT. Registration of received referrals to the PRC varied from two weeks before RT and two weeks into the start of RT treatment. The intention was to recruit the patient for the study before pain arose related to RT and mucositis. Regarding the patients who underwent surgery before RT, all had recovered from wound and postoperative pain at inclusion in the study. **Results:** The mean age of the participants was 66 years. Most patients were men (61.2%) and a majority were smokers or former smokers (59%). The most common cancer site was the pharynx (40.9%) and the most commonly occurring cancer treatment was a combination of surgery and RT (41.1%). **Conclusion:** This real-life study indicates that severe RT-related pain in HNC patients is not afatality.

Keywords: Oncology, mucositis, Postoperative pain, Radiationtherapy

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This article may be cited as: Behera SK. A study on Pain management in patients undergoing radiation therapy for head and neck cancer. J Adv Med Dent Scie Res 2016;4(4):316-319.

INTRODUCTION

The collection of disorders known as head and neck cancer is diverse in terms of occurrence, management, and prognosis.1 Chemotherapy, radiotherapy (RT), and surgery are possible treatments for HNC, and they can be used in different combinations.2. Two grey (Gy) per day, five days a week, for a total cumulative dose of 50–70 Gy is a typical RT protocol.2 Patients receiving treatment for HNC experience a variety of psychological and physical symptoms that adversely affect day-to-day functioning, such as discomfort, xerostomia, depression, and swallowing difficulties.3. The National Comprehensive Cancer Network Task Force reports that the most frequent physical side effects associated with cancer treatment include nausea, vomiting, and mucositis.4 The harmful effects of radiation therapy (RT) and chemotherapy can cause inflammation of the oral and oropharyngeal mucous membranes, which is known as oral mucositis.5

These therapies can be used singly or in combination. They might cause excruciating symptomatology. This article addresses the treatment of somatic pain brought on by chemotherapy or radiation therapy (RT).

It can be challenging to provide patients with HNC who have RT-related oral mucositis with sufficient pain management, according to previous research.6–11 The Pain and Rehabilitation Centre (PRC), University Hospital, Linköping, Sweden has developed local guidelines for this patient population that follow the WHO ladder, which includes paracetamol, non-steroid anti-inflammatory medications (NSAIDs), and opioid analgesics.12 In addition, every HNC patient receives weekly oral health examinations from the hospital dentist and uses a daily mouthwash containing mycostatin and lidocaine hydrochloride. Gabapentinoids, such as pregabalin, can be used to provide adjuvant analgesia when the pain mechanism is thought to be neuropathic.11 The adverse effects of opioid medication, including constipation, nausea, dry mouth, and decreased alertness, are discussed.9, 13 When swallowing problems are present, fentanyl patches are typically administered to minimise adverse effects such nausea and constipation.13 and fentanyl patches are the most popular opioid option at PRC for this patient population.

In a cohort of patients with HNC having RT, this long-term study assessed the impact of the aforementioned local recommendations on clinical practise and looked at the connections between opioid dosages, oral mucositis, and pain.

MATERIALS AND METHODS

The results showed no statistical difference between the control and intervention group regarding pain, QoL, and psychological aspects. Likewise, no significant difference was seen regarding gender and age between the groups.23 Thus, in this paper, we could consider these two groups as a unified group to study and analyse the issue of the current study.

During 2016–2017, patients with HNC undergoing RT were recruited by the PRC. Recruitment of

patients for the study was based on referred patients from the oncology clinic to the PRC prior to RT. Registration of received referrals to the PRC varied from two weeks before RT and two weeks into the start of RT treatment. The intention was to recruit the patient for the study before pain arose related to RTand mucositis.

Regardingthepatientswhounderwentsurgerybefore RT,allhadrecoveredfromwoundandpostoperativepainati nclusioninthestudy.Thatis,accordingtothelocalguidelin esatthelocaloncologyclinic,6– 8 weeks would pass before the start of radiation therapy. PatientsbecameeligibleforPRCafterreferralfromtheonc ologistasexpectedpaininconnectionwithRToftenrequir esstructuredpaintreatment.

In connection with the first appointment with the responsibleresearchnurses(RN)atPRC,whichtookplace within1–

2weeksafterstartofRT,alleligiblepatientsreceivedwritte nandoralinformationas well as offer to participate in the study. Eligible patients were 18years old or older, able to read, write, and understand Swedish, andscheduled to receive curative RT for HNC. Informed consent was ob-tained from all participants included in the study.

Assessment of oral mucositis: Oral mucositis was diagnosed ac-cording to WHO mucositis index score, as evaluated weekly by aspecialistdentistattheUniversityHospital.TheWHOmu cositisindexmeasurestheseverityofmucositisonafive-pointscalerangingfrom0(normal)to4(severe).Theresult wasdocumentedinthemedicalrecord.Oncea week, two RNreviewedthe degreeof mucositisin themedical record.

STATISTICAL METHODS

Data wereanalyzed using SPSS23.0 for Windows(IBM Corp., Armonk,NY, USA). Descriptive data are presented as median (minimum-maximum).Forinferentialstatistics,non-parametrictests wereused:(1)for comparisonsbetween two independent groups. the Mann Whitney Utestor, forcategorical data, theChi-squaretest; (2)for correlationsbetween two variables, Variables with p(corr) values >0.5 wereconsidered “significant”.

RESULTS

The analysisincluded 83 consecutive casesof patients withvariousHNC(Table1,see“Total”column).Themeana geof the participants was 66 years. Most patients were men (61.2%) and a majority were smokers or former smokers (59%). The most common cancer site was the pharynx (40.9%) andthe most commonly occurring cancer treatment was a combination of surgery and RT (41.1%). All partici-pantswerescheduledtoreceiveRTfortheircancer,witha minimum prescribed radiation dose of 50 Gy and a maximum dose of 68 Gy (10 Gy per week).

Table1: Socio-demographic, clinical, and treatment data of 83patients with HNC and comparison between pain-and mucositis groups.

Variables	Total	In-depth analysis at the cumulative dose of RT 51–60 Gray			
		Mild pain group[a]	Moderate-to-severe pain group[b]	Grade of mucositis[c] 0–1	Grade of mucositis[c] 2–4
Participants,n	83	52	31	34	49
Ageinyears					
Median(min–max)	68(37–87)	68(43–87)	67(58–80)	65(49–79)	68(37–87)
Sex,n(%)					
Female	34 (40.9)	22 (64.7)	12(35.2)	14 (41.1)	20(58.8)
Male	49 (59.0)	30 (61.2)	19 (38.7)	20 (40.8)	29(59.1)
Smokinghabits,n(%)					
Non-smokers	32 (38.5)	22 (68.7)	10 (31.2)	12 (37.5)	20(62.5)
Smokers	17 (20.4)	10 (58.8)	7(41.1)	5 (29.4)	12(70.5)
Ex-smokers	34 (40.9)	20 (58.8)	14 (41.1)	17 (50)	17(50)
Cancersite,n (%)					
Oralcavity	19 (22)	11 (57)	8(43)	8 (36)	11(64)
Pharynx	31 (41)	19 (62)	12 (38)	7 (15)	24(85)
Larynx	11 (10)	7 (83)	4(17)	4 (67)	5(33)
Others	22 (27)	15 (76)	7(24)	13 (65)	9(35)
Cancertreatment,n(%)					
RTonly	11 (13.2)	9 (81.8)	2(18.1)	5 (45.4)	6(54.5)
RTwithchemotherapy	16 (19.2)	10 (62.5)	6(37.5)	3 (18.7)	13(81.2)
RT andsurgery	27 (32.5)	17 (62.9)	10 (37)	14 (51.8)	13(48.1)
RTwithchemotherapyand surgery	9 (10.8)	6 (66.6)	3(33.3)	2 (22.9)	7(77.7)
Cumulativedoseofradioth erapy,gray,	69(51–69)	69(51–69)	69(51–69)	69(51–69)	69(51–69)
median,(min–max)					

Opioiduseyes/no(%)					
Yes(%)	59 (71)	35 (59.3)	24 (40.6)	20 (33.8)	39(66.1)
No(%)	24 (28.9)	17 (70.8)	7(29.1)	14 (58.3)	10(41.6)
Opioiduse(mg/day)[d], median(min–max)	85(0–431)	61(0–431),	121(0–401)	23(0–150)	121(0–431)
Concomitantofopioid-andNSAIDuse					
Yes(%)	36 (43.3)	21 (58.3)	15 (41.6)	13 (36.1)	23(63.8)
No(%)	47 (56.6)	31 (65.9)	16 (34)	21 (44.6)	26(55.3)
Acetaminophenuse					
Yes(%)	63 (75.9)	40 (63.4)	23 (36.5)	23(36.5)	40(63.4)
No(%)	20 (24)	12 (60)	8(40)	11 (55)	9(45)

n, total number of participants; RT, radiotherapy; Ex-smokers, former smokers; OM, oral mucositis; NSAID, non-steroidal anti-inflammatory drugs.[a]Mildpaingroup=function-related pain(OralCancer PainQuestionnaire), numerical rating scale (NRS)≤4 at measurement point (MP)52–61.[b]Moderate-to-severepaingroup=function-relatedpain,NRS≥5atMP52–61.[c]GradeofmucositisatMP52–61.[d]OpioiduseatMP 52–61.

DISCUSSION

In addition to focusing on MP 51–60, which was the time point of maximum opioid doses, highest grade of mucositis, and highest pain intensities, we also examined the temporal dynamics involved (longitudinal features).

One of the study's benefits, from a pathophysiological perspective, is that the data was organised based on the cumulative radiation dosage (Gy) rather than the duration (weeks) in which the patients were included. We were able to connect the real radiation dose to the onset of mucositis thanks to this tactic. This study discovered, as anticipated, that radiation dose was associated with the development of mucositis and discomfort in individuals with HNC during RT.

Following local standards for pain management at PRC, the majority of patients (67% at MP51-60) reported only mild discomfort (NRS 0–4). This result is in line with a previous study that also found that patients with HNC receiving RT experienced minor pain;14 However, the study did not disclose the tactics employed to alleviate pain, therefore from a pharmacological perspective, its conclusions cannot be applied to guide clinical practise. Therefore, for most HNC patients using RT, sufficient pain management can be achieved. This is not a surprising conclusion given the numerous studies that have demonstrated how challenging it is to treat this patient group's pain.15, 16 Within two weeks prior to and up to two weeks following RT, every patient was sent to the PRC. Since early intervention was made possible by this early surveillance method, results were likely impacted. Early pain management—that is, giving cancer patients preventive medication during the post-operative phase—has reportedly been linked to better pain control.17

As of right now, the literature does not provide enough data to recommend a particular pharmaceutical approach to treating pain in patients with head and neck cancer. Right now, the WHO pain ladder should be followed by these patients, with some additional advice to utilise local medications (such mouthwash containing lidocaine).18–20 This is consistent with PRC local recommendations, and one of the study's strengths is that it outlines the results of using this method in clinical settings. The majority of patients with HNC had similar gender, age, and smoking habits, which implies good validity.

Nonetheless, there are clear restrictions. Because of the small sample size (n=83) in this uncontrolled investigation, it's possible that the results are not fully representative of populations of individuals with HNC, which restricts how broadly these findings can be applied. In such a tiny sample, detailed subgroup analysis is also challenging. Furthermore, there is a chance that the patients who consented to take part were the healthiest ones (risk of selection bias), which could also have an impact on the external validity. Notably, the patients also experience other stresses that were not measured in the study, such as nausea and vomiting, which can have an impact on the patients' reporting of pain.3,4 Moreover, pregabalin was only used to treat 16% of the patients. For this patient population, randomised controlled trials evaluating adjuvant pregabalin would be beneficial.

CONCLUSION

Thisreal-lifestudyindicatesthatsevere RT-relatedpaininHNCpatients isnotafatality.However, furtherstudiesareneededtodevelopbetterpaintreatment strategies for those patients who do develop severe oral mucositis-relatedpaindespiteadequateopioidtreatment.

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