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ORAL MUCOSITIS-RELATED NEUROPATHIC PAIN IN HEAD AND NECK CANCER PATIENTS RECEIVING RADIOTHERAPY OR CHEMORADIOTHERAPY

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INTRODUCTION:

Painful oral mucositis (OM) is a debilitating complication in Head and Neck Cancer (HNC) patients receiving RadioTherapy (RT) /ChemoRadioTherapy. Therapy-induced pain can be nociceptive and / or neuropathic. Neuropathic pain (NP) in HNC patients often remains underdiagnosed and undertreated. This study's purpose was to identify the OM-induced NP.

PATIENTS & METHODS:

ORAL PAIN AND XEROSTOMIA EVALUATION: Numeric Rating Scale (NRS); Scores: 0 – 10

1 - 4: mild, 5 – 7: moderate, 8 – 10: severe.

NEUROPATHIC PAIN EVALUATION: Douleur Neuropathique 4 questionnaire: DN4; Cut-off value: total score of 4/10.

ORAL MUCOSITIS GRADING: EORTC / RTOG criteria; Grades: I - IV

I: mild, II: moderate, III-IV: severe

Patients completed a DN4 as soon as they reported moderate or severe pain.

RESULTS:

| Variable | N (%) | Mean (SD) |
|--|---------------------|---------------|
| Age (years) | | 63.54 (13.96) |
| Gender | | |
| Male | 20 (76.9) | |
| Female | 6 (23.1) | |
| Cancer Stage | | |
| II | 2 (7.7) | |
| III | 7 (26.9) | |
| IV | 9 (34.6) | |
| Recurrence missing | 2 (7.7) 6 (23.1) | |
| Cancer Site | | |
| Oral / Oropharyngeal | 16 (61.5) | |
| Nasal / Nasopharyngeal | 3 (11.5) | |
| Parotid | 3 (11.5) | |
| Unknown Primary | 2 (7.7) | |
| Other | 2 (7.7) | |
| Type of Treatment | | |
| Radical RT | 11 (42.3) | |
| Postoperative RT | 15 (57.7) | |
| Concomitant Chemotherapy | 20 (76.9) | |
| Radiotherapy Dose (Gray) | | |
| Total Dose | | 62.11 (9.243) |
| Daily Dose | | 2.04 (0.104) |
| Infections (before the DN4 completion) | | |
| Candidiasis | 3 (11.54) | |
| Herpes | 2 (7.69) | |
| Pain medication | | |
| Opioids | 8 (30.77) | |
| NSADs | 7 (26.92) | |
| Adjuvant (Pregabalin) | 1 (3.85) | |

Characteristics of the patients who completed a DN4q (n=26)

| | DN4 | Pain | Oral Mucositis | Xerostomia |
|----------------|--------------------|--------------------|--------------------|--------------------|
| DN4 | | r=0.617 p=0.001 | r=0.752 p<0.001 | r=0.590 p=0.002 |
| Pain | r=0.617 p=0.001 | | r=0.314 p=0.119 | r=0.733 p<0.001 |
| Oral Mucositis | r=0.752 p<0.001 | r=0.314 p=0.119 | | r=0.444 p=0.023 |
| Xerostomia | r=0.590 p=0.002 | r=0.733 p<0.001 | r=0.444 p=0.023 | |

Correlations between DN4 score, intensity of pain, oral mucositis and xerostomia. (Spearman's rho test - r).

| Variable | N (%) | | | Mean (SD) | | |
|-----------------------|--------------|-------------|--------------|--------------|--------------|--------------|
| | Total (n=26) | DN4≥4 (n=5) | DN4<4 (n=21) | Total (n=26) | DN4≥4 (n=5) | DN4<4 (n=21) |
| Pain | | | | 7.46 (1.42) | 8.40 (0.548) | 7.24 (1.48) |
| Mild | - | - | - | | | |
| Moderate | 13(50) | - | 13(61.9) | | | |
| Severe | 13(50) | 5(100) | 8(38.1) | | | |
| Oral Mucositis | | | | 1.96 (0.92) | 3.00 (0.00) | 1.71 (0.85) |
| No | 3(11.5) | - | 3(14.3) | | | |
| Mild | 2(7.7) | - | 2(9.5) | | | |
| Moderate | 14(53.8) | - | 14(66.7) | | | |
| Severe | 7(26.9) | 5(100) | 2(9.5) | | | |
| Xerostomia | | | | 6.50 (2.14) | 8.40 (0.548) | 6.05 (2.13) |
| Mild | 4(15.4) | - | 4(19.0) | | | |
| Moderate | 10(38.5) | - | 10(47.6) | | | |
| Severe | 12(46.2) | 5(100) | 7(33.3) | | | |

Pain, Oral Mucositis and Xerostomia in patients who completed a DN4

| NP descriptors | Total (n=26) n(%) | Negative DN4 (n=21), n(%) | Positive DN4 (n=5) n(%) | p-value |
|-----------------------|-------------------|---------------------------|-------------------------|--------------|
| Burning | 9 (34.62) | 6 (28.6) | 3 (60.0) | 0.302 |
| Painful cold | - | - | - | - |
| Electric shocks | 8 (30.77) | 3 (14.3) | 5 (100) | 0.001 |
| Tingling | 5 (19.23) | 2 (9.5) | 3 (60.0) | 0.034 |
| Pins and needles | 8 (30.77) | 4 (19.0) | 4 (80.0) | 0.020 |
| Numbness | 5 (19.23) | 1 (4.8) | 4 (80.0) | 0.002 |
| Itching | 4 (15.38) | 2 (9.5) | 2 (40.0) | 0.155 |
| Hypoesthesia to touch | 1 (3.87) | - | 1 (20.0) | 0.192 |
| Hypoesthesia to prick | - | - | - | - |
| Brushing | 9 (34.62) | 7 (33.3) | 2 (40.0) | >0.999 |

Statistical significance of the NP descriptors between positive (≥4) and negative DN4 scores. (Fisher's exact test)

Five patients (19.23%) had a positive for NP, DN4 score ≥4. The most common NP descriptor was "burning" (34.62%) followed by "electric shocks" (30.77%) and "pins-and-needles" (30.77%). Statistically significant differences between positive and negative DN4q scores were observed for the "electric shocks", "tingling", "pins-and-needles" and "numbness" NP descriptors. Nine (34.62%) patients didn't report any NP descriptors. A direct correlation was observed between DN4q score and intensity of pain, OM and xerostomia (p<0.02). Pain medication was administered to fifteen (57.69%) patients. Adjuvant medication for NP was administered to 1 (1/5, 20%) patient with positive DN4

CONCLUSION:

Oral mucositis induced NP was assessed for the first time during RT/CRT for HNC. Neuropathic pain was recorded in 5 patients with 1 of them receiving adjuvant NP medication. This study highlights the lack of adequate recognition and management of OM related NP.