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THE TREATMENT IMPACT OF THE INDUCTION CHEMOTHERAPY WITH PACLITAXEL AND CARBOPLATIN ON THE QUALITY OF LIFE IN THE PATIENTS WITH LOCOREGIONAL ADVANCED TONSILLAR CARCINOMA

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Abstract: ***Background:*** *Tonsillar carcinoma is a significant cause of mortality and morbidity in oncological practice which cause severe decrease in quality of life especially in patients with III and IV stages. The objective of the study was to explore the influence of induction chemotherapy with Paclitaxel and Carboplatin on quality of life.*
Methods: *In an open label study, we randomly assigned 80 patients with locoregional advanced tonsillar cancer to receive conventional radiation therapy (the control group) with paclitaxel and carboplatin as induction therapy and to induction chemotherapy with cisplatin and 5 fluorouracil. All patients were evaluated for quality of life and mental status using Medical Outcome Study Short –form, 36 Item Health Survey (SF-36) questionnaire. The follow-up period was 12 months.*
Statistics: *using nonparametric test Krusskall-Wallis (for multigroup ordinal variables) and Pearson correlation coefficient.*
Results: *There is a significant improvement in quality of life in patients treated with paclitaxel and carboplatin treatment compare to those treated with cisplatin and 5 fluorouracil. There where no changes in menthal status.*
Conclusions: *The study suggest that paclitaxel and carboplatin as induction chemotherapy improves quality of life in patients with locoregional advanced tonsillar carcinoma.*

Key words: *Paclitaxel, carboplatin, tonsillar carcinoma, quality of life, SF-36.*

1. Introduction

Tonsillar cancer is less common in oncology practice. Worldwide, tonsillar cancer together with oropharynx and hypopharynx cancers account for about 123,000 new cases per year, with a mortality estimated at 79,000 deaths/year [1]. Usually, tonsillar and oropharyngeal carcinomas are more frequently diagnosed in patients 50-70 years old, men being affected 3 to 5 times more often than women [2].

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2. Objective

Purpose of the study was to assess the impact of the paclitaxel and carboplatin induction chemotherapy on quality of life and mental status in patients with locoregional advanced tonsillar carcinoma. The main end point of the trial was to evaluate if there are differences in quality of life in patients treated with induction chemotherapy consisted in paclitaxel and carboplatin or in cisplatin with 5-FU and versus curative chemoradiation therapy.

3. Materials and Methods

Method : 177 patients with epidermoid tonsillar carcinoma were screened at the Oncology and Otolaryngology Department of Clinical Emergency Hospital of Brasov between January 2005 – January 2011. The inclusion criteria in the study were: histopathological diagnostic of epidermoid tonsillar carcinoma, advanced stage of locoregional tonsillar cancer was established using clinical, head and neck CT scan, lack of distant metastases, surgically inoperable patients. The exclusion criteria were: early tonsillar carcinoma or metastatic disease, any other histopathology of tonsillar cancer, patient refusal to participate in the study, operable patients. All patients have given the informed consent.

In the study were included 80 patients: 29 patients randomized to conventional radiation therapy (control group or Group1), 31 patients randomized to receive paclitaxel and carboplatin as induction therapy (Group 2) and 20 patients randomized to receive induction chemotherapy with cisplatin and 5 fluorouracil (Group 3). The radiotherapy (RT) was delivered at 66-70 Gy total dose on the tumor site, excluding the spinal cord at 40 Gy, according to standard procedures specific to radiation oncology sections [3,4,8]. Paclitaxel and carboplatin chemotherapy were given in three chemotherapy cycles of paclitaxel 175 mg / m² body surface area and carboplatin AUC6, followed by the sequence of radiotherapy to 66-70 Gy total dose, excluding the spinal cord at 40 Gy . Cisplatin and 5-FU (5-fluorouracil) or chemotherapy was given in dosage of 100 mg / m² cisplatin in 30 minutes iv infusion in day 1 and 5-FU in dosage of 1000 mg / m² I.V (24h infusion) days 1-5. There were three cycles every 3 weeks followed by standard radiotherapy according to standard protocols. The study duration was 12 month.

All patients completed SF 36 questionnaire for quality of life evaluation. SF-36 questionnaire was initial used in Medical Outcome Study Short Form-36 Item Health Survey (4) and is now widely used in U.S. for the quality of life evaluation in various chronic diseases. Emerged as a consequence of psychometric theory in assessing the general health of patients, SF-36 form is a valid instrument for assessing the quality of life consisting in a questionnaire with 36 items. The final score is determined by an algorithm included in the rating scale. The questionnaire is divided into 8 sections that define the major parameters of physical and mental health: limitation of physical activity (such as walking, sports, swimming) (PF); problems at the work place or in daily activities caused by underlying disease (RP); intensity of physical pain and / or existence of any underlying disease induced limitations (BP); perception of their own health condition (GH); the energy / vital tone (VT); the extent to which health interferes with normal social status (SF); problems in daily activity caused by disturbances in the emotional area (RE); mental health status (MH) .[9]

We made minor amendament to questionnaire consisting in the fact that it was adapted and simplified (by subgroups of items) to allow an easier and faster self-assessment for both – subjects and examiners. Each sector of work items could be pursued and rated by the patient on three levels, a variable (1-3 points) and depending on the degree of changes to the specific parameters. Thus, severe injure was noted by 1 point, moderate injure with 2 points and no injuries with 3 points. The highest normal state score (for a healthy individual) was set at 24 points. Minimum values: 8 points. Finally, mean scores were calculated for all patients of the three groups and then compared results and findings were included in tables and graphs below. Patients who have found changes (considering the improvements in quality of life an increase in scoring of at least 1.00 points) were analyzed globally and by comparison with control group. Quality of life score was assessed at baseline and at the end of the study.

There were used statistical comparisons and evaluation between initial and final SF 36 mean score, comparisons between chemotherapy - given groups and control radiotherapy - given group, using nonparametric test Krusskall-Wallis (for multigroup ordinal variables) and Pearson correlation coefficient. Statistical data processing and expression of results was done with software 4.5 for Windows XP SP3 STATVIEW at a 95% confidence interval.

4. Results

Data regarding quality of life after filling out the SF 36 questionnaires are presented in tables and charts below:

Table 1

Evolution of quality of life, QoL-SF 36 item mean score in patients treated with ChRT, cisplatin-5FU, paclitaxel-carboplatin and chemoradiation at baseline and after 12 months

	Arm ChRT (n=29)		Arm cisplatin-5FU(n=20)		Arm paclitaxel-carboplatin (n=31)	
	INITIAL	FINAL	INITIAL	FINAL	INITIAL	FINAL
PF	1,5	1,3	1,5	1,8	1,5	2
RP	2	1,5	2	1,8	2	1,9
BP	1,7	1,8	1,8	1,9	1,4	2
GH	1	1,5	1,1	1,7	1	2
VT	1,5	1,5	1,5	1,8	1,6	2
SF	2	1,5	2	1,7	2	1,7
RE	1	1	1,1	1,2	1	1,5
MH	2	2	2	2	2	2

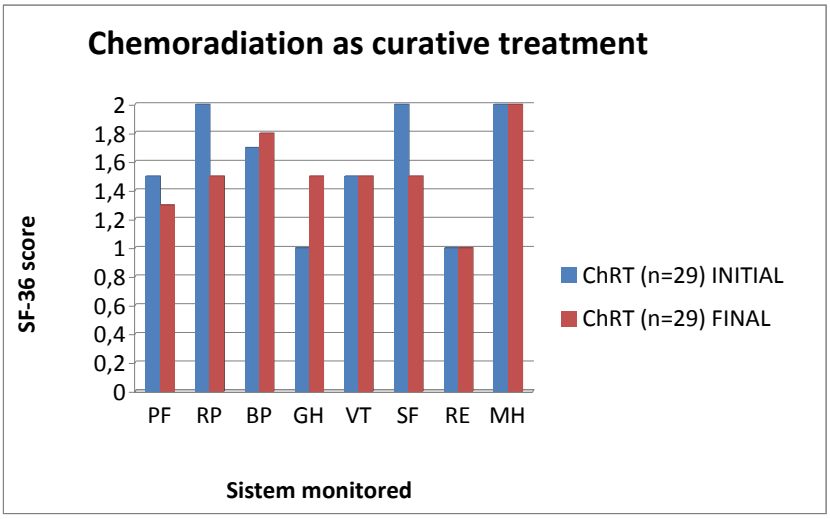

Fig. 1. *Evolution of quality of life, QoL-SF 36 item mean score in chemoradiation arm (n=29)*

Quality of life evaluated by SF 36 questionnaire was clearly improved at the end of the study in the patients treated with induction chemotherapy paclitaxel - carboplatin in addition to a better oncological response at therapy observed in these patients compare with those treated with conventional chemo- and radiotherapy ($p<0.001$) and with those treated with cisplatin-5FU. There is a significant improvement in quality of life overall, the predominant type of growth being settled at medium / excellent level (over 76.5% of patients). It is important to underline that there were improvements in daily fields of activity and work (54.4%). In this area we can include physical performance and perception of symptoms like pain, where favorable changes are seen after treatment. We believe in fact that this functional area of daily activity was highly affected by the persisting symptoms (83.4%) that partly can be partially correct by target therapy in intention to reduce tumor size which can be followed by improvement of respiratory dysfunction with increasing of brain oxygenation, allowing better daily activities.

The lack of painful complications during the chemotherapy with paclitaxel-carboplatin and cisplatin-5FU would be another favorable factor. Chemotherapy led to significant improvements in social interactions and affection area as well as the area of the sensibility. Noted improvements were recorded in approximately 34 - 44% of patients in these functional areas of quality of life, which in patients with this type of pathology is an important gain, knowing the fact that they are in the period when the emotional area is strongly affected by the disease, generating a series of negative psycho side reactions. At the same time, the general perception of their mental state was not affected in any treatment group.

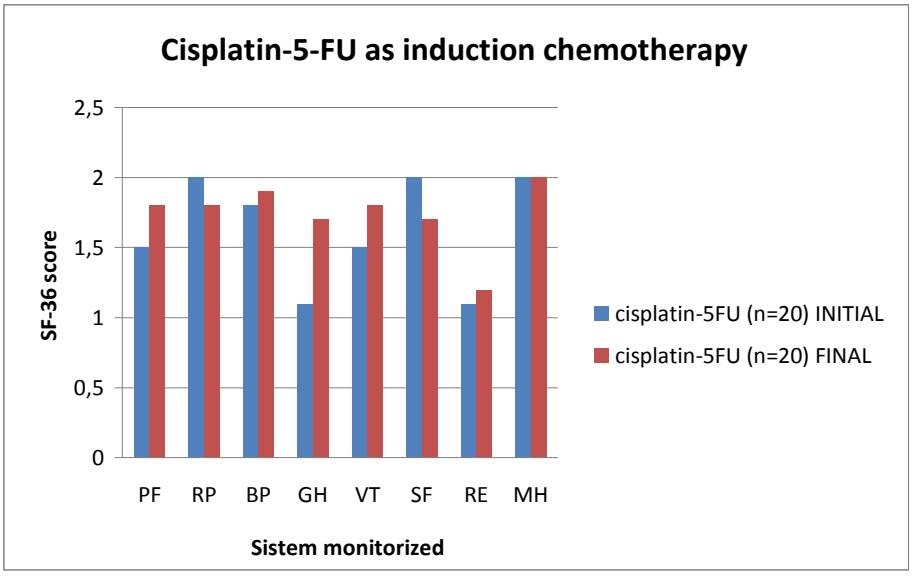

Fig. 2. *Evolution of quality of life, QoL-SF 36 item mean score in cisplatin-5FU arm (n=20)*

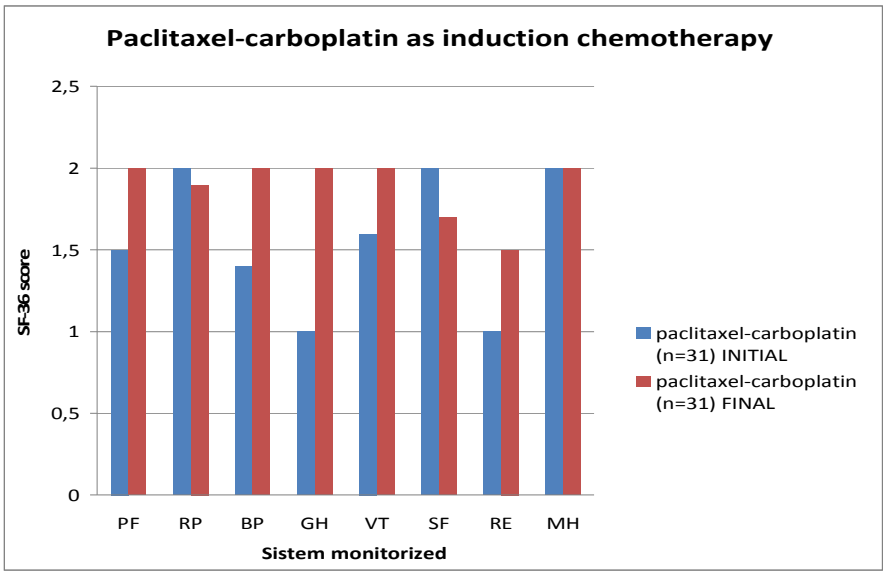

Fig. 3. *Evolution of quality of life, QoL-SF 36 item mean score in paclitaxel-carboplatin arm (n=31)*

These results correlate significantly with those obtained by other authors in similar studies, confirming the hypothesis of beneficial effects on QOL in treatment protocol with paclitaxel and carboplatin given as induction chemotherapy in

patients with locoregional advanced tonsillar carcinoma but only in selected cases [5].

Outcomes of this study suggest that administration protocol with paclitaxel and carboplatin, given as induction chemotherapy conducted in selected cases of locoregional advanced tonsillar carcinoma, improves quality of life of these patients. These data confirm existing studies in the literature [6,7] showing beneficial effects of this type of treatment which, when properly applied improve the overall quality of life, affecting both – survival and psychosomatic state of the patients. Estimation of quality of life (QoL) by SF-36 questionnaire (Medical Outcome Study Short Form-36 Item Health Survey) occurred as a consequence of using psychometric theory of assessing the general health in patients with various disabling conditions, among other questionnaires like used in current practice (QCL HN35, SF 8, QOL AD etc). We believe that SF-36 is a valid and easy tool for assessing the quality of life in patients with advanced locoregional tonsillar cancer undergoing combined radio / chemotherapy.

Relying on the types of treatment available for this type of tonsillar cancer, the effect of the protocol with paclitaxel and carboplatin, given as induction chemotherapy seems to be a beneficial treatment modality, effective in practical use and with minimal side effects when applied in carefully selected cases.

Conclusions

The induction chemoptherapy with paclitaxel and carboplatin compare with cisplatin – 5 FU and with conventional chemoradiotherapy was associated with improving in quality of life in selected patients with locoregional advanced tonsillar carcinoma.

References

1. Alkureishi, L.W., Ross, G.L., MacDonald, D.G., et al.: *Sentinel node in head and neck cancer: use of size criterion to upstage the no neck in head and neck squamous cell carcinoma.* In: Head Neck 2007; 29:95–103.
2. Katz, M.R., Kopek, N., Waldron, J., Devins, G.M., Tomlinson, G.: *Screening for depression in head and neck cancer.* In: Psychooncology 2004;13:269–280.
3. Perry, M.C.: *The Chemotherapy Source Book.* 4th edition. 2007. Lippincott Williams and Wilkins.
4. Pharmaceutical Press. British National Formulary. 62nd edition. 2011. British Medical Association and Royal Pharmaceutical Society of Great Britain.
5. Rogers, S.N., Lowe, D., Brown, J.S., Vaughan, E.D.: *A comparison between the University of Washington Head and Neck Disease-Specific measure and the Medical Short Form* 36, EORTC QoL-C30 and EORTC Head and Neck 35. In: Oral Oncol 1998;34:361–72.
6. Schwarz, R., Hinz, A.: *Reference data for the quality of life questionnaire EORTC QoL-C30 in the general German population*. In: Eur J Cancer 2001;37:1345–1351.
7. Sloan, J., Symonds, T., Vargas-Chanes, D., et al.: *Practical guidelines for assessing the clinical significance of health-related quality of life changes within clinical trials*. In: Drug Inf J 37:23-31, 2003.
8. Sweetman, et al.: *Martindale: The Complete Drug Reference*. 37th edition. 2011.
9. Ware, J.E., Jr., and Sherbourne, C. D.: "The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual Framework and item Selection," In: *Medical Care*, 30:473-483, 1992.