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CHEMO-INDUCED ORAL COMPLICATIONS IN PATIENTS TREATED FOR CANCER AT THE YAOUNDE GENERAL HOSPITAL

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ABSTRACT

Nowadays, surgery, radiotherapy, and chemotherapy are the most used cancer therapies. But the chemotherapy, because of its non-specificity towards neoplastic cells causes many complications among which the oral complications. About 40% of chemotherapy patients develop an oral complication and, this prevalence can go up to 76% in malignant hemopathies. In this study, our objectives were to determine the prevalence, frequency and average extension time for the occurrence of these complications at the Yaounde general hospital. In the other hand, the association of these complications with a few risk factors was evaluated. To achieve these objectives, we conducted a descriptive study over 6 months with prospective data collection in the oncology department of the General Hospital of Yaounde. Our sample was determined consecutively and randomly. The selected patients (1 patient = 1 file), after receiving their chemotherapy cure, were consulted on the 10th day to identify the sprung complications. When a statistical test was required, a value of p<0.05 was considered to be statistically significant. 95 participants (36 men and 59 women) were included in our study. The prevalence of oral complications was 40%. and, four types of toxicity were observed in this population namely: the mucositis (44.74%), the xerostomia (26.32%), the dysgeusia (23.68%) and the oral candidiasis (5.26%). These complications occurred after an average extension time of 08 days and seemed to be frequent in the female sex and in the age group of 30 to 40 years. The risk factors associated with these complications were: the young age (p = 0.025), the unpleasant oral health (p = 0.049; OR = 3.27; CI = [1.09-9.80] and HIV infection (p = 0.01; OR = 4.78; CI = [1.39-16.41]. Thus, chemo-induced oral complications are a reality in Cameroon with a prevalence of 40% reported at the end of this study.

I- INTRODUCTION

Cancer therapies in recent years have undergone major changes to cope with the ever-increasing frequency of cancers and their complications.[1,2] Although today a diversified therapeutic arsenal is available, only three therapeutic modalities are the most used: the surgery, the radiotherapy and the chemotherapy.[3] Chemotherapy, a treatment based on the destruction of neoplastic cells using cytotoxic substances[4], also affects the normal cells from the organism.[5] This lack of specificity gives it important complications, including oral complications. These complications are either directly due to the toxic action of antineoplastic agents on the oral mucosa, or secondary to hematopoietic toxicity.[2,5]

This vulnerability of the oral cavity to chemotherapy is due to the cells conditions which are there and which are rapidly renewed. Management of the cancer patient is often compromised by this vulnerability. In fact, the ulcers and the resulting oral infections have a negative impact on the quality of life of patients, on the antineoplastic protocol instituted and therefore on the patient's prognosis.[6, 7,8] In addition, these complications lead to additional costs for patients related to the purchase of non-specific treatments.[6,9]

It is estimated that about 40 to 50% of patients on chemotherapy have oral complications.[10] This prevalence can go up to 76% in malignant

hemopathies.[11] Nowadays, approximately 20% of cancers worldwide are treated with chemotherapy[4], a good understanding and description of these complications seems to be really necessary. But to do this, an epidemiological representation well detailed must be available especially in developing countries like Cameroon. In addition, the difference in the technical platform and in the oral follow-up care for patients undergoing the chemotherapy in Cameroon could undoubtedly lead to some peculiarities of the oral complications that may occur. Hence the interest of this study on chemo-induced oral complications in patients treated for cancer at the General Hospital of Yaounde (HGY).

II- MATERIALS AND METHODS

We carried out a descriptive study with prospective data collection over a period of 06 months, from October 2013 to March 2014. It was carried out in the oncology department from the General Hospital of Yaounde. We included patients diagnosed with cancer confirmed by pathology examinations, aged at least 18 and having started their chemotherapy cure in the oncology department from General Hospital of Yaounde during the study period. Our sample was determined consecutively and randomly and consisted of all subjects meeting the selection criteria. After obtaining the approval of the national ethics committee, the authorization of the director from the General Hospital of Yaounde and the informed consent of the new participants admitted to undergo chemotherapy cure, they were registered and identified on a file for data collection. Ten days after the administration of the chemotherapy cure, registered participants were consulted to identify the occurence of a possible oral complication. And, only the first oral complication occured was taken into account and registered on the patient's data collection form. Patients who had no oral complications on the tenth day were re-examined a week later. During our study, the tumors were grouped according to their histological type. Thus, three histological types could be highlighted: epithelial tumors, mesenchymal tumors and hematological tumors. Carcinomas, adenocarcinomas, squamous cell carcinomas, cystadenocarcinomas and choriocarcinomas have been classified as epithelial tumors. Mesenchymal tumors have included sarcomas, leiomyosarcomas, rhabdomyosarcomas, kaposi sarcomas, myeloid sarcomas and chondrosarcomas. The hematological tumors were lymphomas, follicular lymphomas, non-Hodgkin's lymphomas, khaler's disease and leukemias. Likewise, the therapeutic protocols administered consisted of three groups such as the protocols with cisplatin included the cisplatin-adriblastin, the cisplatin-endoxan, the cisplatin-etoposide, the cisplatin-5FU, the cisplatin-taxotere, the cisplatinedeticene, the BEP, FAP, TPF ; the adriblastine protocols included AC, ABV, CHOP, FAC, ABVD, carboplatin-adriblastine, CYVADIC; and the protocols without cisplatin or adriblastin included the carboplatin-endoxan, the carboplatin-taxol, the FUFOL, the 5FU-

xeloda, theoxaliplatin-5FU, the FUN. For the comparison of quantitative data, the Mann-whitney and Kruskal-wallis tests was used. The Chi-square test with the Yates correction or the exact Fischer test was used for qualitative variables. For all these tests, a value of $p<0.05$ was considered to be statistically significant. The analysis of the data collected was done with Epi Info software version 7.1.3.10.

III- RESULTS

At the end of our study period, 95 participants out of the 107 eligible participants were included. This sample consisted of 36 men (37.89%) and 59 women (62.11%) with a sex ratio of 0.61 in favor of women. The average age was 46.22 years ± 13.25 years with ages ranging from 18 to 71 years. 25% of participants were under 36 years of age and 75% were under 56 years of age.

III.1- Characteristics of the sample

Among our study population, 62.1% presented with an epithelial tumor, 22.1% with a mesenchymal tumor and 15.8% with a haematological tumor. The adriblastin protocol was used for the follow-up care for 63.2% of patients, the cisplatin protocol and the one consisting neither cisplatin nor adriblastin were used for 23.4% and 9.5% participants respectively. The average number of cures was 5.3 ± 3.3.

III.2- Prevalence of complications

Among the 95 included participants, 38 participants developed oral complications for a prevalence of 40%. Among the participants having presented some complications, 57.89% had a feminine sex and 42.11% had a masculine sex. These complications were more present among participants with ages ranging from 30 to 40 years (Figure 1).
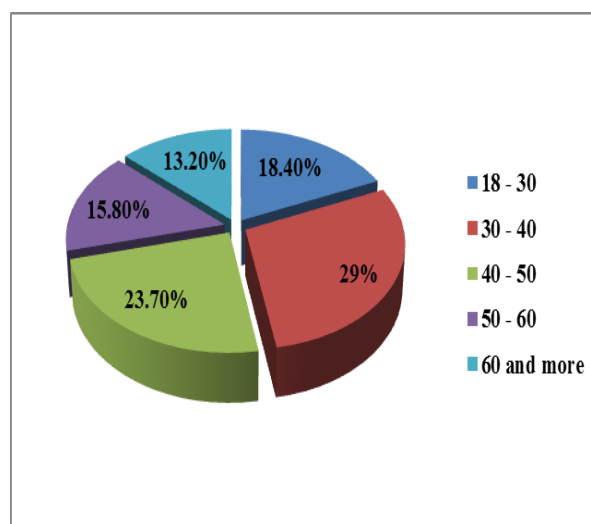

Figure 1: Distribution of complications in each age group

III.3- Prevalence of complications depending on the types of tumors and the chemotherapy protocol used.
The most common tumors in these participants with complications were epithelial tumors (50%). They were followed by mesenchymal tumors (26.32%) and haematological tumors (23.38%). The most common chemotherapy protocol in these participants was the adriblastin protocol (65.79%) (Table 1).

Table I: Distribution of complications according to the chemotherapy protocol.

Protocoles type	Numbers	Percentages (%)
Protocol with adriblastin	25	65.79
Protocol with cisplatin	11	28.95
Protocol without cisplatin and adriblastin	2	5.26
Total	38	100

III.3- Observed complications type
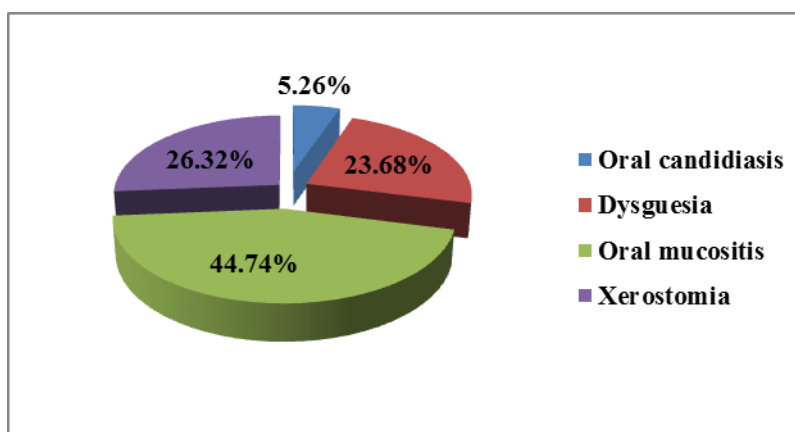The most frequent complication was the oral mucositis with 44.74%.

Figure 2: Distribution of registered complications among the study participants.

III.4- Average extension time for the occurrence of complications
The average extension time for the occurrence of complications was 8.74 days. 25% of complications occured after 2 days and 75% after 7 days.

III.5- Association of complications with some risk factors
A statistically significant association was observed only between the unpleasant oral health, the HIV infection and the mucositis occurence.

Table II: Risk factors and antecedent of patients with mucositis

Risk factors and antecedent	Numbers	OR (CI to 95%)	P.value
unpleasant oral health	11	3.27 (1.09-9.80)	0.049
Epithelial tumors	7	0.35 (0.12-1.03)	0.06
Mesenchymal tumors	6	2.29 (0.73-7.19)	0.20
Haematological tumors	4	1.87 (0.52-6.80)	0.46
Protocol with Cisplastin	5	1.13 (0.36-3.60)	1.00
Protocol with adriblastine	11	1.09 (0.39-3.48)	1.00
Protocol without Cisplatin and adriblastin	1	0.55 (0.06-4.69)	1.00
Tobacco	3	0.83 (0.21-3.24)	1.00
Alcohol	10	1.10 (0.38-3.20)	1.00
High blood pressure	0	-	-
Diabetes	0	-	-
HIV Infection	6	4.78 (1.39-16.41)	0.01

OR= Odds-Ratio; CI= Confidence Interval

LIMITATIONS OF THE STUDY
The main limitation encountered in this study was related to data collection. Indeed, during this study stage, we were not able to consult all our patients on the 10th day. This was due to the fact that not everyone respected their appointments. Consequently, we have been able to miss some neglected toxicities or not felt by the patients.

DISCUSSION
The average age of our study population was 46 years ± 13 years with a female predominance (62.11%). In a

similar study made by Carmen Chan in Chinese cancer patients, a male predominance was observed with an average age of 48.19 years ± 11.89 years.[12] Beyond this similarity in middle age, it is noted that these patients are relatively young. This could be due to improved techniques for early detection of cancer disease. However, the increase of some risk factors, such as HIV and hepatitis infections, deserves to be highlighted.[13] And, the high prevalence of breast cancer in Cameroon in general and within the oncology department from the General Hospital of Yaounde in particular would undoubtedly be at the origin of the female predominance into our study.

Within this sample, a prevalence of 40% was objectified. This prevalence was lower than those found by some authors. Herlofson, in a retrospective study on 39 patients about the side effects of chemotherapy for testicular cancer on the oral mucosa (62%).[14]; Ramirez-Amador, in a prospective study on 50 patients about the lesions of the oral mucosa associated with chemotherapy in patients with leukemia and lymphoma (72%).[11] The difference observed between these results and ours could be explained by the nature of the chemotherapy used. In fact, in these two investigations, all patients received high-dose chemotherapy, unlike those in our study population, whose heterogeneity of tumor types did not always require the administration of intense cures of chemotherapy. This hypothesis joined the result from a similar study carried out by Beier on patients with breast cancer where standard chemotherapy was also used.[15]

Several oral lesions are likely to occur in patients on antineoplastic drugs. However, in our sample with complications, only four types of toxicities were observed namely: the oral candidiasis (5.26%), the xerostomia (26.32%), the dysgeusia (23.68%) and the mucositis (44.74%) (Figure 2). These results were lower than those found in the literature. Wilberg in 2014, in his study on 168 patients with cancers of different locations except those from the head and neck found a mucositis percentage of 12% and a xerostomia percentage of 59%[16]; August Zabernigg in his study on 107 patients with lung cancer found a dysgeusia percentage of 69.9%.[17] While Jenny Mcgreevy in his study on 89 patients had 68.5% of dysgeusia[18]; Beier Jensen in 2008 found 11% of oral candidiasis in his study which included 46 women with breast cancer.[19]

These differences observed with the results obtained into our study could have several origins like the young age from our study population, the low percentage of patients with a smoking antecedent, a single type of cancer therefore implying almost similar chemotherapy protocols and a cumulative dose toxicity of antineoplastics. In fact, in the study of Wilberg, the average age of its study population was 57 years ± 11.8 years compared with the one of 46 years ± 13 years found into our study.[16] In addition, in his study, the patients had already received an average of 8.2 cures of chemotherapy before the beginning of the study, while ours had not yet received chemotherapy before the beginning of our investigation and received only an average of 5.3 cures during the periode of this study.

August Zabernigg and Jenny Mc greevy, had included in their studies a high number of patients with a smoking antecedent (respectively 107 patients out of 197 and 81 patients out of 89), thus showing the role of tobacco in the occurence of dysgeusia.[17,18] Beier Jensen had included in his study 46 women only suffering from breast cancer therefore receiving almost similar chemotherapy protocols.[15]

The extension time for the occurrence of oral complications had an average of 8 days. This average time was close to the one from the literature, which varies from 5 to 7 days.[19] Several factors was considered as risk factors in the occurrence of complications in patients undergoing chemotherapy. These factors included age, the antineoplastic protocol used, the type of tumor and the unpleasant oral health. However, in our study, only the association between young age and the occurence of complications was significant (Table II). This association had also been found by different authors. Tunç ilgenli in 2001[20], JM Andrieu in 1997.[19] Besides of this, a correlation between the unpleasant oral health and the occurrence of mucositis could also be highlighted (Table II). Concerning the antecedents, only the association between HIV infection and the occurence of the oral mucositis could be highlighted (Table II).

CONCLUSION
At the end of our study, we have concluded that chemo-induced oral complications are a reality in Cameroun. Their prévalence was similar to the one found into the literature (40%). These complications occurred after an average extension time of 8 days. And, four (04) types of toxicities have been registered namely: the mucositis, the xerostomia, the dysgeusia and the oral candidiasis. These complications were more frequent into the feminine sex, in the age group ranging from 30 years to 40 years, in the protocol with adriblastin and in the epithelial tumors. Associations between the young age with the occurence of complications, between the unpleasant oral health with the occurence of mucositis and also between the occurrence of this one with the HIV infection have been highlighted.

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