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Research Article

A Pharmacoepidemiologic Safety Study in Oral Cancer Patients in Mombasa, Kenya

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Abstract

Introduction: Chemotherapy for malignant growth patients is a blended gift. It resembles a blade that cuts both ways, improving endurance rate in the patients, guaranteeing better personal satisfaction however at the same time likewise presenting them to different unfavorable medication responses. This orders customary and successive pharmacovigilance concentrates in oncology to protect the patients against the unfriendly impacts and give opportune administration of intricacies which follows. **Methodology:** The examination was embraced to notice the example of associated unfriendly medication responses with disease chemotherapy in oral malignant growth patients matured over twenty years, going to two tertiary consideration clinics around there. Information was examined utilizing SPSS for Windows, adaptation 16.0 Chicago (SPSS Inc.) and introduced as graphic measurements. **Results:** 64.36% patients created 15 distinct kinds of adverse drugs reactions. Alopecia was the most well-known adverse effects followed by nausea, vomiting, anemia, sickness and anorexia. Paclitaxel and Carboplatin routine was protected contrasted with others (p=0.6). Causality appraisal uncovered that a large portion of the adverse effects (82.5%) were in conceivable class of WHO causality evaluation scale. **Conclusion:** Oral cancer disease patients are powerless to an assortment of adverse effects. Pharmacovigilance of anticancer drugs should be explored further and utilization of careful steps should be escalated to diminish the rate of adverse effects.

Keywords: ADR, Oral and Oropharyngeal Cancer

Introduction

Early investigation of oral cancer disease and very much arranged therapy in nick of time is a preeminent health priority as it constitutes 30% of all the cancers in our country[1].

It is important to note that head and neck cancers (except for oesophagus), and therefore oral cancer and pharyngeal cancer, do not get the attention they deserve in papers dealing with the incidence and mortality of

major cancers. Even when African websites and publications dealing with major cancers record head and neck cancer (on average 10% of all cancers), the incidence of cancers of the lip, oral cavity and tongue, pharynx and larynx is often aggregated[2].

Numerous new antineoplastic medications are currently available in the market on account of the sped-up endorsement they get by Food and Drug Administration (FDA) based on 'surrogate end point' as they improve personal satisfaction in malignant growth patients[4]. With numerous new anticancer drugs hitting the market, the exposure of the patients to assortment of adverse effects like fatigue, neutropenia, nausea and vomiting, diarrhoea, mucositis- stomatitis, and hair loss also increases. Shockingly, these adverse effects are accounted as 'normal' and don't impact the helpful choices in larger part of the cases[4].

Formal launch of the National Pharmacovigilance System in Kenya 9th June 2009, Nairobi. The PPB, in consultation with various stakeholders, will review this guideline and tools periodically, to ensure that they continue to meet the goals of the Pharmacovigilance system[4]. still under reporting of adverse drug reaction (ADR) response is wild in oncology as dominant part of the oncologists see the adverse effects as inescapable[4]. It is in such manner; this examination was embraced with the expect to distinguish the example of ADRs in patients being treated for oral cancer disease around Mombasa City.

Method

This was a planned report embraced among oral cavity and oropharyngeal malignant growth (oral cancer collectively) patients attending the two hospitals i.e. Mombassa Cancer Center and Mombassa hospital in Mombasa city from January 2018 to February 2019. These hospitals were picked as they incorporate both hospitals in Mombasa city. The Mombasa Cancer Center is the first of its kind Day Care Center facility based in the heart of Mombasa city. The Hospital is committed to providing affordable, effective and effective treatment for Cancer and Palliative Care in the Coastal Area and beyond. Hospitals create a positive impact on the lives and well-being of all Cancer patients and provide them with the best possible care for Cancer and Palliative Care. The research approaches and investigational tools in this study were as per patients report at both study centers. The entirety of the respondents had given a written informed consent to partake in the investigation and assented to the distribution of the information from there on.

Patients between 20-70 years old and those determined histologically and clinically to have oral and oropharyngeal cancer were included for the investigation. Those with adverse drug reactions caused because of error in administration and medication overdose, pregnant and lactating women's, patients with other comorbidities like end organ damage, human immunodeficiency virus (HIV), Human papillomavirus (HPV), and Hepatitis B infection were excluded. The department of Pharmacovigilance at the Pharmacy and Poisons Board has been actively involved in designing tools and guidelines for detection and reporting of ADRs. In December 2007, the Guidelines for the National Pharmacovigilance System in Kenya were developed followed by sensitization of healthcare workers through a national sensitization workshop in Nairobi and through ad hoc meetings as the opportunity arose. Several other tools were also developed concurrently including the form for reporting poor quality medicinal products, suspected ADR reporting form and ADR Alert Card, which have already been printed. The National Pharmacovigilance Centre (NPC) will be based within the Pharmacy and Poisons Board (PPB), located on Lenana Road, Nairobi. Increased collaboration and joint working and planning

between PPB and public Health programs -ATM[5,6]. Advisor oncologist and nursing staff counseled each persistent for the improvement of any ADR response after every chemotherapy treatment cycle. Subsequently, the suspected adverse drug reaction forms were filled for those patients who experienced ADRs and causality assessment was done with the help of coordinator of pharmacovigilance center using World Health Organization (WHO) Causality Assessment Scale[7]. Patients were followed for an additional a half year post treatment for event of any adverse effect.

The sample size was determined to be 400 at 5% precision and 95% confidence interval dependent on past examinations,[8,9] with remuneration for misfortune to follow-up. At the research centers the randomly chosen days of the same week of the month, the data were collected over six- and half-month period that is from January 2018 till mid-September 2019. In the event that the assessed number of patients didn't arrive at eight patients/day, an extra day was chosen randomly in the following week and if that "additional day" was falling on a previously chosen day, then to eliminate the overlap we randomly drew lots from the cluster of remaining days until overlap could be overcome. Data were analyzed using SPSS for Windows, version 16.0 Chicago (SPSS Inc.) and presented in the form of descriptive statistics. Chi square test was used for statistical analysis and p- value < 0.05 was considered statistically significant.

Results

Out of the total 400 patients, just 188 patients got chemotherapy treatment. Chemotherapy was encouraged to 81 oral cavity cancer and 107 oropharyngeal cancer disease patients. There was a statistically significant difference (p=0.03) in patients experiencing adverse effects and those not experiencing adverse effects (Table 1).

Out of 188 patients, 121 patients (64.36%) developed 15 various types of ADRs as portrayed in Table 2. Alopecia was the most widely recognized adverse effect noted in 32 patients, trailed by nausea in 19 patients and anemia and anorexia in 12 and 11 patients individually (Table 2). Dominant part (66.2%) of the adverse effect happened in male patients. Unfavorable impacts (adverse effect) were regular in the age group of 50-60 years.

Paclitaxel and Carboplatin were the most well-known medication (29.8%) mix endorsed to the patients and furthermore the most secure routine (p = 0.6) as demonstrated in figure 1. Subsequent to performing the causality evaluation, it was tracked down that the greater part of the ADRs (82.5%) were in conceivable class of WHO causality assessment scale while 17.5% of the ADRs were in likely classification. Figure 1 shows ADR profile of various medication routine for oral and oropharyngeal cancer disease patients. For Paclitaxel + Carboplatin group p value was 0.6 and different regimens p value was <0.001. The p value was determined utilizing Chi-Square test.

Table 1: Distribution of patients according to the adverse effects (n = 188)

	Patients experienced adverse effects	**Patients didn't experience adverse effects**	**p value***
Oral cavity cancers (N = 81, 43.0%)	59 (72.8%)	22 (27.1%)	0.007
Oropharyngeal cancers (N = 107, 56.9%)	62 (57.9%)	45 (42.0%)	0.03

*p<0.05- Significant

Table 2: Adverse drug reactions (ADRs) distribution in different organ systems

Organ system involved	ADRs	Frequency, N (%)
Haematological system (15.7%)	Anaemia	12 (9.92%)
	Leucopenia	4 (3.30%)
	Thrombocytopenia	1 (0.83%)
	Neutropenia	2 (1.65%)
Gastrointestinal system (33.06%)	Nausea	19 (15.7%)
	Anorexia	11 (9.01%)
	Diarrhoea	4 (3.3%)
	Disgusea	6 (4.96%)
Skin (32.23%)	Alopecia	32 (26.45%)
	Erythema	3 (2.48%)
	Nail discoloration	4 (3.30%)
General disorders (19.01%)	Fatigue	6 (4.96%)
	Fever	6 (4.96%)
	Headache	2 (1.65%)
	Mucositis	9 (7.44%)

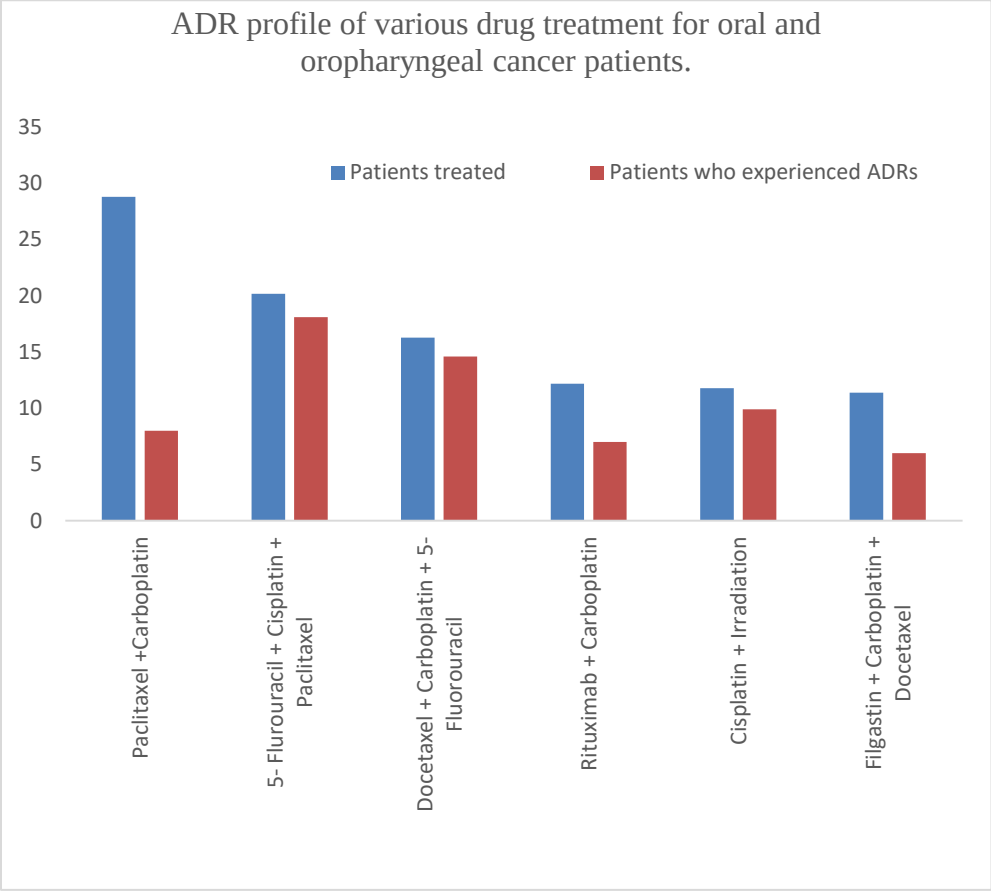

Figure 1: Adverse drug reactions (ADR) profile of various drug treatment for oral and oropharyngeal cancer patients.

Discussion

National Pharmacovigilance and ADR monitoring in Kenya and some developing countries are still in their infancies and are not yet functioning optimally[5,11]. Poor pharmacovigilance framework can prompt treatment disappointment as the patients are not satisfactorily shielded from getting to the destructive and ineffectual prescriptions[12].

Generally utilized chemotherapy drugs used for treating oral cancer disease incorporate taxanes (Paclitaxel and Docetaxel), platinum containing compounds (Cisplatin and Carboplatin), and antimetabolites (Methotrexate and 5-Fluorouracil). Every one of these medications have a wide scope of adverse effect because of their narrow therapeutic effects, endangering personal satisfaction in these patients[13]. Timely reporting and continuous monitoring of the adverse drug reactions in cancer patients ensures their safety. This will further assistance to analyze the modification in pattern of adverse drug effects with time and even the unusual adverse effects can be charted out.

In oncology as well, adverse drug reaction reporting is often overlooked because most of the oncologist accepts that they are inescapable[3,14].

other potential reasons of under reporting of adverse drug reactions in our nation could be for financial incentives, fear of legal aspects, apprehension that the serious ADRs are already documented when a drug is introduced in the market, that a single report would make no difference, ignorance (that only serious ADRs are to be reported), and lack of time or work over load[14,15].

The current investigation revealed that majority (66.2%) of the adverse effects occurred in male patients. Distinctive past examinations depict a contrast in the pattern of distribution of adverse drug effects among both the gender. While in an examination by Jose et al[16], majority (58.6%) of ADRs were noted in females, other investigations revealed male preponderance for adverse drug reactions. majority (58.6%) of ADRs were noted in females, other studies revealed male preponderance for adverse drug reactions[17,18]. In the current investigation majority of ADRs were noted in 51-60 years of age group with the mean age of 52.6 years. while contradictory to other studies[19]. In our investigation for the treatment of oral cancers single, double, and/or triple regimen were preferred depending upon the stage and site of cancer disease. 121 (64.4%) patients out of total of 188 patients developed ADRs in this examination in contrast to the study by Murti K et al[9] in oral cancer patients in Asian region, which showed 87.5% oral cancer patients developed adverse effects to chemotherapy agents[20].

Despite of pre-medication with parenteral steroids, antiemetics, and other classes of drugs, the adverse effects were only reduced but not eliminated completely. Regardless the use of 5-HT3 antagonist like Ondansetron and Granisetron, nausea and vomiting incidence could not be prevented completely, although decreased in frequency. The most frequent adverse effects noted were alopecia, nausea, anemia followed by anorexia. Alopecia started after a week of the first chemotherapy cycle and continued till the complete therapy. Cisplatin with irradiation was found to be the most common agent implicated in ADRs similar to previous studies[8,19,20]. followed by Docetaxel, Carboplatin, and 5- Fluorouracil combined regimen. The treatment drugs were not withheld in any patients because of the adverse effects indicating less severe nature of adverse effect.

In the present investigation, World Health Organization UMC causality scale showed that 82.5% were in possible category while 17.5% of the ADRs were in probable

category, in contrast to the study of Murti K et al[7] which revealed 82% of adverse drug reactions in oral cancer drugs despite their high potential for drug toxicity.

Until adverse effects monitoring is not done for numerous cancers, spectrum of adverse effects of chemotherapy agents could not be examined and smooth functioning of pharmacovigilance program will be at stake. Our study had few limitations. Firstly, all the observations were based mostly on patient complaints and few suitable laboratory investigations. Invasive blood monitoring for confirmation of adverse effects were not done. Therefore, bio- chemical/investigational ADRs like liver function test could not be determined.

Conclusion

Oral cancer disease patients receiving chemotherapy are prone to adverse effects which need to be addressed by more rigorous measures. Considering dissimilarities in inherent makeup of Kenya population, pharmacovigilance in oncology will help in developing a Kenyan database pertaining to side effects of anticancer drugs to help the policy makers.

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