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Aloe vera Prevents Radiation-Induced Dermatitis among the Black Population

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ABSTRACT

Radiation-induced dermatitis is a major complication often encountered following radiotherapy, despite new improvement in irradiation techniques. The toxicity to the skin in this case varies from slight erythema, to ulcer and necrosis. The justification for this study is based on the fact that the literature has not arrived at any international standard of care to prevent radiation-induced dermatitis, thus most physicians use their clinical judgement, based on experience. The aim of the study was to examine the efficacy of *Aloe vera* lotion as a prophylactic agent for radiation induced dermatitis.

Fifty-eight patients each with cervical carcinoma were recruited in the study into groups A (With prophylactic *Aloe vera* treatment) and B (Without *Aloe vera*). The grades of dermatitis in both groups were recorded two weeks after the completion of radiotherapy treatment. The data was analysed using SPSS version 20.

The mean age was 53.2 ± 2.3 years and age ranged between 49 - 73 years. The commonest histological type of cancer of the cervix was squamous cell (87.1%), while the least was adenocarcinoma (5.2%). The maximum grade of radiation-induced dermatitis in both groups was grade III. The grade of skin reactions in group A was very much less than in group B, and this finding was statistically significant ($p<0.001$).

The study demonstrated that *Aloe vera* was effective as a prophylactic agent for radiation-induced dermatitis.

Keywords: Radiation-induced dermatitis, *Aloe vera*, radiotherapy, Cervix, Cancer.

Introduction

Radio-therapy is an integral part of management in oncology and aims at the use of megavoltage dose of ionizing radiation to the target tissue or malignancy for therapeutic purposes, while minimizing the dose to surrounding normal critical tissues.[1,2] Approximately 66-95% of patients diagnosed with cancer will require radiotherapy.[1,2,3] Advances in radiation oncology over the years have significantly improved the prognosis of cancer treatment.[1,2] The ionizing radiation damages the deoxyribonucleic acid (DNA) of the cancer cells which impairs cell growth and ultimately leading to cell death. However, normal cells although also damaged by radiation, exhibit the capacity to cell repair. One of the visible and common manifestations of radiation toxicity is radiation-induced dermatitis which may be acute or chronic skin reactions.[4] The skin reactions may be painful and reduces the quality of life of the patient undergoing radiotherapy.[1,2,4] Despite technological advances in the planning and delivery achieved in the field of radiotherapy, most patients still experience side effect of the treatment.[2,3,4] Radiation induced dermatitis varies from slight erythema to ulcer and necrosis and the severity of skin reaction depends on radiation dose, field size and site of target tissue.[4]

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The patho-physiology of radiation dermatitis has been explained on the basis of effects of radiation on the functional subunit of the skin. Unlike physical burn trauma to the skin which results in instant structural damage in the superficial layers of the skin and progresses deeper layers with severity of the injury, radiation-induced dermatitis results in an altered complex molecular and cellular pathway at the basal layer of the skin that leads to a compromise reparative process or integrity of cell repair. Severity of radiation-induced dermatitis progresses in severity as the dose increases. Finally, the surrounding irradiated normal tissues also are affected which makes skin graft uptake a problem. Skin irradiation manifestations such as transient erythema are termed early if changes occur within the first 70-90 days following radiotherapy or during the course of a fractionated radiotherapy regime.[5,6] The skin manifestations such as atrophy, subcutaneous fibrosis and necrosis are termed late when the effects occur after 70-90 days following irradiation and appear even up to 6 months or years after therapy.[5] The chronic radiation-induced dermatitis is usually and irreversible and progressive condition which is very challenging.[7] The risk factors include radiation dose per fraction, total dose delivered, use of beam-modifying devices, size of the treatment field, site treated, use of concurrent chemotherapy, genetic factors and previous skin and connective tissue disorders. Radiation-induced dermatitis is graded 0 to 3 depending on the severity of the skin reactions.[8]

Freeman[9] stated that "Assessing the burden of skin disease is crucial for evidence-based allocation of resources and to position dermatology in a global perspective". Prevention and management of radiation-induced skin complications is a complex process for the radiotherapist, thus most clinicians depend on their personal experience and clinical judgment.[10] The need for pre- and post-therapy skin care cannot be over emphasized. The treatment of radiation-induced skin reactions include report of simple washing of the body with mild soap and water prior to radiotherapy which helped significantly lowered incidence of moist

desquamation,[11,12] use of topical steroid creams such as methylprednisolone aceponate cream, beclomethasone dipropionate spray, betamethasone cream as prophylactic agents.[13,14,15,16] Other methods include the use of non-steroidal topical creams such as *Aloe vera*,[17] Biafine cream[18,19], Hyaluronidase-based cream which is thought to accelerate the healing process by stimulating fibroblasts and fibrin formation.[20,21] Sucralfate or sucralfate-derivatives which is a persulfated disaccharide in complex with aluminum,[22,23] systemic interventions using amifostine a thiol derivative as a cytoprotective agent against acute radiation-induced skin reactions have been used[24,25] as well as Oral hydrolytic enzymes.[26] Pentoxifylline a drug currently been used in treatment of vaso-occlusive disorders has been used as prophylactic agent.[27] Nutritional supplements and silver-leaf nylon dressings have been shown to have antimicrobial properties and enhanced healing in burns and graft patients.[28,29]

Therefore, documented attempts as shown to either prevent or manage radiation-induced dermatitis appear haphazard with a lot of therapeutic trial. Literature has not arrived at any international accepted standard of care and management. Consequently, this study examines the effect of *Aloe vera* cream prophylaxis among patients with cervical carcinoma, who received radiotherapy to the pelvis. Previous literature review indicates that several authors have documented conflicting results on the effectiveness of the *Aloe vera*[10,17,30,31,32,33]. These researches were carried out in developed countries among Caucasian population, but the same cannot be said among developing world more especially in Nigeria. There is a great need to finding a solution and a common ground on how to manage this complications in our environment, thus necessitated the justification for this study. The study therefore examine the efficacy of *Aloe vera* lotion as a prophylactic agent for radiation-induced dermatitis. This will go a long way to stimulate further research in drug development, alleviate the pain of the patient, improve the quality of life and general outcome of the patient.

Materials and Methods

The study was a prospective cross-sectional descriptive analysis of 116 cancer patients in the radiotherapy department of the University of Benin Teaching Hospital (UBTH). The equipment employed in this study was a multi-modal linear accelerator (LINAC) with photon energy of 8mV to deliver a total dose of 50Gy in 25 fractions over a period of 5 weeks (approximately 2Gy/day) with APPA techniques (antero-posterior and postero-anterior). This is associated with a computed tomography simulator (CT-Sim), a computerized treatment planning system (TPS) and a fully functional mould room. Patients were seen and treated following referral from other departments of UBTH or from all other neighboring hospitals across the six geo-political zones of Nigeria. The department was set up by the Federal Government of Nigeria/ VANMED project in 2007.

The patients recruited for this study were a total of 116 carcinoma of the cervix patients attended to at the department from June 2012 to May 2015. Informed consent was obtained from all participants after adequate and clear explanation of the objectives of the study. Assurance of confidentiality was given. Thereafter, patient's biodata and detailed history were obtained. Approval for the study was obtained from the Ethical and Research Committee. The study was grouped into Group A of 58 patients with carcinoma of the cervix to which a prophylactic application of a commercially available lotion containing *Aloe vera* and 10% lidocaine was applied to the area to be irradiated. This lotion was applied in the morning to the patient's area to be radiated before the irradiation and at night after the treatment in the radiotherapy department. The application of the lotion was started from the very first day of treatment and carried through till 2weeks after treatment with radiotherapy. A second control Group B of 58 patients with carcinoma of the cervix had no application of the prophylactic lotion throughout the period of the treatment with radiotherapy. The treatment period for both groups was 5 weeks (Saturdays and Sundays were excluded). All patients in both groups were subjected to physical examination and further clinical evaluation using a dermascope for up to 2weeks after completion of radiotherapy totaling a period of 7weeks by the trial investigators. The skin reactions were graded using Radiation Therapy Oncology Group (RTOG) acute radiation morbidity scoring criteria. The criterion for inclusion into the study was patient with carcinoma of the cervix with total radiation dose above 40Gy. Exclusion criteria were patients with primary skin lesion, carcinoma of the cervix on radiotherapy with a total dose of less than 40Gy, carcinoma of the cervix with a stage IV status, diabetic patients and history of previous irradiation to the pelvis.

Statistical analysis

Data including patients bio-statistics and demographic information, diagnosis, cancer types and presentation was extracted into a Microsoft excel spreadsheet. The data was analyzed using Statistical Package Software for Social Sciences (SPSS) version 20 (Chicago, IL, USA) with statistics such as mean, median, mode, percentage, ratio of standard deviation being expressed as continuous variables and categorical variables expressed in frequency and proportions. Test of significance was done with Chi-square (χ^2) test of association. The results were statistically significant when the *p*-values were ≤ 0.05.

Results and Discussion

This present study aimed at describing the hospital-based pattern in patients who present with carcinoma of the cervix and were placed on prophylactic treatment of *Aloe vera* lotion in a tertiary hospital in Benin City. *Aloe vera* can be used as a prophylactic agent to reduce or prevent radiation-induced dermatitis[31]. *Aloe vera* of the genus family Asphodelaceae/Aloaceae and sub-family Asphodeleloideae has rosette of large, thick, fleshy leaves. It is an evergreen perennial plant that originates from the Arabian Penisula. However, the plant grows wild in tropical climates around the world and is cultivated for agricultural and medicinal/herbal uses.[34] Economically, it has been estimated with an annual market value of $13 billion globally. *Aloe vera* has anti-inflammatory properties and contains active ingredients such as vitamins, enzymes, minerals, sogan, ligain, saponis, sullcylic acid and amino-acids.[33,34]

A review of the published journals as documented in previous literature reported contrary opinions or conflicting reports[10,17,30,31,32,33]. In this present study, the focus of the study was on the reduction and or prevention, rather than the ways of managing acute radiation induced skin reactions. This study documented in Table 1 an overall mean age was 53.2 ± 2.31years the age range was reported as between 49 year and 73 years. Various reasons in this study may be attributable to race, genetics, associated risk factors and workplace exposure, poverty, illiteracy, tradition or custom and behavioural factors.[35] This finding corroborated with previously documented literature which stated that cancers are diseases that peaked at between the 3rd – 6th decade of life.[36,37,38] More than two third of the population (84.5%) are Christians, while the remaining (15.5%) are Muslims, this may be due to the fact that the predominant religion in South West and Midwest is Christianity. The Binis which form the large part of the population (27.6%) are from Mid-West, while the Yorubas which forms (22.4%) of the population are from South West. This is not far-fetched from the fact that the Binis have close proximity to the facility in this circumstance followed by the Yorubas. It is expected that the Igbo population should be higher than the Hausas based on proximity to the facility, but the presence of Radiotherapy facility in the Eastern part of Nigeria may account for the low turn-out from the East. It must be emphasized that the radiotherapy facility in the Northern part of Nigeria were technically not working during this study which therefore account for the large turn-out of patients among the Hausas. Majority of the patients has formal education, 13.8% has Primary education, 56.9% has secondary education while 10.3% has tertiary education, which implies that they have the ability to follow the information and instructions given throughout the study period.

The commonest histological type of carcinoma of the cervix in this study was squamous cell (87.1%), while the least was adenocarcinoma (5.2%). This is in accordance with literature because approximately (90.0%) of cancer of cervix worldwide are squamous cell type. [39] Most of the patients presented late and 48.3% had stage III disease as shown in Table 2. The maximum grade of radiation-induced dermatitis in both Group A and B was Grade 3. However, the grade of skin reactions in Group A was much less than that recorded in Group B and this finding was statistically significant ($p<0.001$). However, irrespective of the cell type and staging, the same radio-therapeutic protocol and treatment was administered to all the patients. Radiation-Induced dermatitis is an unavoidable side effect observed during the course of ionizing radiation treatment; its alleviation is vital for the uninterrupted completion of the

Table 1: Demographic characteristics of study population.

VARIABLES	Frequency (n = 116)	Percentage (%)
AGE (years)		
Mean ± SD	53.2 ± 2.31	
Range	49-73	
RELIGION		
Christianity	98	84.5
Islam	18	15.5
EDUCATIONAL STATUS		
No formal education	22	19.0
Primary	16	13.8
Secondary	66	56.9
Tertiary	12	10.3
OCCUPATION		
Trading	21	18.1
Civil servant	22	19.0
Artisan	32	27.6
Others	41	35.3
ETHNICITY		
Bini	32	27.6
Yoruba	26	22.4
Hausa	18	15.5
Igbo	21	18.1
Others	19	16.4

Table 2: Clinical profile of patients.

VARIABLES	Frequency (n=116)	Percentage (%)
HISTOLOGICAL TYPE		
Squamous cell	101	87.1
Carcinoma in-situ	9	7.8
Adenocarcinoma	6	5.2
STAGING		
In-situ	9	7.8
Stage I	18	15.5
Stage II	33	28.4
Stage III	56	48.3

Table 3: Effect of treatment on radiation toxicity grading.

RTOG/EORTC GRADING	GROUP A (n, %)	GROUP B (n, %)
Grade 0	35 (60.3)	0 (0.0)
Grade 1	19 (32.8)	25 (43.1)
Grade 2	3 (5.2)	30 (51.7)
Grade 3	1 (1.7)	3 (5.2)
TOTAL	58 (100.0)	58 (100.0)

$\chi 2 = 70.848$; $\boldsymbol{p < 0.001}$

planned treatment.[40] The mechanism by which radiation-induced dermatitis develops is complex and includes a myriad of overlapping events. [41-43] Exposure to X-rays which is a low Linear Energy Transfer (LET) ionizing radiation at the molecular level, causes damage of cells as well as death by generating free radicals and inducing breakage in the DNA strand. [41,42] *Aloe vera* is reported to be a potent antioxidant and inhibits TPA-induced ear edema and tumor promotion in mouse skin.[44] Furthermore, methanol extracts of Aloe arborescens were effective in scavenging reactive oxygen and protecting DNA.[44] *Aloe vera* has been investigated for its radioprotective properties; studies have also shown that the *Aloe vera* leaf extract protects mice against radiation-induced sickness and lethality.[43]

In this study it was observed that sixty percent of the patients treated with prophylactic *Aloe vera* (Group A) had a Grade 0 skin reaction and 32.8% had a Grade 1 radiation-induced dermatitis. This compared with the report of higher percentage of 56.9% of control Group B patients without administration of prophylactic *Aloe vera* presenting with Grade 2 and above radiation-induced skin reactions as reported in Table 3. This result indicates that *Aloe vera* was effective in delaying the development of Grade 2 and 3 dermatitis. Acute radiodermatitis is a primarily inflammatory reaction and pro-inflammatory cytokines, which after tissue irradiation are rapidly activated and also plays a major role in the radiation dermatitis.[45,46] Several studies have shown that *Aloe vera* possesses anti-inflammatory effects that can be intervened by modulating the levels of cytokines and the relevant signal transduction pathway in various study models.[47,48] Over centuries, *Aloe vera* has been used as a wound healing agent [49–51] and to corroborate our observation, researches have also shown that *Aloe vera* lotion has prophylactic ability in reducing radiodermatitis[52] and also enhancing the wound healing process [53]. This study has documented that application of *Aloe vera* lotion during radiotherapy can improve the skin tolerance of the treatment and reduce the incidence of radiation-induced dermatitis. This finding is concordant with previous literature[10,31,33,34] that documented the efficacy of *Aloe vera* as a prophylactic agent against radiation dermatitis and discordant with researches[32,54] which stated that there was no major difference between *Aloe vera* treated and untreated study groups.

In lieu of all these observations, and considering our observations, it can be stated here that *Aloe vera* lotion is effective as a prophylactic agent for radiation induced dermatitis.

Limitations of the study

The limitations of this study include the sample size of this hospital-based research which may not be a true reflection of the general epidemiological situation in Edo State in particular, and Nigeria in general within the study period.

Conclusion

Over the years, the report in literature of the pattern of presentation and documentation of cancers in Nigeria has not changed. The researches carried out have been limited to hospital-based studies. Radiation dermatitis is a commonly encountered side effect of definitive radiotherapy. Management of radiation-induced skin reactions vary from institution to institution depending on guidelines and experiences of the attending radiotherapist. There is therefore a need to document such data and findings, as done in this study, in various institutions.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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