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Dermatological Toxicity of an Anthracycline Antibiotic Doxorubicin

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ABSTRACT

Dermatological toxicity was a common effect of an anthracycline antibiotic Doxorubicin as described here during all the experimental protocols while studying its effect on male reproductive physiology on the albino rat, Rattus norvegicus since rapidly dividing cells are the target of chemotherapy and consequently are toxic to organ system with high metabolic rates, such has hairs, nails and skins. Some noteworthy effects recorded were alopecia, facial edema, nasal irritation, skin irritation, redness of skin, itching, brittleness and ruffeleness of hairs, puritus or allergic reaction, red streaks and wound formation/ skin necrosis at injection site. All the effects were dose and duration dependent. From the foregoing it is concluded that present piece of studies would be useful to dermatologist and in clinical management of cancer patients.

KEYWORDS :

Introduction

Dealing with the side effects of chemotherapy has always been a major concern. Chemotherapy side effects can be debilitating and make life unpleasant. Traditional chemotherapeutic agents generally target rapidly dividing cells and consequently are toxic to organ system with high metabolic rates, such as hairs, nails and skins (Fischer et al. 1997; Chandha and Shenoi, 2004 and Kamil et al. 2010). With this background much of the information described here on the dermatological side effects comes from one decade study in this laboratory on the chemotherapeutic drug Doxorubicin while studying the adverse effect on the male reproductive system of rat.

Materials and methods

Drug

Doxorubicin hydrochloride injection by Oplax (50mg/25ml) Markans Pharma Ltd.

Animals and treatment

Male Wistar strain rats (250.67±6.01 to 200.43±3.06) g in weight were obtained from the breeding colony of Department of Biochemistry, RTM Nagpur University, Nagpur and raised on a commercial pellet diet (Hindustan lever Ltd.) and water ad libitum. The animals were housed at constant temperature (28±2°C) and relative humidity (60±10%) with a 12h light:12h dark cycle. Doses used are summarized in Table-1.

Table-1 Experimental design for doxorubicin treatment

Number of animals and sex	Treatment	Dose (mg/ KgBW)	Route	Duration
6 Males (Control)	Saline	E.V.	I.P.	-
6 Males (Experimental)	Doxorubicin	10 mg daily	I.P.	5 days
6 Males (Experimental)	Doxorubicin	5 mg daily	I.P.	15 days
6 Males (Experimental)	Doxorubicin	2 mg daily	I.P.	30 days
6 Males (Experimental)	Doxorubicin	1 mg daily	I.P.	40 days

Abbreviations: I.P.= Intraperitoneally; B.W.= Body weight; E.V.=Equal volume

Results

Dermatological toxicity was observed in every therapeutic protocol, however, in varying degrees of frequency and severity. The effects were associated with symptoms of weakness, weight loss and diarrhea. Effects observed with all regimens are summarized in Table-2.

Doxorubicin treatment	Dermatological toxicity
10mg/KgBW/5 days	• Facial edema. • Skin irritation/Phlebitis/Erythema. • Itching. • Nasal irritation. • Skin adnexes, especially hair with alopecia, however, temporary.
5mg/KgBW/15 days	• Facial edema. • Redness of skin which sometimes vanished within 30-90 minutes. • Brittleness and ruffleness of hairs. • Swelling along injection site. • Puritus or allergic reaction (skin rash). • Partial alopecia, hair fall more on dorsal side.
2mg/KgBW/30 days	• Dryness of skin. • Red streaks along injection site. • Redness of face. • Partial alopecia.
1mg/KgBW/40 days	• Another skin adnexes, such as figurated hyperpigmentation of skin. • Alopecia prominent on dorsal side. • Severe local skin ulceration due to dermatomyositis due to extravasation of drug on abdominal injection site. • Hyper pigmentation of nails (dark coffee colour). • Hypersensitivity reactions.

Discussion

The dermatological complications of cancer chemotherapy have become an increasingly significant subject (Bronner and Hood, 1983; Hood, 1986; 1996; Payne et al.2005; Kamil et al. 2008; Kamil et al.2010; Sastry et al. 2012; Sastry and Dighade, 2013). Alopecia was the commonest effect observed with Doxorubicin and also consistent to other studies (Hussein et al. 1993; Cece et al. 1996; Alley et al. 2002; Selleri et al. 2005, 2006; Kamil et al. 2010; Sastry et al. 2012; Ganash et al. 2014; Sastry and Dighade, 2013). It may be because of necrotizing effect of peak plasma Doxorubicin level on hair follicle cells, which are actively dividing (Balsari et al. 1994). The dermatological side effects concerned with hyperpigmentation was prevalent and specific to Doxorubicin in the present study as described in the literature (Susser et al. 1999; Kamil et al. 2010). Allergic skin reaction such as pruritus, rashes, itching, edema, phelebitis, injection site reaction (pain/redness/swelling/wound formation) and skin irritation which varied in their symptoms depending upon the quantity of drug, such allergic reactions have been described by Branzan et al. 2005; Kamil et al. 2008; Ganash et al. 2014. Severe local skin ulceration and dermatomyositis at abdominal injection site (peritoneal) might be due o extravasations of drug. Similarly in the present study hypersensitivity reactions were most commonly caused by Doxorubicin and are in

accordance with observation of Asker et al. 2002; Ganash et al. 2014. Hyperpigmentation of nails (dark coffee colour) were concomittent to other drugs such as Docetaxel and Taxanes and other anthracyclines (Gilbat et al. 2009; Ferreira et al. 2010; Halvorson et al. 2010)

Conclusion

The present piece of studies would be useful to dermatologist and clinical management of cancer patients. It is important to be aware of all such effects in order to develop intervention strategies and would minimize or eliminate an expected side effects for better life.

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