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Wistar rat-exposure to sunlight: Impact on markers of hepato-renal functions

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ABSTRACT

The sun, an agent that is capable of inducing free radical generation, has been recognized to play a role in many skin-related pathological processes. While its impact on the prostate gland through vitamin D action has been observed, there is dearth of data pertaining to the effect of sun ray on both the hepato-renal markers in a nocturnal mammalian species. The aim of the study is to determine the effect of sun ray on hepatic and renal markers such as AST, ALT, GGT, ALP, bilirubin, albumin, creatinine and urea in female Wistar rats. Fourteen female Wistar rats (220- 245 g) divided into 2 groups of 7 rats each were used for the study. Rats in groups 1 and 2 were termed test and control respectively. While the rats in group 2 were housed in a standard animal house, group 1 rats were kept in a cage placed in an open field from the hour of 9:00 to 13:00 every day for a period of 6 weeks. Clinical chemistry tests carried out on the animals included serum activities of ALT, AST, ALP, GGT, bilirubin and albumin. Others were total proteins, creatinine, and urea. Sections of both liver and kidney were processed and subjected to hematoxylin and eosin staining technique. Data obtained were analyzed by Student's t test. P≤ 0.05 was considered significant. Results revealed that exposure of Wistar rats to sun rays from the hour of 9:00 and 13:00 each day for a period of 30 days did not result in significant differences in hepatic and renal makers. In addition, tissue histology of both test and control revealed no visible lesion. These results suggest that 4 hourly-exposure to sunlight may not be hepato-nephrotoxic in this mammalian species.

INTRODUCTION

The liver, an organ of great metabolic significance to the body, is known to be highly susceptible to a number of physical (radiant energy), chemical, or biological assaults. The liver parenchymal which constitute significant percentage of cells that make up this organ, are the major site of the synthesis of most of the serum proteins e.g. albumin and many individual components of globulins. In addition, its excretory function especially in relation to bilirubin and some xenobiotics has been documented [1]. Being a major source of many non-functional plasma enzymes, the integrity of plasma membrane of hepatocytes can be assessed using such enzymes. Therefore to determine the condition of the liver or the effects of an agent on it, synthetic markers like albumin as well as excretory (bilirubin) and other markers (AST, ALT, GGT and ALP) are usually assessed. The renal cell on the other hand, is known for its excretory role, the kidney is an organ through which toxic exogenous or endogenous compounds are removed from the body via urine, after these substances might have been metabolically processed to water soluble compounds [2].

While free-radical generating chemical compounds are known in most cases for their abilities to cause hepatocellular damage, a number of physical agents are also capable of inducing oxidative stress which consequently can result in abnormality in histology and biochemistry of hepato-renal axis. One of such physical

agent is the sun. The Sun, the star at the center of the Solar System, that has a diameter of about 1,392,000 km, and has a mass 330,000 times that of Earth affects life on earth in a number of ways, through its rays. Sunlight contains ultraviolet B radiation (290-315 nm) that affects human health in both harmful and beneficial ways [3, 4]. Ultraviolet radiation is a physical carcinogen capable of inducing oxidative stress. While the oxidative stress potential of ultraviolet B (UVB) on the skin is well established, the impact of UVB on the hepato-renal axis after a prolonged period of exposure has not been fully investigated. The aim of this study is to investigate the impact of sunlight on female Wistar rats on hepato-renal axis using both hepatic and renal markers such as AST, ALT, GGT, ALP, bilirubin, albumin, globulin, urea and creatinine as indices of study.

MATERIALS AND METHODS

Experimental Animals and design

Fourteen female Wistar rats weighing between 220 and 245 g were obtained from the Experimental Animal Unit of the Faculty of Veterinary Medicine, University of Ibadan. They were divided into 2 groups, with each group consisting of 7 rats. The rats in group 1 were the test animals while those in group 2 constituted the control animals. The animals in group 2 were kept in cages and fed with standard rat pellets and supplied water without any form of restriction. Group 1 rats were left in an open field from the hour of 9:00 to 13:00 hours every day for a period of 6 weeks. The control rats were kept in cages in the animal house of the Experimental Animal Unit of Faculty of Veterinary Medicine, University of Ibadan (Nigeria), at ambient temperature of 26±2°C. All experimental animals were supplied feed and water *ad libitum*. Blood was collected from each rat by retro-orbital bleeding, dispensed into anti-coagulant free bottle, and centrifuged at 3000 g for ten minutes. The serum obtained was stored at - 20ºC until required for analysis.

Clinical Chemistry and Histopathology

Activities of liver enzymes; ALT and AST were determined using Bergmeyer et al. method [5], while that of serum alkaline phosphatase (ALP) was by Mc Comb and Bowers method [6]. The serum levels of bilirubin and albumin were carried out using modified Jendrassik-Groff [7] & standard bromocresol methods respectively. Levels of total proteins, creatinine, and urea were assessed using Biuret method [8], Jaffé reaction and diacetyl monoxime oxidase method respectively. Hitachi® 902 automated machines (Roche Diagnostic, Germany) was used for these estimations.

Sections of both liver and kidney were collected and fixed in 10% neutral buffered formalin. These were dehydrated in ascending concentration of ethanol, cleared in xylene and embedded in paraffin. Sections 4-5 µm in thickness were prepared and stained with Hematoxylin and Eosin (H & E). The slides were viewed under the microscope at ×400. All experimental procedures were carried out in accordance with guidelines established in the NIH Guide for the Care and Use of Laboratory Animals.

Statistical analysis

Data obtained are expressed as mean ± SEM (standard error of mean). Level of significant was determined using Student's t test. SPSS package version 15 was used for this purpose. P≤ 0 .05 was considered significant.

RESULTS

Table 1: Serum levels or activities of hepato-renal indices in sun-exposed and control rats

Parameters	Control	Sun-exposed
Gamma-glutamyl transferase (IU/L)	35.07±4.32	34.19±1.19
Alkaline phosphatase (IU/L)	48.65±5.44	50.04±2.19
Total protein (g/L)	72.82±2.83	70.73±3.65
Albumin (g/L)	43.05±1.65	41.29±1.94
Globulin (g/L)	39.79±1.27	39.50±2.04
Bilirubin (µmol\L)	9.74±0.92	10.92±1.66
Alanine aminotransferase (IU/L)	35.98±3.04	33.83±2.79
Aspartate aminotransferase (IU/L)	28.53±1.69	30.14±1.08
Uric acid (mmol\L)	166.88±5.20	172.24±6.29
Creatinine (µmol\L)	27.95±2.48	31.66±2.20
Urea acid (mg\dL)	28.69±3.03	30.14±1.99

*Results are expressed as mean ± standard error of mean. *P < 0.05 is significant when compared with control using Student's t test, n=6.*

In **Table 1** results showed that sun exposure to Wistar rats did not result in significant changes in biochemical markers of hepato-renal function as all indices featured non-significant differences compared with control ($p>0.05$). The results in both **Figures 1 and 2** revealed that the renal and hepatic tissues of both sun-exposed rats and control featured no visible lesion as shown in the photomicrographs below.

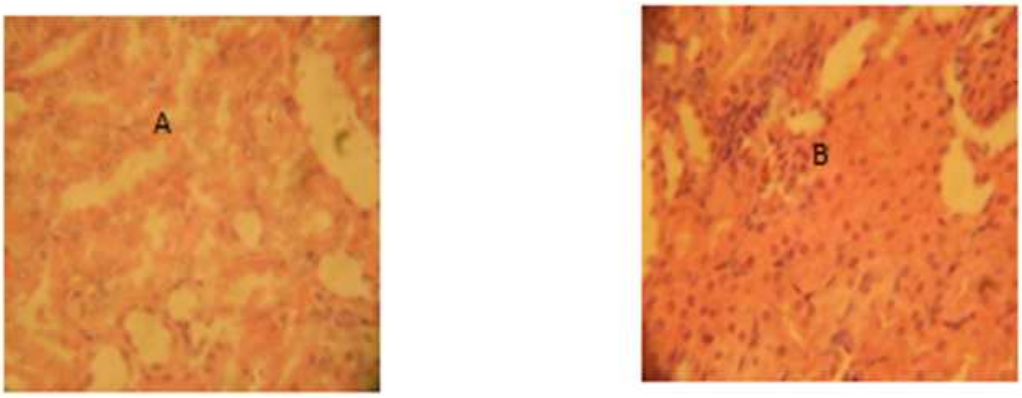

Figure 1: The photomicrographs of kidney of sun-exposed (A) and control (B) rats both showing no visible lesion.

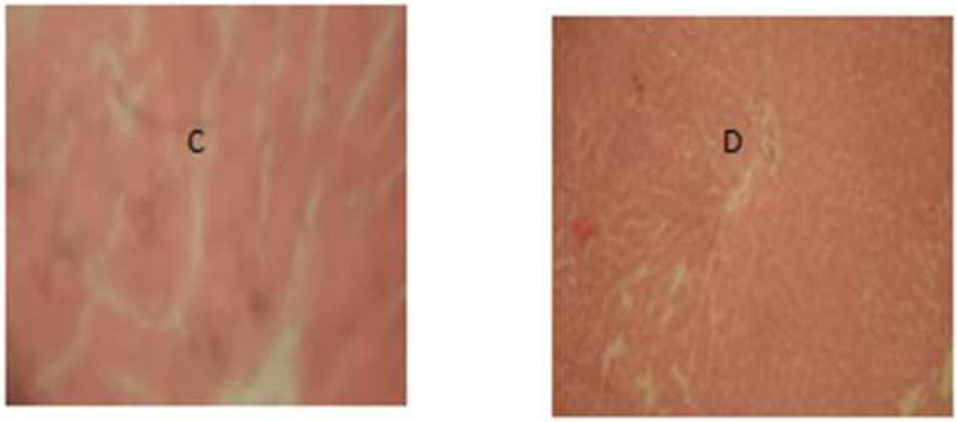

Figure 2: The photomicrographs of liver of sun-exposed (C) and control (D) rats both showing no visible lesion.

DISCUSSION

Both the liver and kidney are indirectly affected by sunlight, since both organs play significant role in the synthesis of endogenously derived vitamin D. Vitamin D is an endocrine hormone that functions to control serum levels of calcium and phosphorus and is produced in the skin after exposure to ultraviolet (UV) radiation. It is also obtained from the diet and supplements [9]. Vitamin D is hydroxylated in the liver to 25-hydroxyvitamin D (25-OHD), the major circulating vitamin D metabolite. In the kidney, 25-OHD is hydroxylated to form 1α, 25-dihydroxyvitamin D [1,25(OH)2D]. 1,25(OH)2D is also produced by nonrenal tissues that possess 1α-hydroxylase [10], including human prostatic cells [11], where it functions locally to control cellular growth and differentiation.

In a succinct account of the interaction between the liver, kidney and skin in UV radiation induced vitamin D synthesis, Alshishtawy [4] noted that UVB rays penetrate the epidermis and release energy that alters a pre-existing

cholesterol metabolite to previtamin D3, which is then slowly converted nonenzymatically to vitamin D3 (cholecalciferol). Cholecalciferol that is bound to a specific vitamin D-binding protein (DBP), is transported to the liver, where it is enzymatically hydroxylated to 25-hydroxyvitamin D (calcifidiol or 25(OH)D). Then, DBP bound 25(OH)D is transported to the kidney and other organs, where it is hydroxylated at the 1 position to produce 1,25(OH)2D, the most biologically active form of vitamin D.

That exposure to sun (via vitamin D) has impact on different organs and tissues of the body can be deduced from the historical definition of vitamin D deficiency, 25-OHD levels of <15 ng/mL or <37.5 nmol/L was arrived at based on the presence or absence of bone diseases (rickets in children and osteomalacia in adults). The recognition that other organs, such as the prostate gland, possess vitamin D receptor and 1α-hydroxylase and respond to the hormone and prohormone strongly suggests that vitamin D is essential for the development of these tissues as well [9]. This is an indication that the quantity/quality of sun exposure can affect this organ. While it has long been recognized that there is a link between physiologic processes in bone and sun exposure via vitamin D, the more recent discovery of an association between prostate cancer and sun exposure is an indication that the level of sufficient vitamin D or optimal vitamin D levels in these sites (e.g. prostate) is unknown but is likely to be higher than for bone. In addition, as far back as 1903, Niels Ryberg Finsen received the Nobel Prize for observing that sun exposure was therapeutic for cutaneous tuberculosis [12], and the idea that UV radiation exposure was healthful rapidly took hold among the public [13].

Another organ known for its relationship with the sun is the skin. As a predisposing factor ultraviolet (UV) radiation has considerable influence on the incidence of skin cancer [14]. For example, Australia is known to have the highest rates of skin cancer in the world [15-18]. And based on the understanding of these high rates and the number of skin cancers that can possibly be prevented, National Goals and Targets for Australia [19] recommended decreased exposure to sunlight for individuals of all ages, and especially for those people at high risk of skin cancer [20, 21]. That such changes in activities could help to reduce incidence of skin cancer can be deduced from recent results. Data emanating from Australia suggest that the incidence of both non-melanocytic skin cancer [21] and malignant melanoma have decreased in recent years. Basal cell carcinoma (BCC) is an example of commonly diagnosed malignant skin tumors that develops characteristically on sun-exposed areas, such as the head and neck. Ultraviolet light exposure has been suggested as an important etiologic factor in BCCs, and BCCs arising from non-sun-exposed areas are, therefore, very rare [22]. Chronic exposure to ultraviolet light (UVL) is an important predisposing factor for BCC, and more than 80% of BCCs are confined to sun-exposed areas of the body, such as the face.

Moreover, it seems that exposure to environmental levels of ultraviolet rays changes the activity and pattern of distribution of some of the cells that are responsible for triggering immune responses in humans. As a result of this, increase exposure to sun rays may enhance the risk of infection especially viral, bacterial, parasitic or fungal infections [23]. In addition, harmful effects of sun exposure can also affect the eye causing clinical conditions such as photokeratitis, photoconjunctivitis, and cataract development [WHO, 2011].

Even with so many of these organs pathologically linked in one way or another to excessive sun exposure, both the liver and renal histology and serum biochemistry of sun-exposed female Wistar used for the present study rats did not reveal any form of abnormality. Since the hepatic and renal biochemical markers were not significantly different in sun-exposed rats compared with control. Histology results also showed no visible lesions for all tissues examined for sun-exposed rats as well as the control group. This is an indication that neither the synthetic ability of the liver nor its excretory function is altered as a result of sun exposure especially if it is from 9:00 to 13:00. In addition the no significant differences recorded for the activities of hepatic enzymes such as ALT, AST, GGT, and ALP suggest that the integrity of the membrane of hepatocytes was not compromised.

Conclusion: Although the UVB of the sun is carcinogenic or generally harmful; but it can be deduced from the results of this study that such harmful effects do not extend to the hepatorenal axis, as all indices show no significant differences compared with control.

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