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Original Research

Histopathology of the Liver following Administration of Artesunate in Adult Wistar Rats

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Abstract
In most of the developing countries especially in Africa antimalaria drugs are taken regularly either to treat or prevent malaria. Fifteen wistar rats of both sexes were randomly divided into 3 groups of 5 each and tested as follows: - Group O- control (water), Group A – 2mg/kg and Group B - 6mg/kg. The animals were sacrificed after the 7th day. There was no mortality caused by the drug but dizziness in the animals. In the group administered with 2mg/kg of oral artesunate there was no form of distortion in the tissue architecture of the liver, but in the group administered with 6mg/kg of artesunate, artesunate caused sinusoidal congestion, infiltration of inflammatory cells and there was loss of tissue architecture. Drugs are produce to combat illnesses but may turn out to be harmful when administered wrongly. In most of the developing countries especially in Africa antimalaria drugs are taken regularly either to treat or prevent malaria. They are taken such that one could even imaging if it is a food supplement.

INTRODUCTION

Malaria is a leading cause of mortality and morbidity in developing areas of the world, and remains a major public health problem in endemic regions [1]. Malaria is a parasitic disease of global importance, with more than 3000 million people in over 100 malaria endemic countries being at risk [2], and is responsible for the death of approximately a million people annually. Over 90% of yearly deaths resulting from malaria occur in sub Saharan Africa [3].

It was from Artemisia annua that the most recent phytochemical agents was isolated from and biologically characterized to exhibit anti-malaria potency. Other synthetic derivatives of artemisinin are artemether, arteether (artemotil), artesunate and artenimol (â-dihydroartemisinin, DHA). Artemisinin and its derivatives are known to exhibit potency against the asexual, and erythrocytic forms of Plasmodium falciparum and Plasmodium vivax [4].

Artemisinins are derived from leaves of a plant called sweet wormwood or sweet Annie (*Artemisia annua*) by Chinese scientists. In china, where they were discovered, “qinqhao” extracts were reported to have antipyretic properties more than 1500 years ago. In 1967 an outstanding coordinated programme was started by the Chinese government to discover antimalarial principles in various medicinal herbs including qinghao. In 1971, a highly active chemical from qinghao known as qinghaosu was obtained which

is called artemisinin [5]. Since this initial discovery, an array of semi-synthetic oil and water soluble derivatives of artemisinin have been developed with variety of formulations entering clinical studies [6] .

Artesunate is one of the major and active antimalaria drugs used in Nigeria; they are relatively cheap and can be obtained virtually in almost all the Pharmaceutical shops across the nation. Although there are still other forms of antimalaria but artesunate is refered in resistant cases.

It is used in combination therapy and is effective in cases of uncomplicated P. falciparum. Several studies on artesunate showed evidence of toxicity on the brain stem [7-9].

The rate of Uncontrolled use of drugs have been a challenge in developing countries, especially in Africa where we have a lot of non-professionals in drug businesses, some hawk along streets, looking for who will patronize them, they sometimes give wrong prescription, and most of the victims are the uneducated class.

The use of these drugs should be controlled and restricted to proven multi-drug resistance on severe malaria in order to preserve their efficacy [10] and avoid emergence of resistant strains. In a country like Nigeria which is malaria endemic area, self medication cannot be ruled out, and purchase of antimalarials in the open market is rampant. The possibility of administering overdose and misappropriation in the usage of antimalarials are very common. Drugs in general are useful in the treatment of diseases but could also produce harmful effects in the individual [6]. Therefore the aim of this study is to investigate the possible effects of artesunate drug on the histology of the liver.

MATERIALS AND METHODS

Drug collection, Preparation and Administration

The artesunate powder for oral suspension (ARTESUNATE ®) was manufactured by MekopharChamical pharmaceutical joint-stock Co. Marketed by Neros Pharmaceuticals Ltd., Lagos, Nigeria. The powder solution was made by distilled water 160mg/80ml (2mg/ml) and administered to the animals orally once a day for a period of 7days.

Experimental Animals

Fifteen wistar rats of both sexes weighing 120-180g obtained from the College of Health Sciences, University of Port Harcourt, Nigeria, were used. They maintained under standard laboratory conditions of 27 ± 2^{o}C, relative humidity 50 ± 15% and normal photo period (12h dark/12h light).

Experimental Design

The rats were randomly divided into 3 groups of 5 each and tested as follows: - Group O- control (water), Group A – 2mg/kg and Group B - 6mg/kg. The animals were sacrificed after the 7th day.

Histopathology

Animals were anesthesized using chloroform before sacrificing. Immediately after dissection, the sections of the livers were placed in a tissue cassette and fixed in 10% formal saline for 24 h after which they were processed using standard histopathological methods, stained with haematoxylin and eosin for microscopic assessment [11]

RESULTS

There was no mortality caused by the drug but dizziness in the animals. In the group administered with 2mg/kg of oral artesunate there was no form of distortion in the tissue architecture of the liver (Plate 2), but in the group administered with 6mg/kg of artesunate, artesunate caused sinusoidal congestion, infiltration of inflammatory cells and there was loss of tissue architecture (Plate 3).

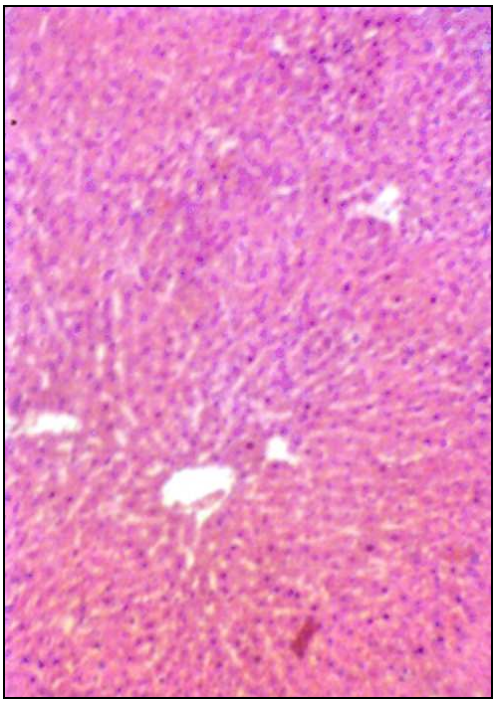

Figure 1. Normal Histology of the liver

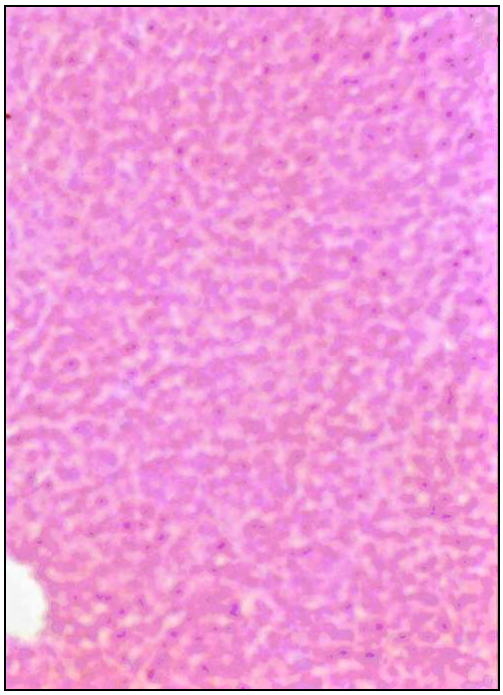

Figure 2: 2ml/kg of Artesunate

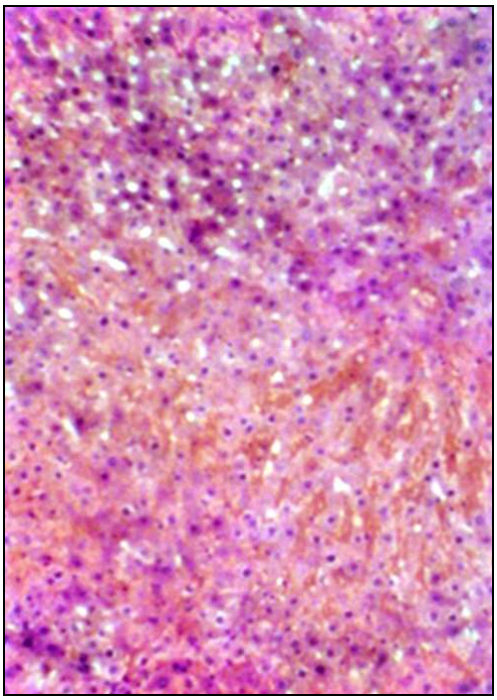

Figure3: 6ml/kg of Artesunate

DISCUSSION

The investigation shows that orally administered artesunate 2ml/kg which may be regarded as a clinical dose (recommended dose) has no effect on the histology of the liver, as the tissue architecture showed normal hepatocyte, sinusoid and central vein. This implies that artesunate administered at 2ml/kg for seven days showed no effect (plate 2). The group administered with 6ml/kg of artesunate showed sinusoidal congestion, infiltration of inflammatory cells and there was loss of tissue architecture (Plate 3). This study agrees with the study carried out by Olurishe et al [12], where animals that received immunosuppressive therapy showed different degrees of haemosiderosis and pathologic involvement ranging from focal necrosis to some congestion in sinusoidal spaces. It also agrees with Izunya et al., [13], where artesunate caused cytoplasmic vacuolation, sinusoidal congestion and inflammation of the portal tracts. Our study is inline with Nwanjo and Oze [6] where artesunate caused toxicity of the liver cells in guinea pigs.

CONCLUSION

Drugs are produce to combat illnesses but may turn out be harmful when administered wrongly.

In most of the developing countries especially in Africa antimalaria drugs are taken regularly either to treat or prevent malaria. They are taken such that one could even imaging if it is a food supplement. It is high time developing countries stood on their feet for proper advocacy, on recklessness of drug abuse most especially in Nigeria. It is therefore important for drug regulating agencies and Pharmaceutical bodies to train and retrain licensed drug peddlers and Pharmaceutical shop owners to always educate drug users on how to take their drugs and emphasis should be laid on the adverse effects when drugs are abuse, which will help to reduce the abuse of drugs in developing country.

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