

Splenotoxic Potentials of Chloroquine, Fansidar, Cotecxin and Amalar

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Abstract

The Histologic studies on the spleen was carried out with Chloroquine, Fansidar, Cotecxin and Amalar to observe any pathologic effect(s) on the tissue on comparative basis. The study revealed some degenerated white pulps and wider interstitial spaces with chloroquine drug not observed in control samples. Also animals with fansidar administration showed clumping of periarteriolar lymphoid cells in the white pulp not shown in the control group without any drug. In the Amalar group the spleen showed sinusoidal dilation in the red pulp with macrophages scattered around it but not in the form of activation. For cotecxin drug there was the degeneration of periarteriolar lymphoid sheaths with residue of the infiltrated cells in the arterioles. It is concluded that chloroquine, fansidar, cotecxin may induce jaundice and splenic disorders.

Keywords: splenomegaly, splenic rupture, anti-malaria drugs.

INTRODUCTION

The spleen is the largest lymph gland in the body formed by the combination of reticular and lymphatic tissue. It is positioned in the left hypochondriac region of the abdominal cavity but located between the fundus of the stomach and the diaphragm. It is oval in shape and enclosed in a fibroblastic capsule, Waugh and Grant (2001). The physiologic functions of the spleen rest in the pulp: the red and the white pulp. The spleen is very central in the metabolic function of the liver e.g. bilirubin by being the conduit of passage of its product including others from the aged and abnormal erythrocytes destruction, the spleen also serves as organ of such destruction.

But very vital in its body defense functions is that of phagocytosis of foreign particles of bacteria, viruses, malaria parasite etc. However, such phagocytic function affects leucocytes and the platelets which perhaps are often those obsolete for body function.

But in hemorrhagic situation, the spleen feeds the circulation with augmented volume of blood. The spleen is also erythropoietic organ as it serves as source of fetus blood formation Guyton, 2006, Hoffbrand 1991 and presence of T. & B. lymphocytes also confirm the immunologic properties of this organ.

However, in infection like malaria the spleen is enlarged (splenomegaly). Such enlargement may lead to splenic pooling of the erythrocytes which may result in anemia. Even in asymptomatic malaria splenomegaly is highly prevalence, Franca, 2005. Also in endemic condition of schistosomiasis and leishmaniasis there abound also splenomegaly. Splenomegaly is very common in tropical West Africa mainly due to malaria, splenomegaly is said to raise Igm levels with hepatic sinusoidal lymphatic, Bates, (1992). Organs tolerated antimalaria drugs need be utilized in malaria treatment as confirmed in spleen reduction with particular antimalaria and not others, Fakunla, (1981). Non tolerated antimalaria by the spleen mean negative effects on the spleen. Based on this, a review of some old and some new antimalaria drugs as per the possible negative effects on the spleen was done. The aim being the advocacy for continuous revalidation and evaluation of antimalaria drugs based on the consumption rate, malaria prevalence, efficacy and side effects and body organs physiologic status. Despite the presence of drug resistance to chloroquine and fansidar, the two drugs are still consumed due to the availability and low costs. The new drugs, Amalar and Cotecxin, are alternative therapy for chloroquine and fansidar but are rather expensive though available in the big urban cities. However, the physiologic consequence i.e. negative effects of both the new and the old drugs seem not to attract much comment like the clinical and parasitological success or failure particularly with the new drugs. The implications are many especially with the high rate of antimalaria consumption the prevalence of malaria and tendency of high organs toxicity. Such characteristics may be the true situation of malaria mortality and morbidity and the resultant aggravation of future death tolls presumed to be caused by malaria but rather due to pharmacologic neglect and physiologic oversight in the disease.

MATERIALS AND METHODS

Thirty (30) albino wistar rats of average weight 0.80kg – 1.41kg were used for the study. The animals were obtained from the stock in the Faculty of Pharmacy animal house University of Uyo and maintained daily with pellets food and water. The animals were of good health when obtained. Consent for use was not obtained

due to the absence of the animal right where the study was done. But the animals were not tortured. Six animals were placed in each drug group including control.

DRUGS ADMINISTRATION

The antimalaria drugs; amalar, fansidar, chloroquine and cotecxin were purchased from a registered pharmacy shop. The drugs were administered based on the weight of the animal derived from the average weight of man; 70kg, according to the methods of Bertram, 2004 and Robert et al. 1979. The drugs were administered orally using canula by-passing the esophagus and delivered into the stomach based also on the curative and preventive dosages of the chloroquine, cotecxin, fansidar and amalar respectively, Jimmy et al., 2007. The effects of the drugs were monitored for the period of 28 days adopted from WHO (1982) model for antimalaria efficacy monitory. However, malaria parasites were not given to the animals in this study.

HISTOLOGY: At the end of 28 days, the animals were anaesthetized with chloroform and the spleen were removed and processed according to the methods of druby and Wallington, 1967. Photomicrography of the sectioned tissues were made and interpreted for results.

RESULTS

The investigation has shown marked effects of chloroquine, fansidar and cotecxin, while amalar drug demonstrated mild effect on the spleen. While chloroquine degenerated the splenic whites pulp and widen the interstitial space of the spleen (plate 1) clumping of periarteriolar lymphoid cells also in the white pulp was observed with fansidar (plate 2). However, cotecxin caused the degeneration of periarteriolar lymphoid sheaths, plate 3. But amalar also caused mild dilation of sinusoidal dilation in the red pulp of the spleen plate 4. But, the control group had their spleen remaining normal, (plate 5).

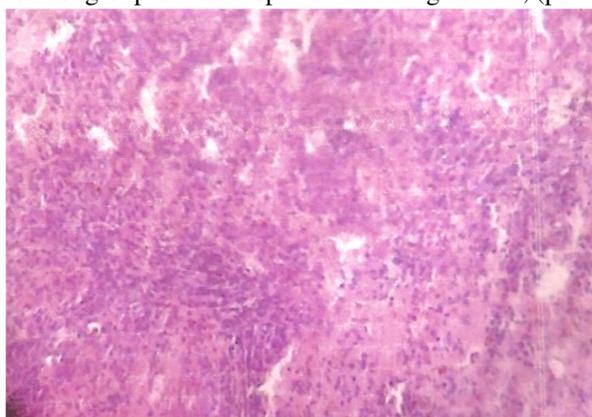


Plate 1: Effect of Chloroquine on spleen

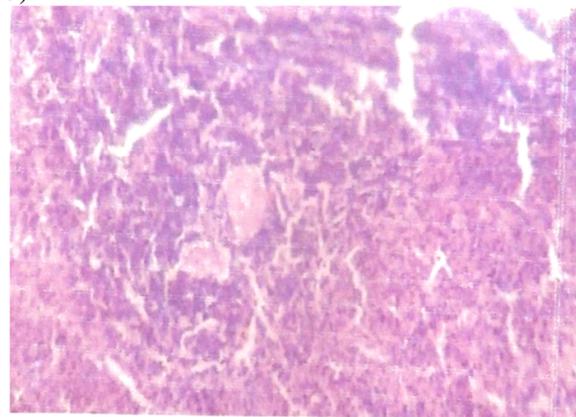


Plate 2: Effect of fansidar on spleen.

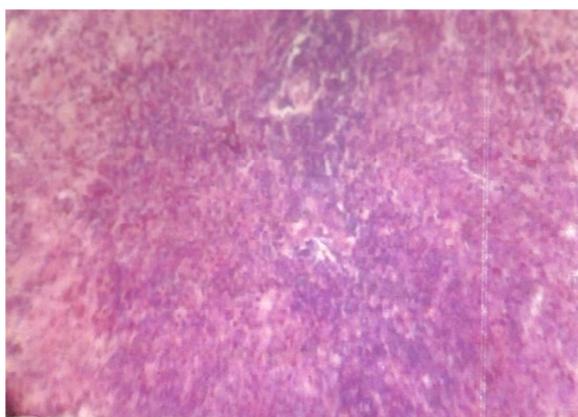


Plate 3: Effect of cotecxin on spleen

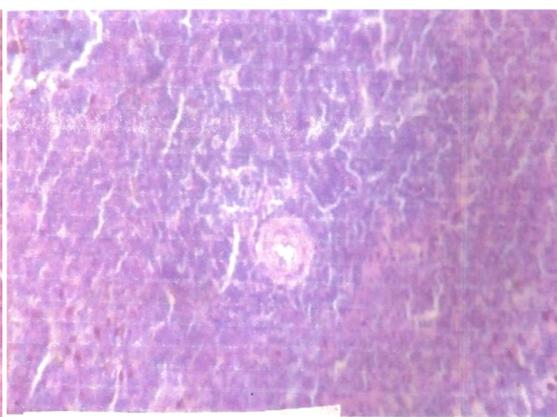


Plate 4: Effect of amalar on spleen.

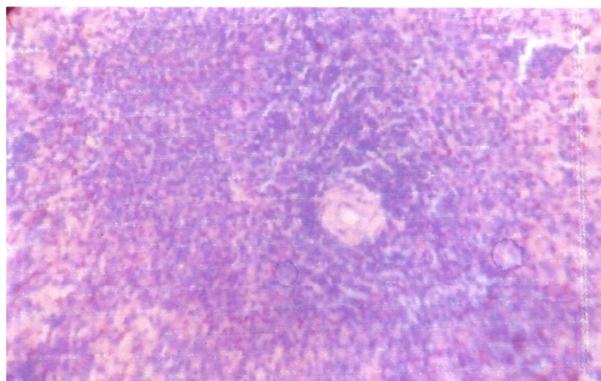


Plate 5: Control

DISCUSSION

The investigation has revealed significant physiologic observations particularly with specific effects of different antimalarials. The chloroquine specifically affected the white pulp causing the degeneration and widening of the interstitial space. The degeneration of the pulp indicates cells destruction of this vital organ and the widened interstitial space implies the abnormal expansion of such space for massive exudation of fluid into the interstitial space. The degeneration could also evolve into erosion and the tendency for the occlusion of the arterioles. The sum total effect of chloroquine action on the spleen is a disorder of it leading to spleen enlargement, splenomegaly (Berkow et al 2001). Splenomegaly is a tropical syndrome in malaria disease observed in West Africa referred to as tropical syndrome, Bryceson et al. 1983. The characteristics of splenomegaly otherwise called the big spleen include spleen of at least 10cm, chronic malaria exposure, raise immunoglobulin (Ig)M levels, hepatic sinusoidal lymphocytosis. In our study, it means the 1gm levels may have been raised though not measured. And increase immune levels also means increase lymphoproliferation which may be of the B cells origin which may result in Leukaemia, Fakunle, 1979.

The hepatic sinusoidal lymphocytosis implies the linkage effect of the spleen with the liver which may result in Jaundice, Guyton 2006. In our study, the induced effects of splenomegaly with chloroquine are correlated with that of malaria disease. It means that taking chloroquine in malaria infection may induced double negative effects in the spleen and will impair physiologic function. This same effect was observed with fansidar though fansidar caused the clumping of periarteriolar lymphoid of the same white spleen pulp but the end result is still splenomegaly, and the resultant impairment of the spleen. Most striking was the effect of cotecxin; a dihydroartemisinin which is supposed to be an alternative drug for the chloroquine and fansidar. Cotecxin caused the degeneration of periarteriolar lymphoid sheath. Such effect will lead to necrosis of the cells of the white pulp such deformation of the spleen pulp will also attract mononuclear and polymorphonuclear infiltrations. These proliferations are the characteristics of splenomegaly. Importantly, the effect of the white pulp degeneration will eventually make the spleen to be very delicate which may result in splenic rupture. Such effects pronounce a deadly signal for a new drug like cotecxin. In a situation of increase malaria attacks as experienced in the tropical West Africa, then splenic rupture would be a significant medical diagnosis for those on cotecxin and splenomegaly for those on chloroquine and fansidar. So where lies the safety of treatment therapy in malaria? Amalar has its effect as it causes sinusoidal dilation of the red pulp though the effect was mild. There is therefore urgent need to reverse the trend of pharmacologic preparations because it appears the drug maiming on the organs is gradually overweighing the effects of the malaria disease and the mortality would also surpass that of the disease. This is why the pathophysiology of malaria disease should be topical in the research of pharmacologic potent drugs in the malaria models and therapeutic application.

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