

Stimulatory Effects of Dihydroartemisinin on the Leucocyte Population of Wistar Albino Rats

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Abstract: Problem statement: Five dosages of Dihydroartemisinin (DHA) which included 1 mg kg⁻¹; a repeated dose of 1; 2; 60 and 80 mg kg⁻¹ were administered orally to albino rats for 5 days. The results of the study showed that dihydroartemisinin treatment significantly elevated the total white cell count (p<0.01); the percentage neutrophil count (p<0.01) and the percentage lymphocyte count (p<0.05). It also increased the percentage monocyte count though its increase was not statistically significant. **Approach:** By increasing the population of neutrophils, lymphocytes and monocytes (which engage in chemo tactic response; microbial killing; microbial ingestion and antibody production) in the blood, dihydroartemisinin demonstrated that it stimulates increase in their population and uses them as part of its own arsenals of warfare against endoparasites (like malaria parasites) and pathogens. **Results:** The results of this study show that dihydroartemisinin stimulated a lot of new white blood cell production by haemopoetic sites of the body. The increases in the total white blood cell count; the percentage neutrophils count and the percentage lymphocyte counts were significant at p<0.01 level of significance. **Conclusion:** The results of the study suggest that the phagocytic and immunological activities of the body's white blood cell population are important components of the efficacious Plasmodium Schizonticidal actions of Dihydroartemisinin in malaria treatment.

Key words: Dihydroartemisinin (DHA), cell count, dihydroartemisinin demonstrated, malaria treatment, microbial ingestion, antibody production, haemopoiesis stimulation, laboratory procedures, dosage regimen, rapid therapeutic effect

INTRODUCTION

The artemisinin antimalarials have been found to be very efficacious and effective in the management of uncomplicated and complicated malaria (Asawamahaska *et al.*, 1994) The Artemisinin Combination Therapy

(ACT) drugs were seen by World Health Organization to be capable of offering new hope for the control of malaria because they have a rapid therapeutic effect in reducing the malaria parasite and diminishing symptoms.

Parasiticidal action of artemisinin has been suggested to occur through their engagement of the

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parasite as an endooperoxide. In the process of this engagement the drug accumulates many times more in the infected cell than elsewhere just like quinacrine which was found to accumulate 500 times more in infected areas. Malaria parasite is suggested to be killed by alkylation of the parasite proteins by the drug.

This study investigated the effects of Dihydroartemisinin (DHA) on the blood cell population of albino rats.

MATERIALS AND METHODS

Dihydroartemisinin (DHA) was administered by oral intubation to 5 Adult test Wistar albino rats which weighed 106-140 g in 4 different treatments. Four adult Wistar rats of 106-140 gm weight served as controls to these test rats DHA was given daily at doses of 1 mg kg⁻¹ (with a 2 mg kg⁻¹ starting dose), 2, 60 and 80 mg kg⁻¹ Dihydroartemisinin (DHA), to 4 sets of test rats for 5 days.

Four young adult wistar albino rats weighing 75-90 g were given the 1 mg kg⁻¹ DHA (with a 2 mg kg⁻¹ starting dose) also by intubation for 5 days and the same dosage regimen was repeated to them after a one week interval (repeat treatment). Four rats which weighed 75-90 g and were of the same age as the test rats served as controls to this group.

The control rats in each of the 5 experiments were given distilled water equivalents of the dosage of DHA taken by their test group in place of dihydroartemisinin, also by oral intubation.

The test and control rats were weighed 10 minutes before the administration of the first dose of a tested dosage regimen and 10 minutes after the administration of the last dose of that dosage regimen.

The test and control rats were sacrificed 24 h after the administration of the last dose of each tested dosage regimen of dihydroartemisinin.

The blood of the sacrificed test and control rats was collected through the subclavian artery into EDTA anticoagulated blood collection bottles before each animal was sacrificed. The total and differential white blood cell counts of the blood of the test and control rats were done using standard laboratory procedures.

RESULTS

The results of our study showed that the total white blood cell count, the percentage neutrophil count and the percentage lymphocyte counts were elevated in the DHA treated rats. DHA treatment significantly (p<0.01) elevated the total blood cell count. The results of the differential leucocyte counts showed that DHA

significantly elevated the percentage neutrophil count (p<0.01) and the percentage lymphocyte count (p<0.01, p<0.05). DHA treatment also increased the percentage monocyte count; did not have much effect on the percentage eosinophil count and had no effect at all on the basophil count.

These effects of DHA on the total white blood cells (on the total and differential WBC counts) were DHA concentration and DHA dose repetition and time dependent.

DISCUSSION

The results of this study show that dihydroartemisinin stimulated a lot of new white blood cell production by haemopoetic sites of the body (Fig. 1-3).

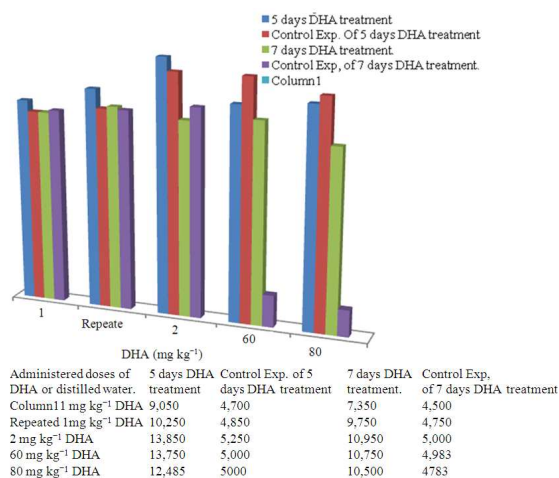


Fig. 1: The Effect of Dihydroartemisinin treatment on the total white blood cell count in mm³

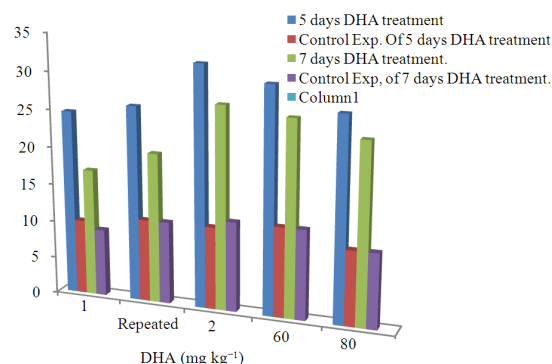


Fig. 2: The Effect of Dihydroartemisinin treatment on the percentage neutrophils count [of the WBC] of Dihydroartemisinin-treated and Control albino rats

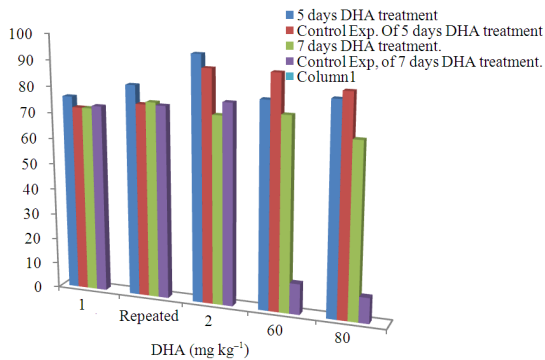


Fig. 3: The Effect of Dihydroartemisinin treatment on percentage lymphocyte count [of the WBC] of Dihydroartemisinin treated and Control albino rats

The increases in the total white blood cell count; the percentage neutrophils count and the percentage lymphocyte counts were significant at $p < 0.01$ level of significance which shows that the haemopoiesis stimulation effect of DHA was very potent. These effects of dihydroartemisinin on haemopoiesis confirm the observation in a previous that the action of artemisinins as antimalarials is linked to their action on intracellular hemin (Meshnick *et al.*, 1994; Ponmee *et al.*, 2007).

Since the white blood cells constitute the disease fighting army of the body, this potent white blood cell population explosion effect of dihydroartemisinin on the blood is a very important aspect of its parasite fighting and elimination strategies as dihydroartemisinin is 90% bound to plasma proteins. The events that take place in the blood during clinical malaria are the hallmark of malaria (Blacklock *et al.*, 1973). The role of dihydroartemisinin in interacting with blood producing cells is significant in malaria as dihydroartemisinin has been found to interact with proteins (Asawamahaskda *et al.*, 1994).

CONCLUSION

The findings of this study suggest that the phagocytic and immunological activities of the white blood cells (especially those of neutrophils and lymphocytes) constitute a component of the plasmodium killing actions of dihydroartemisinin in malaria treatment. This finding is very important as the mechanism of antimalarial action of artemisinin is unsettled (Robert and Meunier, 1998).

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