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Gastric HCL and ulcerogenic potentials of chloroquine, Fansidar and Metakelfin

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ABSTRACT

Comparative gastric hydrochloric acid Secretion was studied in males & females albino rats with three antimalaria drugs; chloroquine® fansidar® and metakelfin®. Of the antimalaria drugs studied, Chloroquine was found to increase stomach hydrochloric acid secretion at (P<0.05) in all the four weeks period of observation. However, fansidar increased gastric hydrochloric secretion during the first and second week of observation after its administration (P<0.05) but the secretion was not significant (P<0.05) in the third and fourth week of observation. Metakelfin showed a significant increase in hydrochloric acid secretion in week one, two and four (P<0.05) but insignificant secretion was observed in week three. It is concluded that chloroquine and metakelfin have the tendency of inducing peptic ulcer but fansidar may be a potent drug for peptic ulcer treatment.

Keywords: Chloroquine, fansidar, metakelfin, gastric secretion and peptic ulcer.

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I. INTRODUCTION

Gastric secretion is the release of chemical substances in the stomach such which include water, hydrochloric acid, pepsin, enzymes etc for the different action on the food taken in for appropriate digestion. The most important of the secretions is the hydrochloric acid which apart from its metabolic properties e.g its action on pepsinogen to pepsin is quite protective eg against gastrointestinal infection and in maintaining the normal pH for enzyme activity. However, the hydrochloric acid secretion is a function of the hydrogen ions and chloride concentration and the metabolic activities (Guyton, 2006). The hydrogen ion are released from the parietal cells when stimulated of food intake, sight of it, smell, embodied in cephalic, gastric and intestinal stimulations.

Some drugs e.g non-steroidal anti-inflammatory drugs NSAIDS eg aspirin, Ibuprofen etc are incriminated as ulcerogenic, Aguwa, 2002, Harvey et al 1992. These drugs are taken as analgesics. Anti-malaria drugs like chloroquine, fansidar and metakelfin are taken for cure and protection against malaria and their frequency of intake is increasing as malaria infection is also on the increase. Chloroquine has gastrointestinal effect; that of stomach churning and retinal damage at high dosage apart from its bitter taste (Ebadi 1997). It is likely such churning could stimulate gastric secretion. However, it was deemed necessary to evaluate its effect along with other drugs in the gastrointestinal system particularly the acidity level during intake. Such evaluation becomes necessary in view of the increase cases of complication arising from malaria which adequate appropriation of medication also depends on the screening of the effects of the antimalarials. Also important would be enactment of drug purchase policy through prescription to reduce high self medication and patronage of fake vendors without knowledge of dispensing Jimmy et al 2000.

II. MATERIALS AND METHODS

Animals: Thirty male and female albino rats, weighing 96g – 183g obtained from the Pharmacy Faculty of the University of Uyo were used for the study. The animals were fed with food pellets and water and accommodated in a well ventilated room having normal temperature. The animals were divided into six groups with five animals in each group including control without anti-malarial.

Drugs Administration: Three drugs, chloroquine®, fansidar® and metakelfin® were used. The drugs were purchased from a registered pharmaceutical shop were the study was done. The drugs were administered per dose/kg weight of each animal as curative and protective. The tablets were ground into powder form and dissolved in 10-15ml of water for mg/ml concentration after step serial dilution. The dissolved drugs were then given using canula by-passing the esophagus to the stomach, Bertram 2004, Robert et al 1979. The effects of the drugs were observed weekly for 28 days using WHO 1982 anti-malaria monitoring model on anti-malaria drugs. However, malaria parasites were not given to the animals but the model was adopted for the drug effects.

Acidity Analysis: At weekly interval, the animals were sacrificed, the stomach removed and the contents squeezed out for the confirmation of acid secretion.

Titrable acidity: For each drug group 1ml of stomach content was dissolved in 5ml of distilled water and filtered using what man filter paper to discard debris. Two drops of methyl orange indicator were added to the content and 0.2N NaoH used in titrating against it to obtain end point.

The titratble acidity was calculated based on the methods of Barker & Silverton 1982, using the following formula;

$$\frac{x.\ 20\text{mmol}}{Y}$$

Where x = litre obtained after titration ie end part
Y = actual volume of the volume
20 mmol=concentration of the sodium hydroxide used.

These was done for 28 days and the results expressed as acidity levels in mmol. Which was a quantitative assay however, qualitative method using Topfer's test which cherry red colour formation indicates Hcl present, Ramnik 2006.

Table 1: Effects of chloroquine, fansidar and metakelfin on stomach acidity

Days	Cholroquine	Fansidar	Metakelfin	Control
7 (week)	3.1 ± 0.16	3.2 ± 0.07	2.6 ± 0.12	1.5± 0.1
14 (week)	2.7 ± 0.01	2.4 ± 0.7	2.4 ± 0.07	1.5 ± 0.1
21 (week)	1.9 ± 0.07	1.8 ± 0.26	1.8 ± 0.26	1.5 ± 0.1
28 (week)	1.9 ± 0.09	1.8 ± 0.16	1.8 ± 0.07	1.5 ± 0.1

III. RESULTS

Chloroquine showed increased in acidity for the four weeks duration (3.1 ± 0.16, 2.7 ± 0.01, 1.9 ± 0.07 and 1.9 ± 0.09) and was significant ($P<0.05$) when compared with control, 1.5 ± 0.1. Fansidar also showed increase in secretion as follows; 3.2 ± 0.07, 2.4 ± 0.7, 1.8 ± 0.26, 1.8 ± 0.16 and was significant ($P<0.05$) as compared with control, 1.5 ± 0.1).

Metakelfin also induced increase secretion as follows; 2.6 ± 0.12, 2.4 ± 0.07, 1.8 ± 0.26 and 1.8 ± 0.07 and was significant for the first, second and fourth week of the administration at $P<0.05$ as compared with control 1.5 ± 0.1.

IV. DISCUSSION

The study has actually shown the gastrointestinal damage that anti-malaria drugs could do to it. This is not the only system that such drugs could affect. Chloroquine has been shown in the study to increase stomach acidity throughout the period of observation ie the twenty eight days as indicated by the titrable acidity and the pH which were all above normal. The increase in stomach acidity is as a result of increase gastric secretion which include those of pepsin and hydrochloric acid. Such acidity increase is likely to affect the mucus and the bicarbonate integrity of the mucosa leading to their reduction and the consequent enhancement of the contractility of the gastric wall and reduced gastric mucosal blood flow, Dask et al 1993. The acidity effect is evaluated in the mechanism of gastric secretion which may enhance production of oxygen species (free radicals) and oxidative stress which chloroquine is likely to have impacted on the gastric mucosal walls of the stomach, Clark et al, 1992 and Galunska, 2002. Apart from the effect on the stomach a change in the pH from normal to such a low degree during the administration of the drug could also cause injury and irritation to other parts of the gastrointestinal system e.g esophagus. Such may lead to heart burn, regurgitation, chest pains and other symptoms eg gastroesophasgeal reflux disease, Ronen, 2000.

However, it is quite surprising that metakelfin a new protective anti-malaria drug is observed to have the same effect on the gastrointestinal system like chloroquine. This is more dangerous as this regimen pattern is that of protection which span more half life than the curative treatment and thus has high tendency of affecting more of the body system and organs. Fansidar is rather observed to have mild effects as the acidity levels were only observed for weeks one and two. But this reaction poses complication in the follow up of a patient who is on fansidar treatment. It means that in the first and second weeks of the treatment there is tendency of increase free radical which malaria parasites are also observed to generate. Such toxic generation may not actually affect the efficacy of the drug but has the tendency of persisting patients morbidity eg pains which means non full recovery which may latter incriminate the drug under parasitological and clinical failure.

The insignificant degree of acidity on the third and fourth observation for fansidar which also means improvement on clinical intervention indicates perhaps a kind of adjustment on the part of the gastrointestinal system such adjustment may include increase production of the mucus and bicarbonate to neutralize the effects of the drug. This is interesting, as fansidar may be a potent drug for the treatment of peptic ulcer. There is therefore need for more investigations into anti-malarials effects on the body physiology rather than total focus on malaria pathology as even the pathophysiology is already complicated in the disease.

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