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Research article

CIMETIDINE, OMEPRAZOLE AND RANITIDINE AS ANTIULCEROGENIC MAKERS IN ULCER INDUCED RAT ILEUM MOTILITY INVITRO STUDIES

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ABSTRACT

Evaluation of the effects of cimetidine, omeprazole and ranitidine were carried out on the contractile motility of rat ileum using electricfield stimulus (EFS). The results showed that omeprazole decreases ileum motility ($P<0.05$) when compared with control groups on days 14, 21 and 28 days. Cimetidine and ranitidine on the other hand increased the motility of the ileum ($P<0.01$) when compared with control groups on different days of studies also. The drugs have minimal effects on days 14 and 21 and a different peak effect on day 28. Comparative motility stimulations with acetylcholine showed its high significant difference ($P < 0.005$) among cimetidine omeprazole and ranitidine. It is concluded that these antiulcerogenic drugs possess excitatory and inhibitory properties which may affect the absorption of food and the degree of ulceration in gastric ulcer patients.

Keywords: Cimetidine, omeprazole, ranitidine, ileum motility.

INTRODUCTION

The motility of the gastrointestinal tract components form major functional rudiment in the passage or transport of basic body needs e.g. water electrolytes and nutrients to all parts of the body. Such motility is a function of well organized layers of muscles functioning as a syncytium as per the activities of electrical signals and action potentials. Essentially, the ileum the final segment of the small intestine occupies a very relevant position in the absorption because of its having the largest surface area. Ileum follows the duodenum and jejunum and is separated from the cecum by the illeocecal valve, Guyton, 2006 Saladin, 2004. The mucosa of the ileum is highly folded with projections; villi and micro villi which form the brush borders. The large numbers of micro villi give the ileum its characteristic nature of having largest surface area. The large surface areas are meant for both attachment of enzyme molecules and for the absorption of products of metabolism of protein, fat and carbohydrate. However, the cells in the ileum diffuse with neuroendocrine system secrets hormones e.g gastrin, secretion and cholescystokinin which are involved in regulatory and metabolism of food substances. The major functions of ileum are the absorption of vitamin B_{12}, bile salts and product of digestion not absorbed by the jejunum. Invivo studies on the general gastrointestinal motility (Guignet, 2008) had provided information on the entire segment whereas our study on the specific segment; the ileum had given details information on that segment. It is aimed at advancing knowledge on the interplay of factors for motility monitored outside the system devoid of interferences which may be inherently pathologic or physiologic.

The significance of ileum motility in our study is brought to bear with its effects in ulceration in any part of the gastrointestinal tract. The relationship of such effects is examined in this study with respect to medication with basic antiulcerogenic drugs, cimetidine, ranitidine and omeprazole. There are controversies regarding the ability of rats ileum to be sensitive to contraction as many studies done on ileum motility are on rabbits and Guinea Pigs, Hyun, 2008, Geert, 1993, Scepanovic, 2006, ADAS, 2008, Stebbing, 2001, Bertrand, 2006. These studies except that of Adas, 2008, which detailed on comparative assay of the motility in two species; the guinea pigs and the mice mainly focused on guinea, pigs. It is therefore necessary to use other species which comparison between the species are drawn, such comparison offers opportunity to understand more about mode of actions of drugs, extracts, chemicals and the interactions with the regulatory mechanics on the motility of ileum in diverse species, Makawana, 2010, Hajazian, 2007, Guignet, 2006, Trailovic, 2009, Borrelli 2004, Giron, 2008, Briejer, 1997. This is the purpose of our present study as it affects antiulcerogenic drugs and motility in rat's ileum and its relative effects on peptic ulceration. Cimetidine, ranitidine and omeprazole are basic antiulcerogenic drugs for the treatment of peptic ulcer. Cimetidine and ranitidine are H_2 antagonists i.e they inhibit the formation of HCL secretion as such molecules are released from the parietal cells at stimulation Tripathi 2008. Cimetidine is effective in reducing ulcer lesions and potent in the treatment of duodenal ulcers. Longterm use of the drug can lead to infertility, centrilobar vacuolation cellular necrosis, bile duct hyperplasia, reduced prostate and seminal vesicle and tumour of the testes. Tripathi, 2008. On the other, a more potent of the H_2 antagonists is ranitidine and of lesser side effects but it is used as comparative therapy in peptic ulcer with omeprazole. Omeprazole is a group of proton pump inhibitor that means it inhibit hydrogen release enhanced by the proton pump thereby reducing the rate of HCL formation which results in

ulceration, it main target enzyme in the action is the inhibition of hydrogen potassium adenosine triphosphatase (H^+ K^+ ATPase) located at the secretory surface of the parietal cells, Hopfer 2006. It is the most, potent of the three antiulcerogenic drugs for peptic ulcer and related disease, Hetzel, 1980 and its inhibitory function is dose dependent. However, the sides effects are almost those of cimetidine e.g. infertility, mental confusion, disruption of pregnancy coupled with fetal lethal effects. The aim of the study is to assess the effects of cimetidine ranitidine and omeprazole on the ileum motility and its related effects on peptic ulceration. The translated effects will spell on the absorption of food substances and therefore in peptic ulcer patients there is likely tendency of low absorption of food and hence affecting the general well being of such patients. Importantly is that these drugs could be used as markers in assessing both physiologic and pathologic status of gastrointestinal tract.

MATERIALS AND METHODS

Forty males and females adult albino wistar rats of average weight between 100-150g were used for the study. They were fed with pellets and water and maintained under standard condition in the animal house. The rats were put into 4 groups with each group having 10 in number. Group one served as control administered with normal saline, group 2 each rat received 20mg/kg of omeprazole, group 3 each rat had 400mg/kg of cimetidine and in group 4 each rat was given 150mg/kg of ranitidine each.

INDUCEMENT OF ULCER:

The rats were starved for 24 hours after which 0.5ml of ethanol was administered to each rat orally using oral canula (Nwafor, 2005). The animals were observed for ulceration two hours after the administration of ethanol by the removal of the stomach, opened along the area of greater curvature to expose the mucosa.

DRUGS ADMINISTRATION

The dosage of the drugs was calculated based on that of the weight of the rats from the average weight of man, Jimmy, 2007, Bertram, 2004. The drugs were administered orally, using canula by-passing oesophagus and administered into the stomach, Robert et al 1979. The effects of the drugs on the contractility of the ulcerated ileum were observed for 14, 21 and 28 days respectively.

Electric field stimulation studies (EFS) with kymograph, Bowen 2008, Udombon, 2004

The rats were sacrificed periodically; 14, 21 and 28 days and ileum was removed from each animal and immersed in tyrode solution. A thread was attached to both ends of the ileum, one end attach to the organ bath and the other end to the writing lever. The threads were held with plasticine. The bath temperature was kept between 30^0 – 38^0C and also aerated and the contraction of the ileum observed on the kymograph recording per 14, 21 and 28 days in milivolt(MVOLT) Student's t. test was used for anlysis of data.

RESULTS

The mean values of ileum motility in milivolt on day 14 for control group, omeprazole, cimetidine and ranitidine groups were 3.6± 0.30, 1.9 ± 0.00, 2.0 ± 0.00 and 2.75 ± 0.25 respectively table 1. From the mean values, omeprazole shown a significant lower motility ($P<0.05$) than control group, cimetidine and ranitidine groups. On day 21, the mean values were 3.5 ± 0.20 for control, 0.5± 0.3, 1.75 ± 0.005 and 2.00± 00 for omeprazole, cimetidine and ranitidine respectively Table 1. The results also showed lower mean values for omeprazole compared with control. Values on day 28 were 1.75± 0.005 for control, 0.40± 0.00, 1.90± 0.00 and 2.0± 0.00 Table 1 for omeprazole, cimetidine and ranitidine respectively. Omeprazole showed a significantly lower value than control ($P<0.005$) while cimetidine and ranitidine values were significantly higher than control ($P<0.001$).

Acetylcholine used as standard in the study showed increase in motility of the ileum than control, cimetidine, ranitidine and omeprazole ($P<0.005$).

TABLE 1: COMPARATIVE ILEUM MOTILITY

DAY	CONTROL	OMEPRAZOLE	CIMETIDINE	RANITIDINE
14	3.6± 0.30	1.9± 0.00	2.00± 0.00	2.75± 00.25
21	3.5±0.20	0.5±0.30	1.75± 0.05	2.00 ± 0.00
28	1.75±0.05	0.40± 0.00	1.9 ± 0.00	2.00± 0.00

DISCUSSION

The study has shown the motility pattern in rat's ileum induced with gastric ulcer. The pattern showed a direct relationship with the different antiulcerogenic drugs based on the treatment period. The study showed a significant decrease in the ileum motility with omeprazole treatment on the different days of treatment, 14, 21 and 28 days. The decrease on the motility could result in decrease absorption of digested foods and such can lead to malabsorption, Benini, 2006. Malabsorption could also lead to malnutrition thus affecting the normal physiological functioning of the body. It means therefore that in the treatment of peptic ulcer with omeprazole the patient may witness malnourishment. But omeprazole, a proton pump inhibitor is the most potent drug in the treatment of peptic ulcer as it inhibit the release of hydrogen ions and hence disrupt its association of with chloride ions; Tripathi, 2008. The lower motility associated with omeprazole in this study indicates its low stretch effect on the ulcer itself hence reducing the bleeding scope and quickening the healing process, Leung, 2002. Treatment with cimetidine and ranitidine showed increase in ileum motility which would increase the absorption of food. But such an increase will stretch the ulcer spots thus increasing the bleeding at the spot and the healing period will increase. Comparing these three drugs in motility studies has shown the potency pattern in which omeprazole has been observed as the most potent. Also that both ranitidine and cimetidine increase the motility has confirmed their class H2- receptor antagonists, Maher, 2008. The three drugs could therefore be used as markers in determining the motility pattern in

the gastrointestinal tract in normal and in a disease situation coupled with magnetic tracking technology, Guignet, 2006. But the stimulating effects of these drugs could be due to direct effects on electrolytes secretion, enteric neurons and gastrointestinal smooth muscle contractions. The use of acetylcholine as standard enhancer in the study compared with the three drugs had proved that the three antiulcerogenic; drugs, cimetidine, ranitidine and omeprazole possess stimulatory and inhibito properties and could be substitutes in comparative blockers and enhancers gastrointestinal studies.

RECOMMENDATION

It is advisable that antiulcerogenic therapy be taken with caution particularly those with major malnutritional anomalies to avert complications. The use of rats in motility studies is highly recommended as it broaden research scope in inter and intraspecies findings, rats high availability in our environment are sources of encouragement for explorative scientists who may not have adequate research funding.

REFERENCES

[1] Adas, R. R. Hema, A., (2008). Evaluation of antidiarrhoea activity of rhizophora mucronata bark extracts on motility in albino mice and isolated ileum. Journal of Alternative Medicine Vol. 7 No.1

[2] Benini, L. Castellani, G., Bardelli, E., Sembenini, C., Bretegani, M. T., Caliari, S., Vantini, I., (2006). Omeprazole causes delay in gastric emptying of digestible meals. Dig Dis. Sci., 41:469-474.

[3] Bertrand, P. P., (2006). Real-time measurement of serotonin release and motility in guinea pig ileum. The Journal of Physiology 577, 689-704.

[4] Bertram, G. (2004): In Basic and Clinical Pharmacology, 9th ed. New York, Chicago, Sanfrancisco, London.

[5] Bowen, R. (2008): In Physiology of Smooth Muscle and Gastrointestinal Motility, 4th ed. New York.

[6] Borrelli, F. Capasso R. Pinto, A., Izzo, A., (2004). Inhibitory effect of ginger Zingiber in officinals on rat ileal motility invitro. Life Sci. 74 (23) 2889-96.

[7] Briejer, M. R., Mathis, C., Schuurkes, J. A., (1997). 5 – HT receptor types in the rat ileum longitudinal muscles: Focus on 5-HT2 receptors mediating contraction. Neurogastroenterol motility. 9(4) 231-7.

[8] Geert, N., Peter, W., Karel, G., Ann. A., Jan, S. and Joseph, L., (1993). Influence of rhein anthrone on peristaltic reflex of guinea pig isolated ileum: Involvement of prostaglandins. Br. J. Pharmacol. 108, 269-273.

[9] Giron, M. C., Annabin, P. B., Sabrina, E. Chiara, B., Chiara, F. and Gaion, R. M., (2008). Cyclic AMP in rat ileum: Evidence for the presence of extracellular Cyclic AMP – adenosine pathway. Gastroenterology. 134(4) 1116-26.

[10] Hetzel, D. V., Dent, J., Reed, W. D., Narievala, F. M., Mackinnon, M. and Miccathy, J. H. (1980) Healing and Relapse of severe peptic esophagitis after treatment with omeprazole. Gastroenterol. 95:903-12.

[11] Hejazian, S. H., Morowatisharifabad and Mahdavi, S. M. (2007) Relaxant effect of carum opticum on intestinal motility in ileum rat. World Journal of Zoology. 2(2) 15-18.

[12] Hyun, C. L., Young, G. K., Jung, H. L., Hcl, S. K. and Hyojin, P. (2008). Effect of Itopride Hydrochloride and Ileal and Coloric Motility in Guinea Pig Invitro. Yonsei Med. J. 49 (3) 472-478.

[13] Hopfer U., (2006). Digestion and absorption of basic nutritional constituents: In textbook of Biochemistry and Clinical Correlations 6th ed.

[14] Leung, W. K., Wong, V. W. S., Chung, S. C. S, Sung, T. T. Y., (2002) Celecoxib Versus Diclofessac and Omeprazole in reducing risk of recurrent bleeding in patients with arthritis. New England J. Med. 347:2104-2110.

[15] Maher O., Nieto J. E., Stanley, S. D., Dore, F., Stanley, J. R. (2008). Evaluation of effect of ranitidine on gastroduodenal contractile activity and gastric emptying in horses. Amj. Vet. Res, 69: 1153-7.

[16] Makwana, R., Molleman, A. and Parsons, M. E. (2010) Pharmacological characterization of cannabinoid receptor activity in the rat-isolated ileum myenteric plexus-longitudinal Muscle preparation Br. T. Pharmacol. 159(8) 1608-1622 W., Nwafor, P. A., Jack, T. Ekanem, A. U., Poh, C. F. (2005). Antiulcerogenic and anti diarrhoeal potentials of metanolic extract of pausinystallia macrosceras stem bark. Nig. J. Nat. Prod. Med. Vol. 9, 63-67.

[17] Guignet, M. and Kucera P. (2006). Magnet tracking: a new tool for invivo studies of the rat gastro intestinal motility. Neurogastroenterology and motility. 18 (6) 476-8.

[18] Saladin K. S., Miller, L. M. S. (2004) In textbook of Anatomy Physiology. 3rd Ed. New York, Sanfrancisco.

[19] Scepanovic, L., Kojic, Z., Suzic, S., Mesic, D., Popovic, D., Mazic, S. and Ilic, S. (2006). Excitatory muscuranic M. receptors mediate in the regulation of Guinea-Pig Terminal motility. Acta Veterinaria (Beograd). Vol. 56, No. 5-6, 397-404.

[20] Stebbing, m. j., Johnson, P. J. Vremec, M. A., and Bornstein, J. C. (2001) Role of X2 –adreno receptors in the sympathetic inhibition of motility reflexes of guinea pig ileum. The Journal of Physiology. 534, 465-478.

[21] Trailovic, S. M., P. A. Robertson, Jelena, N. T. (2009). Inhibitory effect of eugenol on rat motility invitro. Acta Veterinaria, Vol. 59, No. 2-3, 123-131.

[22] Tripathi, K. D. (2008): In essentials of Medical Pharmacology 6th ed. New Dahli

[23] Udombon, N. S. (2004): In Practical Physiology, Clestinnno, Nigeria pp.77-84.