Original article

A Drug Synergism: Mosapride and Ondansetron Combination a Promising Drug Treatment for Gastroparesis

Nazia Rashid[1], Wardah Siddique[1], Irum Nazeer Malik[1], Ayela Eman Zia[2], Muniza Qayyum[1], Binish Anwar[3]

[1]Department of Pharmacology, Fatima Jinnah Medical University, Queen's road Lahore, [4]Department of Pharmacology, CMH Lahore Medical College, [3]Department of Pharmacology, Shalamar Medical and dental College, Lahore

Correspondence to: Nazia Rashid, Email: Email: dr.naziaqamara@yahoo.com

ABSTRACT

Background: Gastroparesis is a common GI disorder. The only FDA approved drug used for its treatment is metoclopramide. Objective was to evaluate the effect of mosapride and ondansetron alone and in combination on intestinal motility of animal tissues and their comparison with serotonin as standard drug.

Methods: This experimental study was done in Combined Military Hospital Lahore and Fatima Jinnah Medical University over 18 months. Isolated tissues obtained from adult healthy rabbits and rats were used in the study. Sample size was calculated by OpenEPI formula. Animals were divided into 5 groups comprising 20 animals in each group. Strips of rabbit ileum and rat gastric fundus tissues were allowed to stand in an organ bath with an isotonic force transducer attached to powerlab (AD instruments). Increasing concentrations of serotonin, mosapride, and ondansetron were applied to tissues and their responses were recorded by the change in the mean force of contraction (grams). Increasing concentrations of serotonin and mosapride were administered in the presence of ondansetron and their responses were recorded. T-test and ANOVA followed by Post Hoc Tukey's test were used for statistical analysis.

Results: There was a dose-dependent increase in the mean force of contraction with Serotonin, mosparide and ondansetron on rabbit ileum and rat gastric fundus tissue. Increasing concentration of mosparide in the presence of ondansetron also showed a dose-dependent increase in response as depicted by the change in the mean force of contraction in grams.

Conclusion: Mosapride has less stimulatory effect on gastrointestinal tissue as compared to when used in combination with ondansetron.

Keywords:

Pharmacology rabbit ileum rat gastric fundus

INTRODUCTION

Gastroeparesis is a chronic gastrointestinal motility disorder resulting from the slowing of gastric emptying in the absence of any mechanical obstruction. The most common symptoms associated with gastroparesis include varying severity of nausea, early satiety, vomiting, epigastric discomfort, abdominal distension, bloating along diarrhoea, or constipation.[1] The etiology of gastroparesis is variable. Most common causes include diabetic gastroenteropathy, idiopathic and post-surgical. Other minor causes include collagen vascular disease, iatrogenic, metabolic diseases and neuromuscular dysfunction, achalasia, functional dyspepsia, gastroesophageal reflux disease, celiac disease, hypertrophic pyloric stenosis, atrophic gastritis. Certain medicines may also be responsible for the symptoms of gastroparesis such as alcohol, proton pump inhibitors, tobacco, anticholinergic drugs, opioids, and progetsterone.[2]

Gastroparesis has a direct impact on health-related quality of life. Hospital admission due to gastroparesis has been increasing over the previous years with significant economic impact.[3] Malnutrition and resultant mineral and vitamin deficiencies are frequently associated with Gastroparesis, leading to autonomic cardiovascular dysfunction as well.[4]

The incidence is 4.6% in Type I and 1.3% in type II diabetes in the USA where 60% of the patients have esophageal symptoms, 60% constipation, and 20% have diarrhea.[5,6] The incidence of gastroparesis is even higher in developing countries due to a higher incidence of diabetes mellitus. According to a recent study, 44% of patients with diabetes mellitus also suffer from diabetic gastroparesis. These patients manifested with stomach

ARTICLE INFO

Article History

Received: 04.09.2024 | Accepted: 27.06.2025

Conflict of Interest: The authors declare no conflict of interest.

Funding: None.

Citation: Rashid N, Siddiqi W, Malik IN, Zia AE, Qayyum M, Anwar B. A Drug synergism: Mosapride and ondansetron combination a promising drug treatment for Gastroparesis. J Fatima Jinnah Med Univ. 2025; 19(2): 74-81.

DOI: https://doi.org/10.37018/HALS6592

fullness (44.5%), early satiety (45.1 %), and nausea (33.1%).[7]

Development of gastroparesis is a complex phenomenon related to many factors such as hyperglycemia, altered serotonin level, dysfunction of myenteric neuronal nitric oxidase synthase, vagal dysfunction, abnormalities of interstitial cells of Cajal, and oxidative stress.[8] Recent studies indicate that low serum serotonin is one of the causes of diabetic gastroparesis and constipation.[9] Treatment of gastroparesis includes lifestyle modification such as good glycemic control through dietary limitation of carbohydrate intake and frequent small meals. Intake of high-fiber diet while avoiding a high-fat diet is also helpful.[10] The only FDA approved drug for treatment of gastroparesis is metoclopramide, which is a dopamine D_2 and $5HT_3$ receptor angtagonist and $4HT_4$ receptor agonist. Other drugs available to treat gastroparesis are erythromycin, cholinomimetic agents and domperidone.[11] Mosapride is a $5HT_4$ agonist used for the treatment of severe constipation. However, it is associated with many adverse effects, such as cardiovascular complications. Ondansetron is a $5HT_3$ receptor antagonist used as an antiemetic in the treatment of gastroparesis.[12] However, there is a gap in literature regarding the comparison of effects of mosapride and ondansetron on gastrointestinal tissues of animals. So the present study was designed to compare the effects of ondansetron and mosapride alone and their combined effects on intestinal motility of animal tissues and to compare them with the standard drug serotonin creatinine sulfate. As both of these drugs act as an agonist and partial antagonists at serotonergic receptors therefore serotonin creatinine sulphate has been used for comparison. The rationale of this study was that combined use of mosapride and ondansteron will reduce the dose of individual drugs and hence the likelihood of developing adverse effects of each drug will also be reduced.

SUBJECTS AND METHODS

This animal experimental research was conducted at department of Pharmacology FJMU and Combined Military Hospital Lahore Medical College over a span of 18 months from January 2023 till June 2024. All the desk work was done in FJMU; however experimental study was conducted in department of Pharmacology CMH Lahore medical college.

The drugs utilized in the study included serotonin creatinine sulphate (Sigma Aldrich), ondansetron hydrochloride dihydrate (Indus Pharma), and mosapride Citrate (Western Pharmaceuticals). Serotonin creatinine sulphate was procured while the other drugs were received as gift samples for the research project. Molar concentrations of solutions were prepared according to molecular weights of drugs.All the calculations for the preparation of molar solutions were done by using a molarity calculator (GraphPad by Dotmatics). The molecular weight of serotonin creatinine sulphate was 405.43g/mol. The stock solution of serotonin creatinine sulphate was prepared by dissolving 40.543 mg of serotonin creatinine sulphate in 10 ml distilled water to prepare a final 0.01 M or $1x10^{-2}$ concentration. Then 1 ml of 10^{-2} solution was dissolved in 9 ml of distilled water to obtain a 10^{-3} concentration and further dilutions of 10^{-4}, 10^{-5}, and 10^{-6} were prepared by following the same procedure.

The molecular weight of ondansetron hydrochloride dihydrate was 365.85 g/mol. The stock solution of ondansetron Hydrochloride was prepared by dissolving 36.5 mg of ondansetron in 10 ml distilled water to get a final 0.01 M or $1x10^{-}$concentration. Then 1ml of 10^{-2} solution was dissolved in 9 ml of distilled water to obtain 10^{-3} concentration and further dilutions were prepared by following the same procedure

The molecular weight of mosapride citrate was 614.0g/mol. The stock solution of mosapride citrate was prepared by dissolving 61.4 mg of mosapride in 10 ml distilled water to get 0.01 M or $1x10^{-2}$ solution. Then 1 ml of 10^{-2} solution was dissolved in 9 ml of distilled water to obtain 10^{-3} concentration and further dilutions were prepared by following the same procedure.

The study involved adult healthy rabbits (weighing between 1 to 1.5 kg, of either sex and non-pregnant) and Albino rats (weighing 150-200g, of either and non-pregnant).The animals were procured from the animal house of CMH Lahore medical college. The animals were placed in the animal house of CMH Lahore Medical College, under optimum hygienic conditions, natural day, and light cycle at normal room temperature. Animals were acclimatized for 1 week before commencement of the study. They had free access to food and water. Before the experiment animals were kept fasting for 18 hours while water was provided.

The animals were divided into 5 groups, with each group consisting of 20 animals of each species. Only one tissue (rabbit lum and rat gastric fundus tissue) was removed from each animal and only once used for experimental work.

Group 1 (serotonin alone group): Cumulative dose-response curve of Serotonin

Group 2 (ondansetron alone group): Cumulative dose-response curve of Ondansetron

Group 3 (serotonin on ondansetron group): Cumulative dose-response curve of Serotonin in the presence of ondansetron

Group 4 (mosapride alone group): Cumulative dose-response curve of mosapride

Group 5 (mosapride on ondansetron group): Cumulative dose-response curve for mosapride in the presence of ondansetron

Rabbits were humanely euthanized. Subsequently, their ileum was carefully dissected and separated from the mesentery. The isolated ileum was immersed in Tyrode's solution, whose composition in millimoles was as follows: 11.90 $NaHCO_3$, 136.9 NaCl, 1.05 $MgCl_2$, 1.8 $CaCl_2$, 0.42 NaH_2PO_4 (pH 7.4), 2.68 KCl, and 5.55 glucose. This solution was freshly prepared daily. Sections of ileum measuring 2 cm in length were suspended in organ baths (Radnoti 159920-X1/C; Radnoti Llc, Covina, CA) containing 25 ml of Tyrode's solution. The bath solution was continuously aerated with carbogen (5% CO_2 and 95% O_2). Initially, a resting tension of 1 g was applied as a preload to the tissue. Prior to drug administration, the tissue was allowed to equilibrate for approximately 30 minutes. Intestinal contractions were recorded using an isotonic transducer connected to the PowerLab data acquisition system (Model: PL26T04, ADInstruments, Sydney, Australia).[13]

Rats were anesthetized with chloroform, after which their stomachs were carefully dissected and separated from surrounding tissues. Strips of tissue measuring 4–5 mm in width and approximately 20 mm in length were prepared. These tissue strips were then mounted in a 25 mL organ bath filled with Kreb's solution, whose composition in mM was: $NaHCO_3$ 25.0, NaCl 118.2, KH_2PO_4 1.3, $CaCl_2$ 2.5, KCl 4.7, $MgSO_4$ 1.2, and glucose 1.7 (pH 7.4). The temperature of the organ bath was maintained at 37 ± 1 °C, and the solution was continuously aerated. A preload of 1.0 g was applied, and the tissue was allowed to equilibrate for 30 minutes before recording responses. Contractions in the rat gastric fundus tissues were recorded using an isotonic transducer connected to the PowerLab data acquisition system (Model: PL26T04, ADInstruments, Sydney, Australia).[14] As the capacity of organ bath was 25 ml, 25 µL of $1x10^{-6}$ molar solution was administered to get a final concentration of $1x10^{-9}$ or 0.001 micromoles in the organ bath. Then after getting maximum tissue response for up to half an hour, the next concentration of 50 microliter of $1x10^{-6}$ was administered to get a final concentration of $3x10^{-9}$ or 0.003 µM in the organ bath. The same procedure was followed to administer increasing concentrations.[15] Cumulative dose-response curves of increasing concentration of Serotonin creatinine sulpahate, Ondansetron and mosapride alone were constructed. Then increasing concentration of serotonin and mosapride were administered after the pretreatment of tissue with ondansetron. For this purpose, tissue was initially exposed to 1µM of ondansetron solution for 30 minutes.[16]

All the Data was entered in the latest available version of GraphPad prism (version 8.01). The number of animals in each group were denoted as 'n'. Data was expressed as Mean ± SEM. T-test was used to compare the difference between the two groups whereas one-way ANOVA followed by Post Hoc Tukey's test was used for comparison among the large number of groups. A p-value <0.05 was considered significant.

RESULTS

Group 1 (serotonin only): The cumulative dose-response curve for increasing concentrations of serotonin was plotted on rabbit ileum and rat gastric fundus tissue. There was an excitatory effect on intestinal contraction as evidenced by a change in the mean force of contraction from 16.83 ± 3.2 to 29.7±4.3 on rabbit ileum and from 9.602±1.69 to 13.03±1.7 on rat gastric fundus tissue.

Group 2 (ondansetron only): The cumulative dose-response curve for increasing concentrations of ondansetron alone was plotted and the response was depicted as a change in the force of contraction. There was a dose-dependent increase in the mean force of contraction as evidenced by a change in mean value from 9.66 ± 3.76 to 13.66±4.43 on rabbit ileum and from 5.405±1.473 to 6.3 ±1.46 on rat gastric fundus tissue.

Group 3 (serotonin on ondansetron): The cumulative dose-response curve of increasing concentrations of serotonin creatine sulphate was plotted in the presence of a fixed concentration of ondansetron (1µM) on rabbit ileum. There was an increase in response as shown by a change in the mean value of Force of contraction from 13.084±1.74 to 21.82 ± 2.8 on rabbit ileum and 8.345±1.611 to 10.2±1.6 on rat gastric fundus tissue.

An unpaired t-test was used to compare the means of the effect of serotonin alone and serotonin in the presence of a fixed concentration of ondansetron on rabbit ileum. A p-value of 0.006 showed a significant difference between the two groups. Similar significant results were obtained on rat gastric fundus tissues.

Group 4 (mosapride only): The cumulative dose-response curve for increasing concentrations of Mosapride alone was plotted and the response was depicted by the change in the force of contraction. There was a stimulatory effect on intestinal motility as shown by the change in mean force of contraction from 15.84 ±2.94 to 15.97 ± 2.98 on rabbit ileum and 5.6±2.55 to 6.2±2.6 on rat gastric fundus tissue.

Group 5 (mosapride on ondansetron): The cumulative dose-response curve of increasing concentrations of Mosapride was plotted in the presence of a fixed concentration of ondansetron. There was an increase in

force of contraction as shown by a change in the mean force of contraction from 18.24 ±2.69 to 19.28±2.7 on rabbit ileum and 7.716±1.20 to 9.9 ±1.5 on rat gastric fundus tissue. An unpaired t-test was used to compare the means of the effects of mosapride alone and mosapride in the presence of a fixed concentration of ondansetron. A p-value of <0.0001 showed the significant difference between the two groups. Similar results were obtained on rat gastric fundus tissues.

Comparison of all groups serotonin alone, ondansetron alone, serotonin on ondansetron, mosaride alone and mosapride in the presence of ondansetron were made by using ANOVA followed by post hoc Tukey's test. These results showed that excitatory effects induced by ondansetron and mosapride in combination are comparable to that of serotonin alone. There were significant differences among various groups as shown in graph.

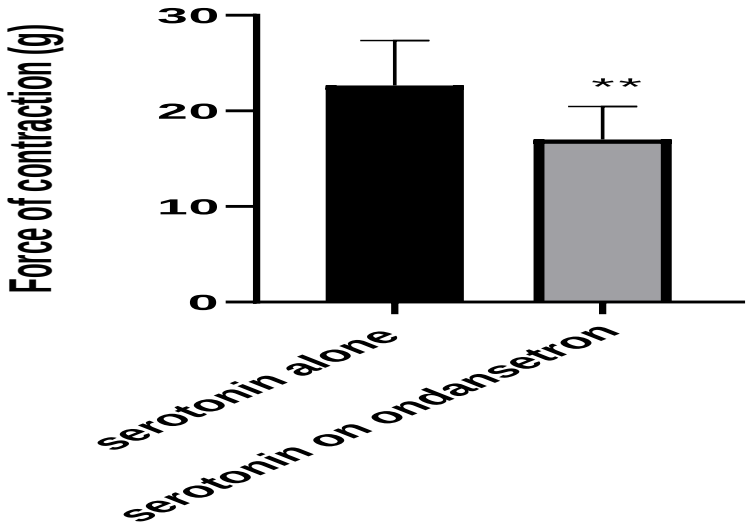

Figure 1: Comparison of the effect of serotonin alone and serotonin in the presence of ondansetron on rabbit ileum. (*** p value < 0.001, **p value <0.01, *p value < 0.05)

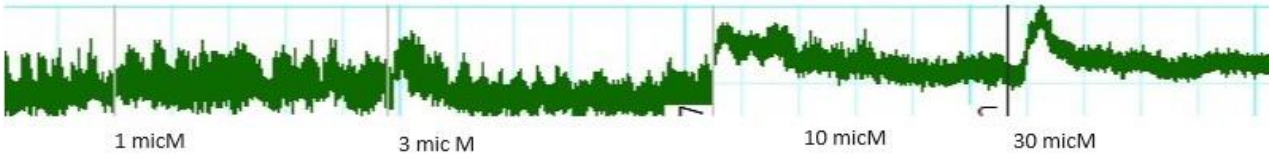

Figure 2: Tracing showing the effect of increasing concentrations of serotonin alone on rabbit ileum.

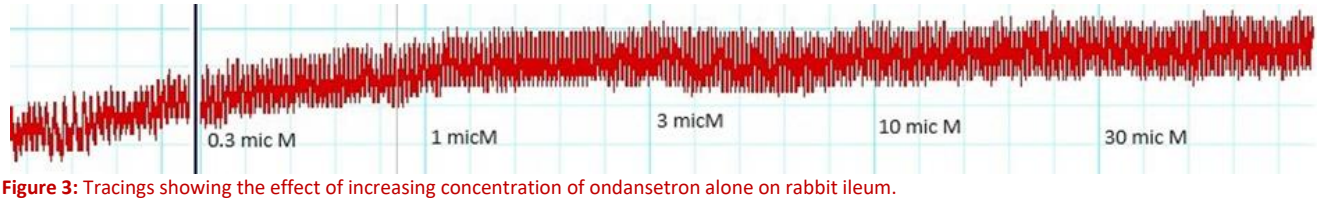

Figure 3: Tracings showing the effect of increasing concentration of ondansetron alone on rabbit ileum.

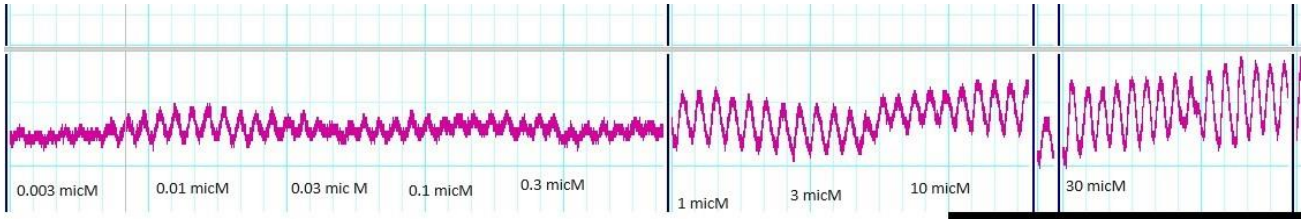

Figure 4: Tracing showing the effect of increasing concentration of serotonin in the presence of a fixed concentration of ondansetron on rabbit ileum.

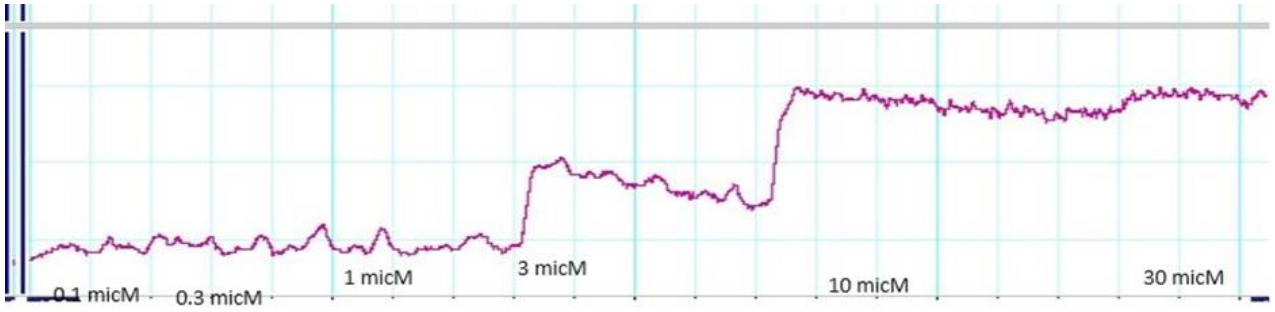

Figure 5: Tracing showing the effect of increasing concentration of serotonin alone on rat gastric fundus tissue.

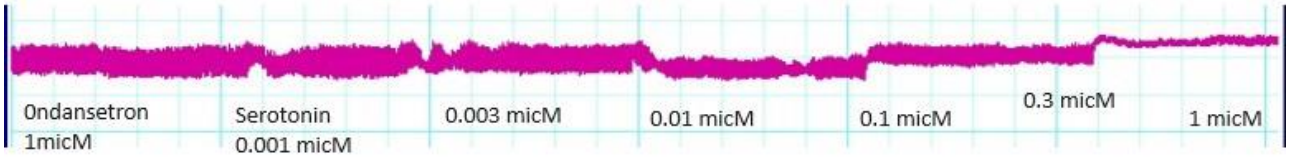

Figure 6: Tracing showing the effect of increasing concentration of serotonin in the presence of a fixed concentration of ondansetron on rat gastric fundus tissue.

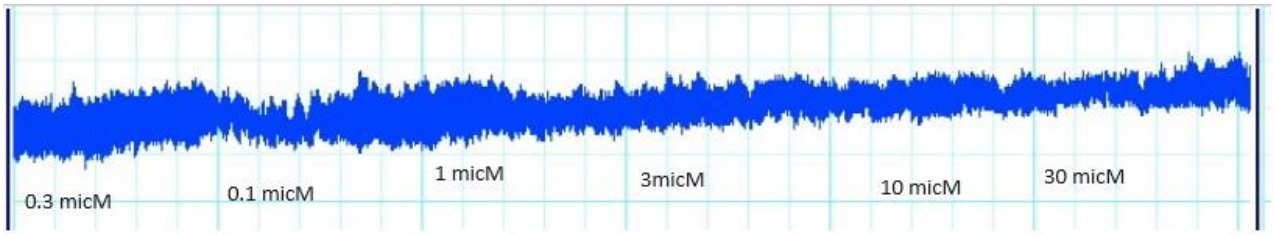

Figure 7: Tracing showing the effect of increasing concentrations of mosapride on rat gastric fundus tissue.

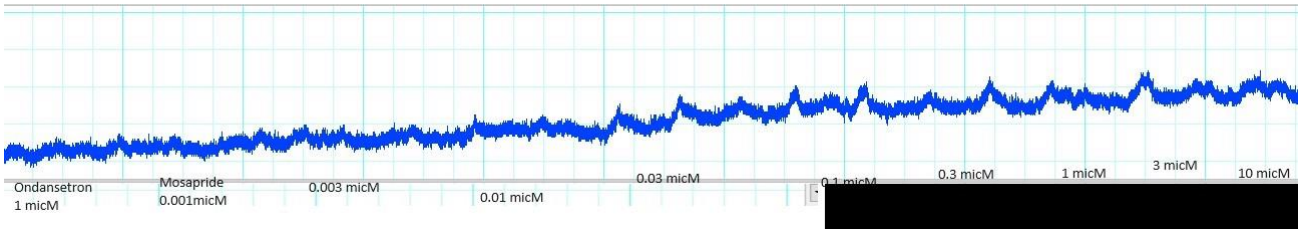

Figure 8: Tracing showing the effect of increasing concentration of mosapride in the presence of a fixed concentration of ondansetron on rat gastric fundus tissue.

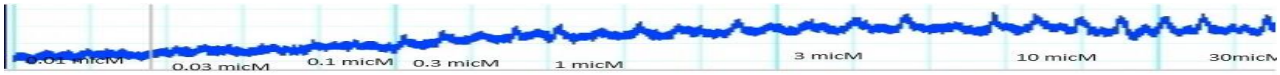

Figure 9: Tracing showing the effect of increasing concentrations of ondansetron alone on rat gastric fundus tissue.

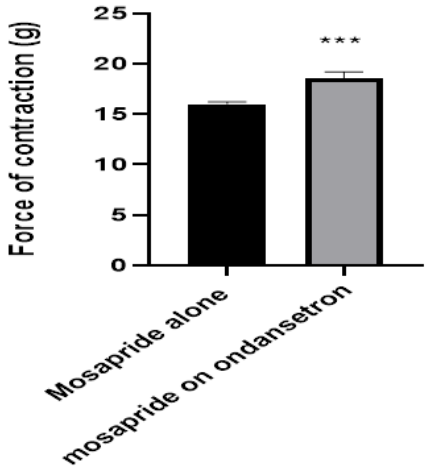

Figure 10: Comparison of effect of increasing concentration of mosapride alone and mosapride in the presence of a fixed concentration of ondansetron on rabbit ileum. (*** p value < 0.001, **p value <0.01, *p value < 0.05)

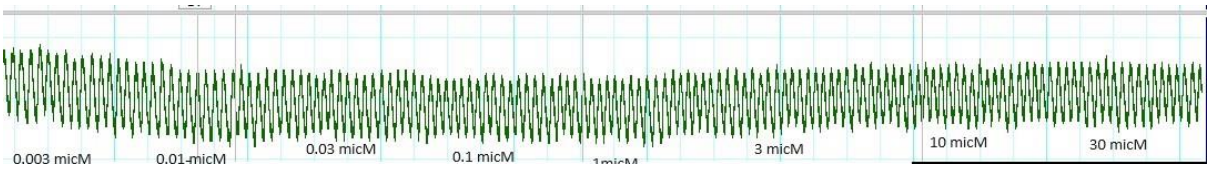

Figure 11: Tracing showing the effect of increasing concentration of mosapride alone on rabbit ileum.

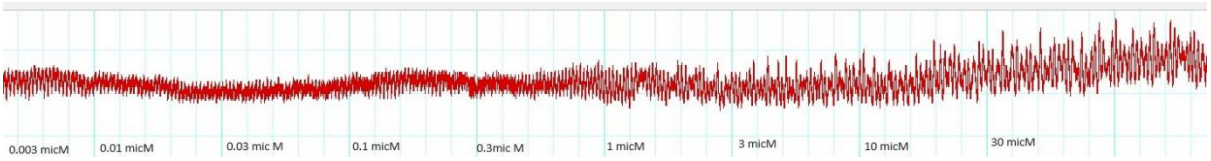

Figure 12: Tracing showing the effect of increasing concentration of mosapride in the presence of a fixed concentration of ondansetron.

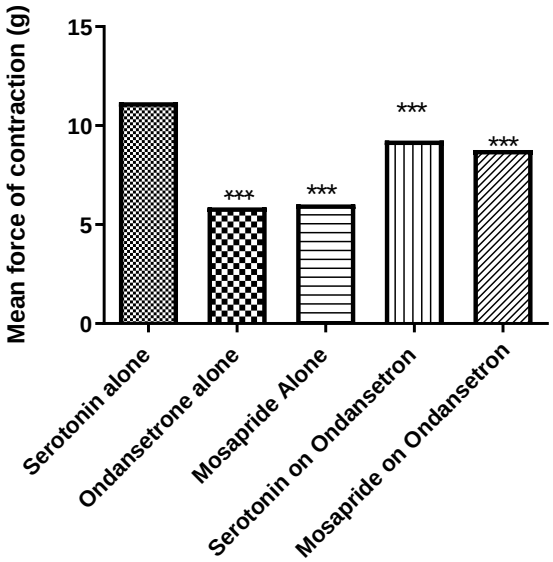

Figure 13: Comparison among Serotonin , ondansetron, mosapride alone , serotonin on ondansetron , mosapride on ondansetron. (* pvalue < 0.05, ** p value < 0.01 , ***P value < 0.001)

DISCUSSION

There is very little data available on drug treatment for gastroparesis. So this study was designed to compare the effect of two drugs, Mosapride and ondansetron, used as gastrokinetic and as an antiemetic agent respectively, in the management of gastroparesis.

It was found that serotonin caused a dose-dependent increase in response as evidenced by the increase in the force of contraction (Mean 16.83-29.73) in rabbit ileum and (9.6-13.03) in rat gastric fundus tissue. This result is consistent with a previous study done by Salvador and colleagues who demonstrated the mechanical effect of serotonin on rabbit small intestines[17]. This result was also in accordance with a recent study reporting the dose-dependent stimulatory effect of serotonin on rat stomach tissue due to stimulation of various serotonergic receptors.[18]

The localized effects of ondansetron on gastrointestinal tissues are not much explored.Haga K and his colleagues also reported that $5HT_3$ antagonists possess the ability to enhance intestinal motility[19]. Ondansetron exerts dose-dependent effects on intestinal motility through stimulation of $5HT_2$ receptors as well and these effects can be counteracted by yohimbine a $5HT_2C$ receptor antagonist[20]. Increasing concentrations of serotonin were administered in the presence of a fixed concentration of ondansetron and the effect was noted. The dose-response effects of increasing the concentration of serotonin alone were compared with the dose-response effects of serotonin in the presence of ondansetron. There was a significant decline in the response of serotonin in the presence of ondansetron (p-value <0.0001).These results are in line with a previous study done by Azal and colleagues due to antagonistic action of ondansetron on serotonin $5HT_3$ receptors.[21]

The increasing concentrations of mosapride were administered on rabbit ileum and rat gastric fundus tissue. The stimulatory effect was more prominent in rat gastric fundus tissue. This effect was observed due to more distribution of $5HT_4$ receptors on the stomach and upper GIT.[22] These results are in accord with Akrab et al who demonstrated the effect of mosapride and levosulpride in GIT.[23]

Our results revealed that increasing concentration of mosapride in the presence of fixed concentration of ondansetron showed an enhanced stimulatory effect on Gastrointestinal motility .This effect might be due to the stimulation of cholinomimetic receptors by ondansetron and $5TH_4$ receptors by mosapride as suggested by previous researchers.[24]

Limitations: The major limitation of study was non availability of resources like well equipped animal house and a powerlab in Fatima Jinnah Medical University.

CONCLUSION

An effect of ondansetron and mosapride is observed on intestinal motility of rabbit ileum and rat gastric fundus tissue. Mosapride when used alone on gastrointestinal tissues has very less stimulatory effect which can be enhanced when used in combination with ondasnteron. This drug combination may help to decrease the dose as well as the adverse effects of individual drugs which is the key strength of this study. This drug combination may be helpful in management of gastroparesis if further studies are conducted in animal models followed by human intervention.

Acknowledgments

I am indebted to Vice chancellor Professor Dr Khalid Masood Gondal who granted me permission to conduct this research work. Also I am highly thankful to Professor Dr. Muniza Qayyum, Dr. Lubna Amer, Dr. Waqar and Dr. Sehrish for their continuous support in this research work. The whole funding for this research work was provided by the Department of Pharmacology, FJMU, Lahorse.

Author Contributions

Dr. Nazia Rashid: Conception and design, analysis and interpretation of data, drafting the article, critical revision for important intellectual content, final approval.

Dr. Wardah Siddiqi: Conception and design, analysis and interpretation of data.

Dr. Irum Nazeer Malik: Analysis and interpretation of data, drafting the article.

Dr. Ayela Eman Zia: Acquisition of data, conception and design, analysis and interpretation.

Dr. Muniza Qayyum: Analysis and interpretation of data, proofreading.

Dr. Binish Anwar: Conception and design, analysis and interpretation of data.

REFERENCES

1. Szeto L, Yazdian A, Parkman HP. Atypical causes of gastroparesis: prevalence, gastric emptying, and clinical features. J Clin Gastroenterol. 2022 May 1;10-97.
2. Bardaro SJ, Guerron AD, Romanelli J, Soriano I, King K, Gibbs KE, et al. Gastroparesis: an evidence-based review for the bariatric and foregut surgeon. Surg Obes Relat Dis. 2023 Mar 4.
3. Yekutiel N, Chodick G, Knop J, Cavlar T, Tsukinovsky S, Toren G, et al. The epidemiology and burden of gastroparesis: real-world data from a large healthcare provider in Israel. Neurogastroenterol Motil. 2023; e14522.
4. Petri M, Singh I, Baker C, Underkofler C, Rasouli N. Diabetic gastroparesis: an overview of pathogenesis, clinical presentation and novel therapies, with a focus on ghrelin receptor agonists. J Diabetes Complications. 2021 Feb 1;35(2):107733.
5. Ye Y, Jiang B, Manne S, Moses PL, Almansa C, Bennett D, et al. Epidemiology and outcomes of gastroparesis in the United Kingdom. Gut. 2021 Apr 1;70(4):644-53.
6. Asghar S, Shahid S, Sajjad H, Nasir JA, Usman M, Abdul Nasir J. Gastroparesis-related symptoms in patients with type 2 diabetes

mellitus: early detection, risk factors, and prevalence. Cureus. 2023 Mar 5;15(3).
7. Ahmed SS, El-Hafez HA, Mohsen M, El-Baiomy AA, Elkhamisy ET, El-Eshmawy MM. Is vitamin B12 deficiency a risk factor for gastroparesis in patients with type 2 diabetes? Diabetol Metab Syndr. 2023 Mar 1;15(1):33.
8. Zavaleta MJ, Yovera JG, Marreros DM, Robles LD, Taype KR, Gálvez KN, et al. Diabetic gastroenteropathy: an underdiagnosed complication. World J Diabetes. 2021 Jun 6;12(6):794-802.
9. Jin B. Role of serotonin in gastrointestinal dysmotility associated with diabetes and COVID-19 [dissertation]. Reno (NV): University of Nevada, Reno; 2021.
10. Shakhatreh M, Jehangir A, Malik Z, Parkman HP. Metoclopramide for the treatment of diabetic gastroparesis. Expert Rev Gastroenterol Hepatol. 2019 Aug 3;13(8):711-21.
11. Young CF, Moussa M, Shubrook JH. Diabetic gastroparesis: a review. Diabetes Spectrum. 2020 Aug 1;33(3):290-7.
12. Picot C, Berard A, Grenet G, Ripoche E, Cucherat M, Cottin J. Risk of malformation after ondansetron in pregnancy: an updated systematic review and meta-analysis. Birth Defects Res. 2020 Aug;112(13):996-1013.
13. Siddiqui WA, Mazhar MU, Malik JA, Talat A, Zaffar S, Rashid H, et al. The spasmolytic effect of Astragalus sarcocolla on intestinal smooth muscle of rabbit in vitro: potassium channel opening. Cureus. 2020 Jul 8;12(7).
14. Chen G, Zhu L, Liu Y, Zhou Q, Chen H, Yang J. Isoliquiritigenin, a flavonoid from licorice, regulates gastrointestinal motility in vitro and in vivo. Phytother Res. 2009 Apr;23(4):498-506.
15. Jespersen B, Tykocki NR, Watts SW, Cobbett PJ. Measurement of smooth muscle function in the isolated tissue bath: applications to pharmacology research. J Vis Exp. 2015 Jan; (95):e52324.
16. Hamambulu P, Goma FM, Choongo K, Simfukwe N, Lwiindi L, Mwenya KC. Effects of Steganotaenia araliacae root extract on contractile function of isolated rat ileum. J Prev Rehabil Med. 2021 May 30;3(2):32-41.
17. Salvador MT, Murillo MD, Rodriguez-Yoldi MC, Alcalde AI, Mesonero JE, Rodriguez-Yoldi MJ. Effects of serotonin on physiology of rabbit small intestine. Can J Physiol Pharmacol. 2000 Apr 10;78(5):359-66.
18. Dey YN, Mahor S, Sharma D, Wanjari MM, Kumar D, Sharma J. Possible role of serotonin in gastrokinetic activity of Amorphophallus paeoniifolius tuber. Phytomed Plus. 2022 May 1;2(2):100275.
19. Haga K, Asano K, Inaba K, Morimoto Y, Setoguchi M. Effect of Y-25130, a selective 5-HT3 receptor antagonist, on gastric emptying in mice. Arch Int Pharmacodyn Ther. 1994 Nov 1;328(3):344-55.
20. Amemiya N, Hatta S, Ohshika H. Effects of ondansetron on electrically evoked contraction in rat stomach fundus: possible involvement of 5-HT2B receptors. Eur J Pharmacol. 1997 Nov 27;339(2-3):173-81.
21. Afzal A, Bakhtiar BT. Ondansetron: a newer aspect of dose–response relationship on ileal smooth muscle of rabbit. Pak J Pharm Sci. 2016 Jan;29(1):119-24.
22. Usai-Satta P, Lai M, Oppia F, Cabras F. Effects of prokinetics on the digestive tract. Curr Rev Clin Exp Pharmacol. 2022 Nov 1;17(3):161-5.
23. Akrab SN, Al Gawhary NE, Shafik AN, Morcos GN, Wissa MY. Role of mosapride and levosulpiride in gut function and glycemic control in diabetic rats. Arab J Gastroenterol. 2023 Mar 4.
24. Komada T. Elucidation for gastrokinetic effects of a novel 5-HT4 receptor agonist, CJ-033466, and pharmacological characterization of 5-HT receptor subtypes.