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Original Research Paper

Physiology

TO STUDY AND COMPARE THE EFFECT OF SSRI ANTIDEPRESSANTS ON MOTILITY OF ISOLATED RABBIT GUT.

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ABSTRACT **Introduction:** Metabolism is the primary process by which medications are cleared, as it is how they are activated or deactivated which shows that the metabolism of medications is critical to their efficacy. The small intestine, like the rest of the gastrointestinal tract, is an intelligent organ. It generates a wide variety of motor patterns to meet motility requirements in different situations The isolated rabbit gut preparation is one of the classical preparations in physiology and pharmacology for bioassays, or the study of drug action and autonomic control of motility. **Materials And Methods:** This was an in vitro experimental study which was performed on isolated rabbit gut preparation in order to explore the effect of anti-depressant drugs. In the present study total 24 samples of rabbit gut (age group 2-4.5 years) were enrolled. The samples were randomized as follows: Acetylcholine (D1), Sertraline (D2) Citalopram (D3). **Result:** Effect of SSRI Anti-depressants (Sertraline and Citalopram) was observed which showed substantial decrease in amplitude and frequency on isolated gut motility. **Conclusion:** Anti-depressants exhibit anti-muscarinic properties as both have significant effects on the muscarinic receptor. Anti-depressant drugs showed substantial decrease in gut motility by affecting the amplitude and the frequency.

KEYWORDS : Anti-depressants, Acetylcholine, Sertraline, Citalopram.

INTRODUCTION:

Metabolism is the primary process by which medications are cleared, as it is how they are activated or deactivated which shows that the metabolism of medications is critical to their efficacy. Medications are initially exposed to a vast number of bacteria and active enzymes released by these bacteria, including oxidation-reduction enzymes, transferases, and other metabolic enzymes. As a result, the gut flora's metabolism of pharmaceuticals has a significant effect on the pharmacokinetics and pharmacodynamics of medications [1].

The small intestine, like the rest of the gastrointestinal tract, is an intelligent organ. It generates a wide variety of motor patterns to meet motility requirements in different situations. Its basic motor function after a meal is to mix the chime with exocrine and intestinal secretions, agitate its contents too Uniformly and evenly expose them To the mucosal surface and to propel them distally at a rate that allows optimal absorption of food components, and reabsorption of bile [2] .

Maintenance of intestinal barrier integrity is essential to a healthy status. Diverse chronic disorders, including inflammatory bowel disease, diabetes, and rheumatologic disorders, are associated with a disruption of intestinal barrier function[3]

Numerous organs and tissues of the gastrointestinal smooth muscle exhibit "autonomous" action. Segmental or peristaltic motility patterns are based on phasic contractions, which are organised into phasic patterns by spontaneous pacemaker activity in the colon, small intestine, and stomach. Although the level of coupling between pacemaker activity and contractions is heavily reliant on neurological and other regulatory inputs, pacemaker activity is intrinsic to gastrointestinal muscles and does not depend on hormonal or brain inputs. Low-amplitude contractions are produced by basic slow wave activity, and each cycle's frequency of contractions is modulated by inhibitory or excitatory neuronal inputs [4] Gastrointestinal motility is regulated by Motilin (MLN), a peptide hormone, that was firstly identified from the pig's upper intestinal mucosa and it has a stimulatory action in gastrointestinal motility.

Various other research study, show that animals who had disruptions in acetylcholine production during prenatal development saw major abnormalities in their gastrointestinal health. Intestinal dysbiosis or germ overgrowth, loss of healthy gut motility or dysmotility, lack of colonic movement/constipation, failure to flourish, and even mortality occurred. As a result, it was determined that acetylcholine is essential for long-term gut motility and survival [5]

The isolated rabbit gut preparation is one of the classical preparations in physiology and pharmacology for bioassays, or the study of drug action and autonomic control of motility. This preparation is included in many "in-house" laboratory manuals of various colleges and research institute, and in some commercially prepared manuals dealing with physiology and pharmacology [6].

Therefore, in this work we aimed to evaluate changes in permeability induced by Anti-depressant drugs on isolated rabbit gut preparation.

MATERIALS AND METHODS:

Laboratory based experimental study was performed on isolated rabbit gut (ileum) preparation, conducted in the Experimental Laboratory, Department of Physiology, B.R.D. Medical College, Gorakhpur. Prior to the sacrifice, rabbits were fasted overnight, kept in comfortable surrounding by maintaining temperature, humidity and light. The animal experiments were performed after obtaining animal ethical clearance from the Institutional Animal Ethics Committee (IAEC), as per the guidelines of "CPCSEA" Government of India.

The Chemicals/drugs Used In The Study:

1. Acetylcholine Chloride, Sertraline, Citalopram

Statistical Analysis:

For statistical analysis a SPSS v20 (IBM©, Chicago, IL, USA) software was used. Quantitative results have been provided as a mean and standard deviation (SD) and have been measured, if appropriate, by the ANOVA (F) method. Different demographic and test parameters were calculated and tabulated in the master chart and analysed. The data normality were also checked and nullified as per principle. The qualitative results is provided as numbers and percentages and contrasted, if possible, with the Chi-square (X2) method. The value of P was considered statistically significant, when it stood to be <0.05.

RESULT:

TABLE-1: Effect on Basal Amplitude treating with Acetylcholine & Anti-Depressants (Sertraline and Citalopram).

Acetylcholine & Anti-depressants [sertraline, Citalopram]				
	Basal Amplitude (mm)	Acetylcholine	Sertraline	Citalopram
MEAN±SD	3.00±1.64	10.25±1.99	2.33±1.63	3.25±1.08
Minimum	1.000	7.500	1.000	2.000
Median	2.750	10.50	2.000	3.000
Maximum	6.000	12.00	5.000	5.000
P-Value	F=31.63 P <0.0001		P 0.8891	P 0.9931

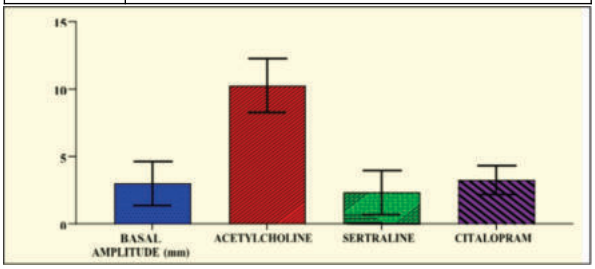

Figure 1: graphical representation of mean Basal Amplitude treating with Acetylcholine & Anti-Depressants (Sertraline and Citalopram).

TABLE- 2: Effect on Basal Frequency treating with Acetylcholine & Anti-Depressants (Sertraline and Citalopram)

Acetylcholine & Anti-depressants [sertraline, Citalopram]				
	Basal Frequency (/min)	Acetylcholine	Sertraline	Citalopram
MEAN±SD	9.33±1.21	11.33±0.82	10.67±0.52	10.67±0.82
Minimum	8.000	10.00	10.00	10.00
Median	9.500	11.50	11.00	10.50
Maximum	11.00	12.00	11.00	12.00
P-VALUE	F=5.496	P 0.0041	P 0.0681	P 0.0681

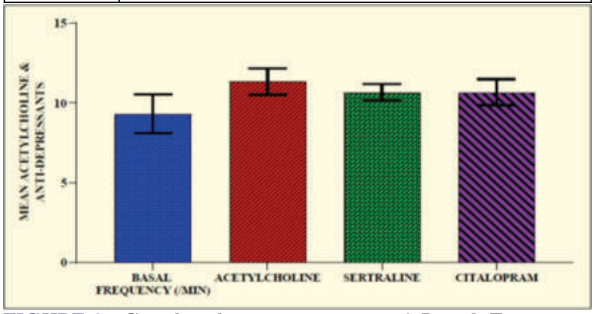

FIGURE-2: Graphical representation of Basal Frequency treating with Acetylcholine & Anti-Depressants (Sertraline and Citalopram).

DISCUSSION:

The main aim of this experiment was to explore the effect of the anti-depressants group of drugs on basal amplitude and basal frequency of the isolated rabbit gut contractions. The anti-depressants were subdivided into 2 subgroups namely Sertraline, Citalopram, respectively.

With this study it was found that instillation of Ach (10^{-6} M), the basal amplitude as well as the basal frequency of the isolated gut muscle contraction increased significantly thereby demonstrating its role in isolated gut muscle contraction , who observed in the study that an excitatory neurotransmitter is synthesized in cholinergic neurons [7] and these cholinergic neurotransmitter are principal excitatory neurotransmitter in the gastrointestinal tract responsible for elicitation of contractions [8]. The pathophysiology of many extra-intestinal stress-related illnesses, such as anxiety, depression, or chronic pain syndrome, as well as the modification of gut motility, visceral sensitivity, and intestinal secretion caused by stress, are well recognised to involve 5-HT [**9,10**]. Antidepressants have been used for quite some time as it believed to improve gastrointestinal function being the main focus restoration of normal GI motility. With Sertraline (10^{-6} M to 10^{-3} M) and Citalopram (10^{-6} M to 10^{-3} M), effect on the basal amplitude and basal frequency of the isolated rabbit gut muscle contractions was recorded. Our observation found significant decrease of the basal amplitude but they did not alter the basal frequency of isolated rabbit gut contractions significantly. The possible reason for significant decrease of basal amplitude might be, selective serotonin reuptake inhibitor antidepressants (SSRIs) have been demonstrated to have depressive effects on cardiac myocytes and vascular smooth muscle cells by blocking Ca^{2+} channels [11] similar types of study observed by the by Pacher P et al [12] this study observed that fluoxetine and citalopram likely relax intestinal smooth muscle by blocking Ca2+ channels, and hence this might be the reason for the significant decrease of basal amplitude after instillation of anti-depressants on isolated rabbit gut muscle preparation [13].

CONCLUSION:

Anti-depressants exhibit anti-muscarinic properties as both have significant effects on the muscarinic receptor. Anti-depressant drugs showed substantial decrease in gut motility by affecting the amplitude and the frequency.

- The effect of Anti-depressant drugs (Sertraline and Citalopram) was
- observed on amplitude and it was found that the amplitude decreased with
- both the Anti-depressant group of drugs i.e. Sertraline and Citalopram but
- the decrease in amplitude was seen more with Sertraline than Citalopram.
- Statistically, a significant difference was observed in basal amplitude.

In case of frequency both the drugs didn't showed much significant effect. However, on comparison of both the drugs with one another, Sertraline showed reduction in frequency more than Citalopram. Statistically, a non-significant difference was observed in basal frequency.

Competing Interests: Authors have declared that no competing interests exist.

Ethical Approval: Institutional Animal Ethics Committee

REFERENCES:

1. Yuan Xie, Fangdi Hu, Dawei Xiang, Hui Lu, Wenbin Li, Anpeng Zhao, Longji Huang & Rong Wang (2020): The metabolic effect of gut microbiota on drugs, Drug Metabolism Reviews, DOI: 10.1080/03602532.2020.1718691.
2. Otterson MF, Sarr MG. Normal Physiology of small intestinal motility. Surg Clin North Am.1993;73(6):1173-92
3. Ciccia F, et al. Over-expression of paneth cell-derived anti-microbial peptides in the gut of patients with ankylosing spondylitis and subclinical intestinal inflammation. Rheumatology (Oxford). 2010;49:2076–2083.
4. Szurszewski, JH. Physiology of the Gastrointestinal Tract. Johnson, LR., editor. New York: Raven Press; 1987. p. 393-422.
5. Brown JC, Mutt V, Dryburgh JR. The further purification of motilin, a gastric

motor activity stimulating polypeptide from the mucosa of the small intestine of hogs. Can J Physiol Pharmacol. (1971) 49:399–405. 10.1139/y71-047
6. Sacre S, et al. Fluoxetine and citalopram exhibit potent antiinflammatory activity in human and murine models of rheumatoid arthritis and inhibit toll-like receptors. Arthritis Rheum. 2010;62:683–693
7. Dr. Linda J. Dobberstein, DC, Board Certified in Clinical Nutrition July 13, 2018; Memory Neurotransmitter & Gut Health Linked
8. Montgomery LE, Tansey EA, Johnson CD, Roe SM, Quinn JG. Autonomic modification of intestinal smooth muscle contractility. Adv Physiol Educ. 2016 Mar;40(1):104-9. doi: 10.1152/advan.00038.2015. PMID: 26873897.
9. Gross ER, Gershon MD, Margolis KG, et al. Neuronal serotonin regulates growth of the intestinal mucosa in mice. Gastroenterology 2012;143:408–17 e2. [PubMed: 22609381]
10. Larauche M, Mulak A, Tache Y. Stress and visceral pain: from animal models to clinical therapies. Exp Neurol 2012; 233:49-67 [PMID: 21575632 DOI: 10.1016/j.expneurol.2011.04.020]
11. Kitazawa T, Ichikawa S, Yokoyama T, Ishii A, Shuto K. Stimulating action of KW-5139 (Leu13-motilin) on gastrointestinal motility in the rabbit. Br J Pharmacol. (1994) 111:288–94. 10.1111/j.1476- 5381.1994.tb14058.x
12. Pacher P, Ungvari Z, Kecskeméti V, Friedmann T, Furst S. Serotonin reuptake inhibitors fluoxetine and citalopram relax intestinal smooth muscle. Can J Physiol Pharmacol. 2001 Jul;79(7):580-4. PMID: 11478591.
13. Li Z, Chalazonitis A, Huang YY, et al. Essential roles of enteric neuronal serotonin in gastrointestinal motility and the development/survival of enteric dopaminergic neurons. J Neurosci 2011;31:8998–9009. [PubMed: 21677183]