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RESEARCH ARTICLE

CITALOPRAM: A NOVAL ANTIDEPRESSANT

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Abberevations:

ACh Acetylcholine,
5-HT Serotonin, 5-HT4-receptors.

ABSTRACT

Background and Objectives: There are several life threatening deadly diseases in our world but 'Depression' out power them all in recent years. It is a nightmare now a days that could destroy a whereby strong and healthy person emotionally, mentally and physically in days to month's time. The discovery of selective serotonin receptor antagonist act as a miracle in the treating depression as it greatly reduces the time for therapeutic outcome but also improve the efficacy. The present study was designed to observe the effects of citalopram on gastrointestinal smooth muscles in vitro.
Method: Contractile response of acetylcholine, serotonin & citalopram on isolated rabbits ileum was recorded on power lab USA.
Results: The percent responses with acetylcholine, serotonin and citalopram were 100, 140 and 5.45 percent respectively indicating that citalopram has a depressant effect on motility.
Conclusion: Inability of paroxetine to enhance the serotonergic transmission in vitro causes a decrease in its qualitative response.

INTRODUCTION

Studies have shown that depression occur because of change in the levels of biogenic amines (serotonin, nor-epinephrine and dopamine). Several preclinical studies carried out in the past suggested, that selective serotonin antagonist has a great role in treatment of depression; they also decreases the decreases the time for therapeutic effects to appear as compared to traditional or older antidepressants (Ferres *et al*., 2013). Selective serotonin reuptake inhibitor are free of untoward effect as compared to traditional antidepressant; but, nausea & vomiting occurs as its main adverse effects which was severe in the start of therapy but gradually it settle down. To explore the underlying basis of this adverse effect, we observed the effects of citalopram; on ileal smooth muscles of rabbits in vitro. (Afzal *et al*., 2015; Coates *et al*., 2006) As serotonin is the major neurotransmitter in the gastrointestinal tract, which inturn causes release of acetylcholine. So acetylcholine & serotonin-mediated intestinal activity was taken as control in our research study (Jabeen *et al*., 2007).

METHODS

This experimental study was carried out in Multidisciplinary Lab Army Medical College Rawalpindi, from May 2013 to August 2013.

Chemicals : Acetylcholine Chloride, Serotonin Carnitine Sulfate and Citalopram Hydrochloride were purchased from local market.

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All the solutions and dilutions (10^{-} to 10^{-} M) were prepared fresh at the time of experiments (Noor *et al*., 2011).

Preparation of tissue

Eighteen healthy rabbits weighing from 2.0-3.0 Kg were randomly divided into three groups (n=6). Overnight fasting rabbit was sacrificed, ileum was taken out and cut into 2 inches pieces[7]. The isolated tissue was transferred to organ bath containing tyrode's solution of 50ml capacity (in mM: NaCl, 136.8mM; KCl, 2.7mM; $MgCl_2$, 0.5mM; $CaCl_2$, 1.3mM; NaH_2PO_4, 0.14mM; $NaHCO_3$, 12.0mM, Dextrose, 5.5mM) and aerated with 95% oxygen and 5% carbondioxide[11]. One end of the ileal strip was attached to the bottom of oxygen tube in tissue bath and the other end was connected to a research grade force Displacement transducer (Afzal *et al*., 2015). After equilibration the isotonic ileal smooth muscle activity was recorded through the Displacement Transducer on Power lab (Tanko *et al*., 2012).

Group 1 Cumulative concentration response curve of acetylcholine (n=6)

Using varying concentrations (10 9-10 6M) we construct the cumulative dose-response curves of acetylcholine. Tissue sensitization was prevented by using new tissue each time (n=6). As this was our control group; so, serotonin and citalopram induced contractions are compared with acetylcholine induced contractions (Afzal *et al*., 2015).

Group 2 Cumulative concentration-response curve of serotonin (n=6)

Serotonin mediated isotonic contractions were recorded using concentrations 10 9 to 10 6 M in the same manner as that of acetylcholine (Afzal *et al*., 2015).

Group 3 Cumulative concentration-response curve of citalopram (n=6)

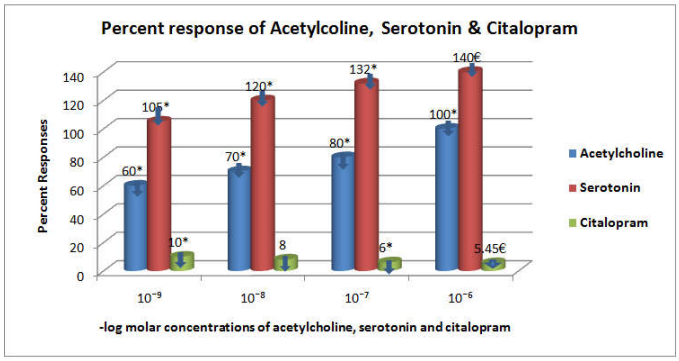
In similar manner as for group 1 and 2we record the contractile response of citalopram.

Statistical analysis

The results have been expressed as means±standard deviation . The arithmetic means of amplitudes of contractions and SDs were calculated using Post hoc tuky test SPSS version 20.

RESULTS

Citalopram exert a very depressive response on ileal smooth muscle activity right from the beginning (10^9M) and even straight line is observed at many occasion. To evaluate this decrease in citalopram-induced ileal contractility we compare its response with acetylcholine and serotonin mediated response. Maximum constrictor response of serotonin was 40% more than maximal acetylcholine response. Citalopram causes a significant decrease in ileal smooth muscle contractions from 100 % (control group) to 5.45 % but their means of amplitude of contractions was found statistically significant.



*P- value significant (< 0.001)
P- value non-significant (0.001)

Figure 1. Cumulative dose response curve of Acetylcholine, Serotonin & Citalopram

DISCUSSION

The present study was carried out to to find out the possible reason that may underlies in causing severe nausea & vomiting at the start of therapy with citalopram. Acetylcholine and serotonin gradually increases the ileal smooth muscle contractility, whereas citalopram in contrast to acetylcholine & serotonin decreases the smooth muscle contractility. Acetylcholine mediated ileal contractions is taken as a standard for comparison in our experimental study (Chetty *et al*., 2006). Acetylcholine increases the motility throughout the gut due to smooth muscle contraction which involves depolarization of smooth muscle cells & calcium influx via M_3 receptors[9]. Stimulation of smooth muscles of the gut increases tone & motility, may cause colicky pain (Tuladhar *et al*., 2002). Serotonin produced 140 percent of acetylcholine mediated response on ileal smooth muscles of rabbit (Camelleri, 2002). Serotonin act through 5-HT_4 (G- protein coupled receptors) of usual 7-transmembrane serpentine type located on both cholinergic interneurons and motor neurons[1] on enterocytes and indirectly via 5-HT_3 receptors (a member of nicotinic family of Na+/K+ channel protein) on mucosal nerves and vagal afferents effects the intestinal motility (Mujezinovic *et al*., 2011). Serotonin mediated stimulation of 5-HT_4 receptors leads to an increase in the acetylcholine release; thus increasing the intestinal activity (Pithadia and Jain, 2009). Our results that citalopram causes a remarkable decrease in intestinal motility in vitro was also confirmed by the study of Milne RJ and Ownen MJ along with their co workers in the past. The decrease in amplitude of contractions of ileal smooth muscles by citalopram is because of the fact that citalopram also does not have the weak inhibitory effect on nor- epinephrine reuptake has some affinity for α_1 receptors and also has some antihistaminic activity (Milne and Goa, 1991; Owens *et al*., 1997). These findings was also confirmed by the study of Janssen and his colleagues (Janssen *et al*., 2010)

Conclusion

Citalopram decreases the intestinal motility due to its weak inhibitory effects on nor-epinephrine reuptake and antihistaminic activity.

Conflict of interest

Author show no conflict of interest

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