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Study of Antinociceptive Effect of Paroxetine and Elucidation of Its Mechanism of Action in Acute Pain in Albino Rats

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Pain is the most common reason patients seek medical care. Increased level of monoamines (serotonin and norepinephrine) in synaptic clefts lead to changes in pain threshold and induce antinociception. The study was carried out to evaluate antinociceptive effect of paroxetine in albino rats and to probe into its possible mechanism of action. Albino rats of either sex of average weight 100-200gms were used. The drugs used were paroxetine 5mg/Kg, pethidine 5mg/Kg(active control), naloxone 5mg/Kg, ondansetron 0.1mg/Kg and normal saline 1ml/Kg. Antinociceptive effect tested by using thermal method i.e. tail flick response. Statistical analyses indicate significant difference between value of control when compared with paroxetine i.e., paroxetine shows antinociceptive effect. The effects of paroxetine were comparable to that of pethidine. Naloxone, an opioid receptor antagonist and Ondansetron, a 5HT-3 receptor antagonist when combined with paroxetine blocked its antinociceptive action. This finding suggests and involvement of serotonergic mechanisms (5-HT3 subtype), and the opioidergic system.

Key words: Antinociception, Paroxetine, SSRI

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test drug, paroxetine has antinociceptive effect comparable to that of standard, pethidine. When naloxone and ondansetron were administered along with paroxetine, the antinociceptive effect was comparable to that of the control group indicating that the antinociceptive effect of paroxetine was blocked by naloxone and ondansetron. This suggests the contribution of opiodergic and serotonergic mechanisms in the antinociceptive action of paroxetine. The antinociceptive effect of paroxetine+naloxone and paroxetine+ondansetron was comparable to that of paroxetine indicating that the antinociceptive effect of paroxetine was not blocked completely by either naloxone or ondansetron.

Table 2: Reaction time (sec) before and after drug administration

Groups	Reaction time before drug administration (Sec)	Reaction time 60min after drug administration (Sec)	Mean difference	Signi-ficance t	P value
Group I	6.8±1.0	0.3±0.3	7.1±1.0	2.33	0.07
Group II	6.9±0.6	9.0±1.0	2.1±1.3	4.04	0.01*
Group III	7.6±1.4	9.1±1.4	1.5±0.7	5.15	0.004**
Group IV	6.81±.7	7.5±1.6	0.7±0.4	4.45	0.007*
Group V	7.0±1.6	8.0±1.5	1.0±0.3	9.68	0.001**

P-Value <0.05 *Significant P-Value <0.005** Highly Significant

Table 3: Comparison between groups

Groups Compared	Mean Difference	P-Value
I-II	1.8	0.001*
I-III	1.2	0.041*
I – IV	0.4	0.85
I – V	0.7	0.37
II-III	0.6	0.54
III – IV	0.8	O.29
III – V	0.5	0.77

P-Value <0.05 *Significant

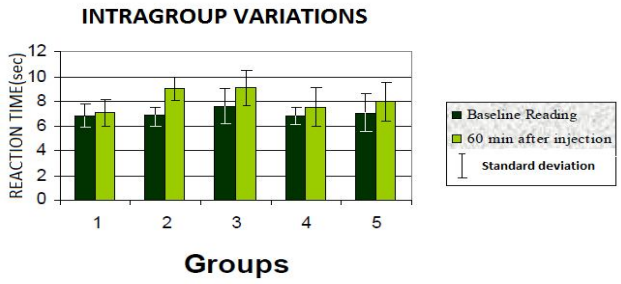

Fig 1: Reaction time (sec) before and after drug administration

DISCUSSION

In the present study analgesic effect of a potent SSRI, paroxetine was evaluated using tail-flick method in albino rats and we tried to explore the mechanism of its action using opioid and serotonin receptor blockers. The results indicate that the paroxetine has analgesic action and it is comparable to that of pethidine. The results of this study are consistent with that of studies done by Erdem et al. [7], Masand et al.[8] and Gray et al.[9]

This antinociceptive action of paroxetine was significantly inhibited by naloxone, suggesting the involvement of opioidergic mechanisms. [10] Similarly ondansatron, a 5-HT3-receptor antagonist, inhibited the analgesic effect of paroxetine suggesting the involvement of serotonergic mechanisms also. The antinociceptive effect of paroxetine+naloxone and paroxetine+ondansetron was comparable to that of paroxetine indicating that the antinociceptive effect of paroxetine was not blocked completely by either naloxone or ondansetron. Also when naloxone and ondansetron were administered along with paroxetine, it showed some amount of antinociceptive effect. As both naloxone and ondansetron could not block the analgesic effect of paroxetine completely, it can be assumed that the analgesic action of paroxetine could be due to multiple mechanisms.

However our study is very primitive in the method and parameters used to evaluate analgesia. Further studies need to be done in various other acute and chronic models using different species to establish efficacy of paroxetine as an analgesic.

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