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A CONTROLLED DOUBLE BLIND CLINICAL TRIAL OF BUSPIRONE AND DIAZEPAM IN GENERALISED ANXIETY DISORDER

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Buspirone hydrochloride is a now non-benzodiazepine, non-barbiturate, non-narcotic tranqualizer. It is an 'agaspirodecanedione', lipophilic and a heterocyclic compound.

Absorption of buspirone from gastrointestinal tract is virtually complete. Peak plasma level is achieved in less, than one hour after a single dose. The elimination half life of the drug ranges from 2 to 8 hours in healthy subjects and is significantly lengthened in renal and hepatic disease. Although mechanism of the anxiolytic effect of buspirone is undetermined, complex interactions with several central nervous system neurotransmitters, especially serotonin are thought to be contributory. Unlike benzodiazepine buspirone lacks hypnotic, anticonvulsant and muscle relaxant properties and has been termed anxio-selective (Eison and Temple, 1986; Skolnick et al., 1985).

In a few double blind clinical trials, buspirone in 15-30 mg/day doses, improved symptoms of anxiety, assessed by standard rating scales, similar to diazepam and clorazepate (Cohn et al., 1986; Feighner et al., 1982; Goldberg and Finnerty, 1979, 1982). Like diazepam, buspirone is effective in patients with mixed anxiety-depression (Feighner et al., 1982; Cohn et al., 1986).

In healthy volunteers buspirone does not impair psychomotor or cognitive function (Smiley and Moskowitz, 1986). Because of its lack of euphoric effect, buspirone appears unlikely to become a drug of abuse (Cole et al., 1982, Griffith et al., 1986).

AIMS OF THE STUDY

1. To compare the anxiolytic efficacy of buspirone and diazepam in treatment of patients suffering from generalized anxiety disorder.
2. To evaluate safety and tolerability of buspirone in such patients.

MATERIAL AND METHODOLOGY

Patients suffering from generalised anxiety disorder according to DSM-III (APA, 1980) criteria were screened from the out-patient department. Specific inclusion and exclusion criteria were used.

On inclusion of patient in study, patients history, physical examination and rating on Hamilton Anxiety Rating Scale (HARS) were done. Basal lab investigations were also carried out.

Patients were randomly distributed to two groups, Group A (Buspirone) and Group C (Diazepam).

Both drugs were administered orally in the form of tablets, each tablet containing 5 mg of the drug. The dosages used were 15-45 mg/day, given in three divided dosage.

The drugs were administered for a period of 4 weeks. Weekly assessment was done using:—

(a) Patients and Physician's Global Impressions.
(b) Physical examination and

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(c) Hamilton Anxiety Rating Scale.

At the end of 4 weeks basal lab investigations were repeated.

A total of 60 patients were included in the study with 30 patients in each group.

The X^2 test and 't' test were employed for data analysis wherever applicable.

Patients in both group were comparable in age sex and duration of illness.

RESULTS AND DISCUSSION

Table I shows the clinical improvement. In group A (buspirone) 16 completed the 4 week study of whom 12 showed significant improvement. In drug group C (diazepam) 21 completed the study of whom 16 showed significant improvement.

Table II depicts the improvement in mean HARS scores reduction. There was 64.24%, reduction in group A (buspirone) and 66.52% was in group C (diazepam). There was no significant difference in the two groups. In the buspirone group, the improvement according to the HARS symptom profile was in the cardio-vascular, symptoms, tension somatic (sensory) autonomic symptoms, anxious mood and insomnia while in the diazepam group, the improvement according to the HARS symptom-profile was in the anxious mood, tension, insomnia, cognitive symptoms, somatic (sensory), cardiovascular-symptoms and autonomic symptoms. However the mean total daily dosage required by the patients in the buspirone group was 36.56 mg/day which is more than what has been reported (Goldberg and Finnerty, 1982; Pecknold et al., 1985; Rickels et al., 1982). However, Fontain et al. (1987) reported diazepam to be significantly better than buspirone in reduction of anxiety.

Table III shows the most common side effects observed in patients of both drug groups. Drowsiness and sedation were predominant in the diazepam group while buspirone group reported insomnia headache and G. I. disturbances., which are similar to the reports of Rickels et al. (1982), Nurton et al. (1982) and Colin and Wilcox (1982). Side effects observed in the patients who completed the study were however, of mild to moderate

TABLE I. *Clinical improvement*

	Completed	Less than 50% reduction in HARS scores	50-74% reduction in HARS scores	75% & more reduction in HARS scores
Buspirone (n=30)	16	4	7	5
Diazepam (n=30)	21	5	5	11

TABLE II. *Improvement : HARS scores.*

	Mean pre-treatment HARS score	Mean post-treatment HARS score	% reduction	Mean total daily dosage at end of 4 weeks
Buspirone (n=16)	25	8.94	64.24	36.56 mg/day
Diazepam (n=21)	24.76	8.29	66.52	25.71 mg/day

TABLE III. *Side effects*

Buspirone	*Diazepam*
1. Insomnia	1. Drowsiness
2. Headache	2. Sedation
3. G. I. disturbances	3. Dryness of mouth
4. Urticaria	4. Euphoria
5. Giddiness	5. Giddiness
6. Dryness of mouth	6. Nausea/Vomitting
7. Visual disturbances	7. Restlessness

TABLE IV. *Dropouts*

	1st week	2nd week	3rd week	4th week
Buspirone (n=14)	7	6	1	—
Diazepam (n=9)	6	3	—	—

intensity in both the groups. Laboratory investigations showed no abnormalities in both the groups.

Table IV shows the patients who dropped out of the study. The dropout in the 1st week was similar in both the groups with one patient of the diazepam group being withdrawn due to pregnancy.

However, more patients in the buspirone group (7) dropped out midway in the trial as compared to 3 in the diazepam group of whom 2 opting out due to drowsiness. No information is available about any of the drop-outs in the buspirone group. However, there was no difference in the mean pretreatment HARS scores of the patients who completed the study and those who dropped out, in either of the two groups. In this context, Pecknold et al. (1985) and Feighner et al. (1982) noted a lag time of 1 to 2 weeks in the onset of anxiolytic effect of buspirone and hence motivation of the patient for better compliance may be necessary. In this study of the 16 patients on the drug diazepam who showed significant improvement, at least 50% reduction in HARS scores, 8 improved within 2 weeks, and 8 after 2 weeks; while of the 12 on the drug buspirone, who had significant improvement 2 improved within the 2nd week while as many as 10 did so after 2 weeks.

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