A Comparative Study of Geriforte in Anxiety Neurosis and Mixed Anxiety-Depressive Disorders

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ABSTRACT
This was a double-blind, placebo-controlled study with 20 patients in each group. They were suffering from mixed anxiety-depressive disorders, and were aged between 18-50 years.

Ratings were done by employing the Hamilton Anxiety Rating Score and Hamilton Psychiatric Rating Scale for Depression. The results showed that Geriforte had a definite anxiolytic but not antidepressant effect.

INTRODUCTION
In the last two decades pharmacotherapy is increasingly being recognised as one of the most effective methods in the management of anxiety disorders (Rickels, K., 1978). Clinical use of benzodiazepines has gained significant attention in the management of anxiety (Hollister, L.E., 1972b). However, dependence potential and side effects of the benzodiazepines have resulted in more emphasis being placed on the search for non-benzodiazepine and herbal preparations in the management of anxiety and psychosomatic disorders. Several experimental and clinical studies have evaluated the therapeutic properties of indigenous drugs advocated in ancient Indian medical literature for the management of mental disorders. The antistress property of Geriforte [D'Sousa, Alan (1989), Ghosh, S. (1985), and Bopardikar, S.M. (1988)], an indigenous Ayurvedic remedy comprising about 60 herbs (prominent ones being Chyavanprash concentrate, Shilajeet, Capparis spinosa, Cichorium intybus, Terminalia arjuna, Vitis vinifera) has already been reported by Dubey, G.P. et al (1988) and Singh, N. et al (1978).

In our earlier open study [Shah, L.P. et al (1990)], we have observed the beneficial effects of Geriforte in patients suffering from anxiety neurosis as per DSM-III R criteria. There was significant reduction in the total Hamilton Anxiety Rating Scale (HARS) score at the end of 4 weeks. On analysis of the individual parameters on this scale, it was observed that Geriforte significantly helped to relieve depressive mood; hence we decided to evaluate the efficacy and safety of Geriforte in mixed anxiety-depressive disorders.

MATERIAL AND METHODS
In a double-blind placebo-controlled study, 40 patients fulfilling I.C.D. 10 criteria for mixed anxiety-depressive disorder were enrolled in the study after getting their informed written consent. Twenty patients received Geriforte (Group 1), while the other 20 (Group 2) received identical looking placebo tablets, both in the dose of 2 tabs t.i.d. for a period of 4 weeks. No concomitant medications were given. Weekly assessments were done on:-

1. Hamilton Psychiatric Rating Scale for Depression (HPRSD), (Appendix 'A').
2. Hamilton Anxiety Rating Scale (HARS), Appendix 'B'.
3. Clinical monitoring of vital parameters.
4. Clinical global evaluation for side effects.
In Group 1 (Geriforte), there were 12 patients in the age range of 18-30 years, 5 in the 31-40 year and 3 in the 41-50 year ranges. The corresponding figures in Group 2 (placebo) were 8,9 and 3 respectively.

While there were 14 males and 6 females in group 1 (Geriforte), the placebo group had 10 of each sex. All the patients belonged to the low socio-economic category.

The distribution of patients according to the duration of illness is shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Duration of illness</th>
<th>No. of patients on</th>
<th>Geriforte</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 6 months</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6 months - 1 year</td>
<td>8</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>1 year - 2 years</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>More than 2 years</td>
<td>–</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

RESULTS
Out of 20 patients receiving Geriforte, 15 (75%) completed the study period of 4 weeks, whereas 11 patients (55%) out of 20 on placebo did likewise. Table No.2 gives more details.

<table>
<thead>
<tr>
<th>Table 2: Distribution of patients according to number of weeks completed in the study period (n=40)</th>
<th>No. of patients on</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Geriforte</td>
</tr>
<tr>
<td>4 weeks</td>
<td>15</td>
</tr>
<tr>
<td>3 weeks</td>
<td>2</td>
</tr>
<tr>
<td>2 weeks</td>
<td>3</td>
</tr>
<tr>
<td>1 week</td>
<td>–</td>
</tr>
</tbody>
</table>

Efficacy:
Reduction in anxiety score on HARS: Table 3 gives the mean total score on HARS in patients in both groups.

<table>
<thead>
<tr>
<th>Table 3: Mean total score on HARS following Geriforte and placebo administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>Geriforte</td>
</tr>
</tbody>
</table>

In patients receiving Geriforte, there was a 48.9% fall in mean HARS scores at the end of 4 weeks, whereas in patients on placebo, the score decreased by only 30.6% at the end of 4 weeks.

Reduction in the score on HPRSD: Table 4 gives the mean total score on the HPRSD.

<table>
<thead>
<tr>
<th>Table 4: Mean total score on HPRSD following Geriforte and placebo administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>Geriforte</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
</tbody>
</table>

There was not much difference in the 2 groups in HPRSD scores at the end of 4 weeks. In patients on Geriforte, HPRSD scores dropped by 35.98%, whereas in the placebo group, they dropped by 29.19%.

Clinical global evaluation: The impressions of the clinicians are shown in Table 5.
Table 5: Clinical global evaluation

<table>
<thead>
<tr>
<th>Degree of improvement</th>
<th>Geriforte</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marked</td>
<td>15%</td>
<td>5%</td>
</tr>
<tr>
<td>Mild to moderate</td>
<td>35%</td>
<td>25%</td>
</tr>
<tr>
<td>No change</td>
<td>45%</td>
<td>60%</td>
</tr>
<tr>
<td>Worse</td>
<td>5%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Thus 50% of patients of mixed anxiety-depression who received Geriforte, showed satisfactory improvement in their clinical status at the end of 4 weeks, whereas only 30% of the patients on placebo showed some clinical improvement.

Tolerability and Safety: No side effects were reported or observed in either group.

Reduction or discontinuation of drugs was not required in either group.

Vital parameters (pulse and BP) were within normal range throughout the study period.

DISCUSSION

In our earlier open study (1990), we had observed significant improvement in patients of anxiety neurosis following 4 weeks of Geriforte treatment.

In this double-blind, placebo-controlled study we have observed improvement in HARS scores in patients of mixed anxiety-depression following 4 weeks of Geriforte treatment in comparison with placebo (Table 6), but no significant difference in HDRS score between the two groups of patients was noted.

Table 6: Mean total score on HARS before and after Geriforte therapy in patients of anxiety neurosis

<table>
<thead>
<tr>
<th>Week 0</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.72</td>
<td>17.24</td>
<td>13.94</td>
<td>12.89</td>
<td>10.94</td>
</tr>
</tbody>
</table>

These findings are in agreement with those reported by Boral, G.C. et al (1989).

Dubey, G.P. et al (1988) have reported decreased levels of catecholamines following Geriforte treatment in anxiety neurosis. Geriforte probably reduces increased turnover of catecholamines by reducing sympathetic outflow in anxiety associated with stress and hence helps in alleviating the symptoms of anxiety.

The fact that Geriforte had a definite effect in anxiety but no effect on depressive symptoms in patients with mixed anxiety-depressive disorder probably indicates that the effect of Geriforte is pharmacological and based on decreased symptomatic outflow; since catecholamines are reduced in depression, it is to be expected that Geriforte will have minimal effect on such symptoms.

CONCLUSION

In view of the above findings, Geriforte can be considered to have anxiolytic but no antidepressant properties (Boral, G.C. et al, 1989).

ACKNOWLEDGEMENT

We thank the Dean, Seth G.S. Medical College and K.E.M. Hospital for permission to carry out the study, the Research society of our institution for their help in conducting the clinical trial and The Himalaya Drug Co., Bombay for supply of drugs and financial assistance.
The Hamilton Psychiatric Rating Scale for Depression (HPRSD)

It is the most widely used depression rating scale. It is a one-page, 21-item scale, rated in three or five rating scales. Rating is based on a clinical interview and on observations of behaviour made by an experienced psychiatrist. Male and female subjects are rated slightly different.

The scale can neither be used for diagnostic purposes nor to differentiate types of depression. The rater has to judge for himself how to balance frequency and severity. Moreover, some symptoms have less weight than others.

When HPRSD is used in drug evaluation trials, outpatients are usually selected on the basis of having a minimum of 14 score points on the first 17 items of the scale. For inpatients, a minimum score of 20 points is usually selected.

The scale has the following 21 items:

- depressed mood
- anxiety, somatic
- guilt
- gastrointestinal symptoms
- suicide
- somatic symptoms, general
- insomnia, initial
- loss of libido
- insomnia, middle
- hypochondriasis
- insomnia, late
- loss of weight
- work and interests
- diurnal variation
- agitation
- depersonalization
- anxiety
- paranoia
- obsessions or compulsions

The Hamilton Anxiety Rating Scale (HARS)

This is the oldest and probably most frequently used anxiety scale. It is a simple one-page, 14-item, five-step rating scale. Each item represents a set of symptoms grouped together according to their nature (for instance anxious mood is the combination of worries, anticipation of the worst, apprehension and irritability).

The rating steps are defined as: not present, mild, moderate, severe, very severe and disabling. Two sub-scores are calculated from the complete scale: somatic anxiety and psychic anxiety both being derived from seven-item scores.

The HARS has only been validated for neurotic anxiety states. Usually a minimum score of 20, including a score of at least 2 for 'anxious mood' and tension, is the criterion for inclusion of
patients in drug studies. The scale almost exclusively rates subjective experience, not objectively observed behaviour or observed signs.

The items are:

- psychic anxiety
- somatic anxiety
- anxious mood
- muscular symptoms
- tension
- sensory symptoms
- fear
- cardiovascular symptoms
- insomnia
- respiratory symptoms
- intellectual problems
- gastrointestinal symptoms
- depressed mood
- genitourinary symptoms
- nervous behaviour
- autonomic symptoms

REFERENCES


