ANXIOLYTIC NEEDED FOR ELECTIVE PRE-OPERATIVE
PATIENTS IN CONTROL OF ANXIETY AND DEPRESSION.

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ABSTRACT

Introduction and objectives: High levels of preoperative anxiety and depression have unfavourable effects on induction, maintenance and recovery from anaesthesia. There is a need to assess the anxiety and depression to understand the experience of sufferings in the hospital setting. So, a study was planned to determine the effect of anxiolytics used preoperatively in patients admitted for planned surgical procedures. Methodology: In this prospective observational study adult patients of either sex scheduled to undergo planned surgery were selected randomly for a period of three months in two groups: Group A (control) patients did not receive any anxiolytic and group B (case) patients received anxiolytics preoperatively at night before the day of surgery. All eligible patients completed a questionnaire (Hospital Anxiety and Depression score) in the morning of their surgical operations. The questionnaire, having both anxiety and depression domains contains a list of questions which were asked to the patients and scorings was done accordingly. HADS score of two groups were compared using independent t-test. All statistical analyses were carried out using the IBM-SPSS ver.20 data processing software. Result: Total 613 patients are obtained. Among them 203 (33%) were in group A (received no anxiolytic) and 410 (67%) in group B (received anxiolytic). There was statistically significant difference in mean score between case and control groups. Conclusion: Preoperative anxiety and depression were common which were ameliorated by anxiolytics. So surgeons and anaesthetics should be aware of personal anxiety of patients.

KEY WORDS: Anxiety, depression, HADS.
INTRODUCTION
Anxiety is actually an adaptive response which prepares a person to face the challenges of life.\textsuperscript{[1]} The terms anxiety and fear although related, are distinct from each other. The fear experienced by a patient is a subjective phenomenon that varies from patient to patient.\textsuperscript{[2]} Depression is a disorder of mood (not of thought process as in schizophrenia) and hence classified as affective disorder.\textsuperscript{[3]} Anxiety and depression both may occur due to variety of reasons and common in pre-operative surgical patients. Preoperative anxiety is described as an unpleasant state of uneasiness or tension that is secondary to a patient being concerned about a disease, hospitalization, anaesthesia and surgery, or the unknown.\textsuperscript{[4]} High levels of preoperative anxiety and depression disrupt the homeostasis of the respiratory, circulatory, metabolic, or immune systems, causing numerous postoperative complications, lead to unfavorable physiological response such as tachycardia and hypertension, have unfavorable effects on induction, maintenance and also recovery from anaesthesia.\textsuperscript{[5]} It also causes a number of undesirable effects which may place the patient at greater perioperative risk. The incidence of preoperative anxiety has been estimated to vary from 11 to 80% in the adult.\textsuperscript{[6]} Often such patients are prescribed with some anxiolytics preoperatively. In clinical practice, patients presenting with symptoms of both anxiety and depression are a common experience and their labelling into one or other category is difficult and mostly arbitrary. There are lacunae in knowledge about this in our hospital setting, where maximum patients come from rural areas. There is a need to assess anxiety and depression, in order to understand the experience of suffering in our setting of medical practice. Prevention of preoperative anxiety and depression with anxiolytic premedication improves preoperative outcomes and decreases inpatient stay in surgical patients. So our objective of this study is to determine how night time anxiolytic therapy affects pre-operative anxiety & depression and what is the comparative efficacy of different anxiolytics when used for this purpose.

MATERIAL AND METHODS
This observational cross-sectional study was conducted in September -November 2014. Adult (>18 years of age) patients of either sex, who were admitted for elective surgical procedure in the Surgery, Otorhinolaryngology, Orthopaedics and Gynaecology and Obstetrics department of Burdwan Medical College and Hospital during this period were enrolled in this study. Subjects with gross central nervous system disorder, those who were unable to understand or communicate and patients with history of substance abuse were excluded from the study. Eligible patients were explained the study and enrolled.
All eligible patients were divided into Group A comprising patients received no anxiolytic, and group B comprising patients received anxiolytics used in our hospital preoperatively at night before the day of surgery. Group B was further divided to assess effectiveness of anxiolytics in reducing anxiety and depression into a) patients received alprazolam, b) patients received diazepam and c) patients received lorazepam.

**Hospital Anxiety and Depression Scale (HADS)**

The HADS is a questionnaire commonly used to assess levels of anxiety and depression. It is composed of 14 items presented as statements which the subject rates based on their experience of anxiety and depression and divided in two subscales: anxiety (HAD-A) and depression (HAD-D). Each subscale contains 7 questions and each question is rated on a four-point scale (0-3). Thus the sum of each graded item renders total HADS and subscale scores. The maximum score is therefore 21 for depression and 21 for anxiety. HADS is now divided into four ranges: non-case (0-7), borderline case (8-10) and case (11+).

All eligible patients were introduced a Hospital Anxiety and Depression Scale (HADS) questionnaire half an hour before the planned surgical procedure and asked to complete. The questionnaire has been annexed in annexure-I. After completion, questionnaires were collected and sum of each graded item was done. According to sum all patients were divided into three groups 1) non-case, 2) borderline case and 3) case.

**Statistical Analysis**

HAD-A and HAD-D score of two groups were compared using Mann-Whitney U test and effectiveness of different anxiolytics was determined by using Kruskal-Wallis H test. All statistical analyses were carried out using the IBM-SPSS ver.20 data processing software. $P$-value < 0.05 was considered significant.

**RESULT AND ANALYSIS**

Total numbers of patients who underwent planned surgery during the study period was 630 (Number of patients from surgery department: 459, otorhinolaryngology: 133, orthopaedics: 29 and gynaecology & obstetrics department: 9). Out of them 613 patients were enrolled in the study. Seventeen patients refused to give consent and hence excluded from the study. Among them 203 patients were in group A and 410 patients were in group B. Number of non-case, borderline case and case among Group A and Group B according to HAD-A score were shown in figure 1 & 2.
Figure 1: Number of non-case, borderline case and case among Group A according to HAD-A score.

Figure 2: Number of non-case, borderline case and case among Group B according to HAD-A score.

Number of non-case, borderline case and case among Group A and Group B according to HAD-D score were shown in figure 3 & 4.

Figure 3: Number of non-case, borderline case and case among Group A according to HAD-D score.
Comparison of HAD-A scores between group A & B (among male)
A Mann-Whitney U test was run to determine if there were differences in HAD-A scores between males of group A & B. Distributions of the HAD-A scores among male for group A and group B were not similar, as assessed by visual inspection. HAD-A scores for group A (mean rank = 255.85) were significantly higher than for group B (mean rank = 173.47), p = 0.00 (<0.05). Median HAD-A score was significantly higher in group A (median=2) than in group B (median=1).

Comparison of HAD-A scores between group A & B (among female)
Distributions of the HAD-A scores among female for group A and group B were not similar, as assessed by visual inspection. HAD-A scores for group A (mean rank = 136.51) were significantly higher than for group B (mean rank =92.24), p =0 .00 (<0.05). Median HAD-A score was statistically significantly higher in group A (median=2) than in group B (median=1).

Comparison of HAD-D scores between group A & B (among male)
Distributions of the HAD-D scores for group A and group B were not similar, as assessed by visual inspection. HAD-D scores for group A (mean rank = 233.33) and group B (mean rank = 186.39) were significantly different, p = 0.00 (<0.05). Median HAD-D score for group A (median=2) and group B (median=2) was same but statistically significant.
Comparison of HAD-D scores between group A & B (among female)

Distributions of the HAD-D scores among female for group A and group B were not similar, as assessed by visual inspection. HAD-D scores for group A (mean rank = 94.00) and group B (mean rank = 107.62) groups were not statistically significant, p =0 .09 (>0.05). Median HAD-D score was statistically not significant but equal in group A (median=1) than in group B (median=1). Comparison of effectiveness of different anxiolytics used (alprazolam, diazepam, and lorazepam) pre-operatively for HAD-A & HAD-D are given in table 1 & 2.

Table: 1 Comparison of effectiveness of different anxiolytics used pre-operatively for HAD-A

<table>
<thead>
<tr>
<th>HAD-A score</th>
<th>Alprazolam Number (%)</th>
<th>Diazepam Number (%)</th>
<th>Lorazepam Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=7 (non-case)</td>
<td>N=183 (44.63)</td>
<td>N=143 (34.88)</td>
<td>N=84 (20.49)</td>
</tr>
<tr>
<td>8-10 (borderline case)</td>
<td>n=151 (82.51)</td>
<td>n=104 (72.73)</td>
<td>n=67 (79.76)</td>
</tr>
<tr>
<td>&gt;11 (case)</td>
<td>n=2 (1.09)</td>
<td>n=21 (14.68)</td>
<td>n=5 (5.95)</td>
</tr>
</tbody>
</table>

Table: 2 Comparison of effectiveness of different anxiolytics used pre-operatively for HAD-D

<table>
<thead>
<tr>
<th>HAD-D score</th>
<th>Alprazolam Number (%)</th>
<th>Diazepam Number (%)</th>
<th>Lorazepam Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=7 (non-case)</td>
<td>N=183(44.63)</td>
<td>N=143(34.88)</td>
<td>N=84(20.49)</td>
</tr>
<tr>
<td>8-10 (borderline case)</td>
<td>32 (17.49)</td>
<td>13 (9.09)</td>
<td>31(36.90)</td>
</tr>
<tr>
<td>&gt;11 (case)</td>
<td>152(83.06)</td>
<td>68 (47.55)</td>
<td>52(61.90)</td>
</tr>
<tr>
<td>&gt;11 (case)</td>
<td>19(10.38)</td>
<td>62(43.35)</td>
<td>1(1.19)</td>
</tr>
</tbody>
</table>

A Kruskal-Wallis test was run to determine if there were differences in HAD-A score between individual anxiolytic groups (alprazolam, diazepam, lorazepam) and also noanxiolytic groups. Pair wise comparisons were performed using Dunn's procedure with a Bonferroni correction for multiple comparisons. HAD-A score was significantly different between the different levels of Anxiolytic activity (p =0 .00). Post-hoc analysis revealed statistically significant differences in HAD-A score between the alprazolam (median =1)-noanxiolytic group, diazepam (median = 1)-noanxiolytic group and lorazepam (median = 1)-noanxiolytic group (p =0 .00) but not between other groups. HAD-D score was statistically significantly different between the different levels of antidepressant activity (p =0 .00). Post-hoc analysis revealed statistically significant differences in HAD-D score between all groups except diazepam-noanxiolytic group.
DISCUSSION

Anxiolytics are effective in reducing anxiety and depression pre-operatively in planned surgical procedures. In our hospital settings, maximum numbers of patients come from rural areas and from low socio-economic status. We observe that the degree of their pre-operative anxiety and depression are usually higher than patients come from urban areas or high socio-economic status. There are lacunae in knowledge regarding effectiveness of anxiolytics and what should be the most effective anxiolytic on these types of pre-operative patients. Also this type of study had not performed in our tertiary care hospital, so we have conducted this study.

Result of our study suggests that the administration of diazepam/alprazolam/lorazepam reduces anxiety and depression in pre-operative patients. Use of any one of the above mentioned drugs is superior to use of no anxiolytic in efficacy parameter evaluated in our study (HAD scale). In a double blind study[8] with halazepam and diazepam 125 patients were treated for 4 weeks and at the end, diazepam was found slightly more efficacious in reducing anxiety neurosis. This is also supported by other studies.[9, 10, 11] Hackett et al[12] compared diazepam, venlafaxine SR and placebo in 540 patients with GAD and result showed no significant differences in response. Feltner et al. evaluated the efficacy of a 4-week treatment with lorazepam, paroxetine or placebo in 169 generalised anxiety disorder subjects. Imanishi et al.[13] showed no significant difference in depression (HADS) when aromatherapy massage given in patients of breast cancer. In our study we also find that, any one of the anxiolytics significantly reduces anxiety and depression both in males but in case of females, only anxiety is reduced, not depression.

When the effectiveness of different anxiolytics (alprazolam, diazepam and lorazepam) are compared with no-anxiolytic group in reducing anxiety, it is found that each anxiolytic effectively and significantly reduces anxiety but there is no statistically significant difference between alprazolam-diazepam, alprazolam-lorazepam and diazepam-lorazepam group. But when the same are compared in case of reducing depression, it is found that alprazolam and lorazepam are effective but not diazepam and there is also statistically significant difference between alprazolam-diazepam, alprazolam-lorazepam and diazepam-lorazepam group.

CONCLUSION

Patients received anxiolytic preoperatively reported effective relief of their anxiety and depression symptoms. This part is very much neglected in our hospital settings. So
Surgeons/anesthetics must acknowledge that there is a need to investigate their current practice and that they have a responsibility to address patient anxiety and depression effectively.

CONFLICT OF INTEREST

We do not have any conflict of interest.

ANNEXURE-I

Hospital Anxiety and Depression Scale Scoring Sheet.

<table>
<thead>
<tr>
<th>Anxiety Item</th>
<th>Yes definitely</th>
<th>Yes sometimes</th>
<th>No, not much</th>
<th>No, not at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I wake early and then sleep badly for the rest of the night.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2. I get very frightened or have panic feelings for apparently no reason at all.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3. I feel miserable and sad.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4. I feel anxious when I go out of the house on my own.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>5. I have lost interest in things.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>6. I get palpitations, or sensations of ‘butterflies’ in my stomach or chest.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>7. I have a good appetite.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. I feel scared or frightened.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>9. I feel life is not worth living.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>10. I still enjoy the things I used to.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>11. I am restless and can’t keep still.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>12. I am more irritable than usual.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>13. I feel as if I have slowed down.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>14. Worrying thoughts constantly go through my mind.</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Anxiety 2, 4, 6, 8, 11, 12, 14
Depression 1, 3, 5, 7, 9, 10, 13
Scoring 3, 2, 1, 0 (For items 7 & 10 the scoring is reversed)
GRADING: 0 - 7 = Non-case 8 – 10 = Borderline case 11+ = Case

REFERENCE


