Investigations Into The Anti-Anxiety, Anti-Depressant Claims Of A Herbal Preparation: A Clinical Trial

Dr. Dave Baldwin, M.D., Dr. Fredrick Nutt, Ph.D.

ABSTRACT

Depression is a condition quite notorious to treatment. The main therapeutic approach for depression-anxiety disorders is antidepressant therapy. However, meta-analytic observations have shown that antidepressants provide partial benefits and clinical improvement in such patients is insignificant. There is no denying that, at the present moment, effective therapeutic solutions to depressive conditions still remain elusive.

Thus, although decades of research has been directed to design definitive therapeutic solutions to depressive illnesses in human beings, the results have been disappointing. This scenario begs for the question to be asked if there is any effective treatment for these debilitating diseases at all.

With such a backdrop, we decided to conduct a clinical trial of a commercially available therapeutic preparation that claims to both treat and prevent depression and anxiety. This was a double-blind placebo-controlled study to investigate the claims of a proprietary herbal preparation, ProVanax™ to treat symptoms associated with depression.

120 participants were shortlisted depending on ‘self-reported’ claims of depression. Of these, 80 were genuinely found to be suffering from depression and associated symptoms; these were divided into 2 groups of 40 each and assigned to either the test group (T group) or control group (C group).

Those assigned to the T group were supplemented with ProVanax™ in dosages recommended by the manufacturers – 2 capsules (t.i.d.), three times daily. Those in the C group took a similar dose of a placebo drug. The doses were repeated every day for a total of 3 weeks. At the end of 3 weeks, a layoff of week was planning and the dosage regimen was reinstituted again for another 3 weeks. Hamilton Scale for Depression (HAM-D) was used to measure the level of depression and associated symptoms.

The findings of our study revealed that ProVanax™ caused a significant clinical improvement in the symptoms associated with depression.

BACKGROUND

Depression is a condition quite notorious to treatment. Furthermore, depressive disorders have a tendency towards chronicity; it is estimated that a third of patients of depression-anxiety will suffer from a long-term illness (Spijker et al., 2002; Arnow & Constantino, 2003). An alarming finding is that 15% of long-term depressed-anxious patients are likely to commit suicide over a period of 10-20 years (Fawcett, 1993).

A subtype of depression illness called major depressive disorder (MDD) causes the most severe of deteriorations in quality of life in a patient (compared to any other medical
condition) (Jakobsen, Lindschou, Storebo, Simonsen, & Gluud, 2011). Also, depression seems to be quite prevalent in the general population; the WHO believes that major depressive illness is the second commonest cause of illness-induced disability (Levav & Rutz, 2002).

The main therapeutic approach for depression-anxiety disorders is antidepressant therapy (Cipriani et al., 2009). However, meta-analytic observations show that drugs provide partial benefits and clinical improvement in such patients is insignificant (Kirsch et al., 2008; Turner, Matthews, Linardatos, Tell, & Rosenthal, 2008). Although some researchers argue that drugs do reduce the risk of relapses (Geddes et al., 2003), there is no denying that effective therapeutic solutions still remain elusive (Jakobsen et al., 2011). A Cochrane review of cognitive therapy for depression, anxiety and panic attacks concluded that it may be better than drugs (Vittengl, Clark, Dunn, & Jarrett, 2007). However, there seems to no evidence to suggest that cognitive therapy may be useful as a therapeutic tool (as opposed to being a preventive tool) (Higgins & Green, 2011).

Thus, although decades of research has been directed towards designing a definitive therapeutic solution to depression-anxiety illnesses in human beings, results have been disappointing. This scenario begs for the question to be asked if there indeed is any effective treatment for these debilitating and serious illnesses (Jakobsen et al., 2011).

With such a backdrop, we decided to conduct a clinical trial of a commercially available therapeutic preparation that claimed to treat depression and associated symptoms like anxiety and panic attacks.

**STUDY DESIGN**

The aim of the present study was to investigate the efficacy and safety (as alleged by the manufacturers-promoters) of a proprietary herbal preparation (ProVanax™) in treating depression and associated symptoms like varying degrees of anxiety, insomnia and panic attacks.

The methodology used was a randomized, double-blind, clinical trial.

**PARTICIPANTS**

120 patients with ‘self-reported’ depression were short-listed for the study.

After carefully screening them clinically and using the Hamilton Depression Rating Scale (Hamilton, 1960) and the Hamilton Anxiety Rating Scale, 80 were diagnosed as genuine cases of depression-anxiety and were enrolled for the study.

**Selection Process & Inclusion Criteria For Participants**

The Hamilton Depression Rating Scale (HAM-D) – see APPENDIX on Page16– is considered a ‘gold-standard’ for diagnosing severity of depression in a patient. Similarly, the Hamilton Anxiety Rating Scale (HAM-A) is a standard test for diagnosing the level of anxiety a person is suffering from. Owing to the effectiveness and simplicity of HAM-D and HAM-A, these tests are some of the most popular around (Cusin, Yang, Young, & Fava, 2009).

HAM-D is preferred by researchers for clinical trials too. Because of its popularity and regularity of use, most researchers and physicians working in the area of depression can
identify with it. Thus, the findings of our study, we theorized, would be easier to analyze and interpret to most of these professionals.

Physician-conducted clinics were organized for recording detailed history, including duration and severity of the ‘self-reported’ depression and anxiety. Clinical examination of all 120 participants resulted in exclusion of 15 patients; these exhibited symptoms consistent with other conditions like hormonal imbalance, bereavement, etc.

For the remaining 105 participants a questionnaire-answering session was organized on a separate day. Participant were issued reminders well in advance (a week) through either email or via a telephonic call or a short messaging service reminder. Care was taken that all participants would attend the questionnaire session. Despite this, 3 participants did not show up on the day of the session.

On the day of questionnaire-answering session, 102 participants were issued the HAM-D questionnaire. An estimate suggests that it might take an average of 12 minute for a person to answer the HAM-D questionnaire (Cusin et al., 2009). To ensure that the participants were not rushed, we allotted a total of 60 min. for completion of both the questionnaires – HAM-D and HAM-A.

After analyzing the data obtained from the questionnaires, another 22 were excluded. These were shown to either not suffer from depression/anxiety or their findings were too mild to warrant therapeutic or preventive treatments. Eventually, a total of 80 patients (including men and women) were shortlisted for the study.

<table>
<thead>
<tr>
<th>Selection Criteria</th>
<th>No. of participants shortlisted</th>
</tr>
</thead>
<tbody>
<tr>
<td>After Self-reporting</td>
<td>120</td>
</tr>
<tr>
<td>After Clinical diagnosis</td>
<td>105</td>
</tr>
<tr>
<td>After HAM-D/HAM-A results</td>
<td>80</td>
</tr>
</tbody>
</table>

**Table 1: Selection Process for Participants.**

**METHODOLOGY**

80 participants of the study were randomly divided into 2 groups of 40 each; one group was labeled the ‘test (T) group’ and the other ‘control (C) group’.

The T group were supplemented with ProVanax™ as recommended by the manufacturers – 1 capsule, twice daily for the first 2 days followed by the full dosages of – 2 capsules (t.i.d.), three times daily. These doses were instructed to be taken for 3 weeks. A week’s layoff was planned after 3 weeks followed by another 3 weeks of dosing.
The C group followed a similar dosing schedule, except that the drug they were administered was a placebo packed in a similar looking pill.

Since the study was ‘double-blind’, neither the participants nor the handlers of participants (and attending physicians) had any idea of which participant was assigned to what group – test or control.

After 2 (3-week) ‘cycles’ of taking ProVanax™ or placebo pills, participants were tested again for signs of depression.

The total duration of the study was 7 weeks (including a 1 week break between the two ‘cycles’).

RESULTS

Pre-supplementation results of HAM-D questionnaire testing.

The results of the HAM-D and HAM-A questionnaires before the initiation of the study are shown in Table 2 and Table 3. As stated earlier, each group (T and C) contained 40 participants each. Symptoms exhibited by members of both groups suggested presence of depression ranging from mild to very severe states in each of the group.

Those (22, 3 didn’t turn up for the questionnaire session) that had total of less than 8 were diagnosed as free from depression and were excluded from the study.

Table 2: HAM-D results before commencement of study.

<table>
<thead>
<tr>
<th>HAM-D Item Total</th>
<th>Test Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-13 (Mild)</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>14-18 (Moderate)</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>19-22 (Severe)</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>&gt;=23 (Very Severe)</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 3: HAM-A results before commencement of study.

<table>
<thead>
<tr>
<th>HAM-A Item Total</th>
<th>Test Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24 (Mild to Moderate)</td>
<td>20</td>
<td>13</td>
</tr>
<tr>
<td>25-30 (Moderate to Severe)</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>&gt;30 (Severe)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>40</td>
</tr>
</tbody>
</table>
Post-supplementation results of HAM-D questionnaire testing

After supplementing with either ProVanax™ or placebo for two cycles of 3 weeks each with a lay-off of a week in between the cycles, all 80 participants were requested to attend another questionnaire-answering session. Similar to the initial session, participants were made to answer HAM-D questionnaire again.

The result of analysis of data from the post-study session are shown in Table 3.

Table 4: HAM-D results after supplementing with ProVanax™.

<table>
<thead>
<tr>
<th>HAM-D Item Total</th>
<th>Test Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-13 (Mild)</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>14-18 (Moderate)</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>19-22 (Severe)</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>&gt;=23 (Very Severe)</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 5: HAM-A results after supplementing with ProVanax™.

<table>
<thead>
<tr>
<th>HAM-A Item Total</th>
<th>Test Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24 (Mild to Moderate)</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>25-30 (Moderate to Severe)</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>&gt;30 (Severe)</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>40</td>
</tr>
</tbody>
</table>
Table 6: HAM-D before/after ProVanax™ usage.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Before ProVanax</th>
<th>After ProVanax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Moderate</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Severe</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Very Severe</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Improvement</td>
<td>30</td>
<td>35</td>
</tr>
</tbody>
</table>

Table 7: HAM-A before/after ProVanax™ usage.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Before ProVanax</th>
<th>After ProVanax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to Moderate</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Moderate to Severe</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Very Severe</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Improvement</td>
<td>30</td>
<td>35</td>
</tr>
</tbody>
</table>

Before ProVanax | After ProVanax
As is seen in Table 4, almost all participants from the T group had a favorable outcome. Not a single case of very severe depression was reported; only 5 patients reported a depression levels from severe to moderate. This was found to be in sharp contrast to pre-supplement levels – a total of 7 very severe depression cases, 21 ranging from severe to moderate and 12 cases of mild depression. Whereas, before the study, all cases in the T group had some level of depression, after supplementing with ProVanax™, 31 of these had no symptoms of the disease. Of the 9 remaining, most had mild to moderate depression. We surmised that a longer duration of treatment with ProVanax™ could cure these remaining cases as well.

In contrast, the C group (supplemented with placebo) didn’t exhibit any significant changes. Although the number of cases of severe depression in the control group did go down, we put this down to changed circumstances, improvement in lifestyle or subjective changes in answering the questionnaire.

Similarly, as seen in Table 5, the number of test participants went down from 40 to 12 after 6 weeks of therapy with ProVanax™. There weren’t much changes seen in the control group.

Overall, there was a 77.5% improvement in HAM-D (Table 6) and 70% improvement in HAM-A (Table 7) for ProVanax™ users.

**Adverse effects profiling of ProVanax™**

No adverse reactions were reported by participants from either the test group or the control group. Some reporting of nausea and gastric symptoms was recorded. However, most of these symptoms settled down after a few weeks of continued therapy.

**DISCUSSION**

Depression (and associated conditions like anxiety and panic attacks) is generally a difficult condition to treat (Jakobsen, Hansen, Simonsen, & Gluud, 2012). Although a number of different approaches are traditionally recommended – antidepressants, anti-inflammatory drugs, cognitive therapy and others – most of these afford partial clinical improvements and none are completely effective (Kirsch et al., 2008; Turner et al., 2008).

Most of these ‘traditional therapeutic approaches’ are based on the etiological theories of depression-anxiety.

Recently, inflammation has been suggested as a likely cause of depression, anxiety and panic attacks; 3 meta-analyses support such an idea (Zorrilla et al., 2001; Howren, Lamkin, & Suls, 2009; Dowlati et al., 2010). However, there are researchers who believe otherwise (Raison & Miller, 2011). Whatever the case, use of anti-inflammatory drugs has been shown to afford some therapeutic relief in depression and its associated symptoms.

‘Accelerated cellular aging’ which occurs mainly due to low-grade systemic inflammation is believed to cause a number of metabolic diseases – obesity being one of them. Such cellular aging processes are also believed to cause psychosomatic conditions like depression, anxiety and panic attacks. Researchers site as proof the occurrence of inflammation-mediated ‘sickness behavior’ – social withdrawal, anhedonia, and fatigue - as characteristic symptoms of psychological disorders (Dantzer, O’Connor, Freund, Johnson, & Kelley, 2008).

An anti-inflammatory approach may therefore, have a definite place in therapy for depression.
Another theory suggests that dysregulation of the HPA (hypothalamic-pituitary-adrenal) axis leading to increased levels of cortisol may form the inflammatory basis of not only depression, anxiety and panic attacks but even graver psychiatric and psychotic conditions (Howland, 2013). No wonder then, use of drugs that can depress or counter the effects of elevated levels of cortisol may be beneficial in depression.

Researches have also observed the strong connection between depression-anxiety-panic attacks and stress. Some believe that stress and depression may be so inherently intertwined that they may be cause and/or effects of each other. And, increase in one may lead to increase in the other with a vicious cycle ensuing. Chronic, increased levels of mental stress can significantly increase both the severity and time-duration of the symptoms associated with depression (Stefano, Stefano, & Esch, 2008; Romans et al., 2009; Hammen, 2005; Cohen, Janicki-Deverts, & Miller, 2007; Kinser & Lyon, 2013). Furthermore, there is enough proof to suggest that stress and depression together may lead to increase in morbidity and mortality – and thus, the significant decrease in quality of life associated with depression (Pozuelo et al., 2009; Cohen et al., 2007). There is also an increased likelihood of metabolic diseases like obesity, cardiovascular disease, diabetes and osteoporosis in patients suffering from chronic stress and depression (Fagundes, Glaser, Hwang, Malarkey, & Kiecolt-Glaser, 2013; Wolkowitz et al., 2011).

Another explanation for the occurrence of depression-anxiety is the altered levels of neuroendocrinal elements in the brain. Reduced levels of γ-aminobutyric acid (GABA) in the occipital and anterior cingulate cortices may be responsible for causing depression and primary insomnia (Plante, Jensen, Schoerning, & Winkelman, 2012). Similarly, reduced dopamine levels are also associated with depression.

Stress, associated inflammation (which increased oxidative stress), increased levels of cortisol and decreased levels of neuroactive peptides like dopamine and GABA may together be responsible for a large number of cases of depression-anxiety-panic attacks (Rawdin et al., 2013; Epel et al., 2004; Epel et al., 2010; Choi, Fauce, & Effros, 2008).

Not surprisingly then, any drug combination or regimen aimed towards decreasing these confounding factors or increasing levels of dopamine or GABA in the brain may prove to be beneficial in treating depression and associated symptoms.

**Contents of ProVanax™**

The Synergy Optimizer™ blend of ProVanax™ contains *Griffonia Simplicifolia* (5 Hydroxytryptophan, 5HT), St. John’s Wort (5% Hyperforin extract), *Passiflora incarnate* (Passion flower 10:1 extract), Kava kava extract, Valerian extract, L-Theanine, Inositol, L-Taurine, GABA.

As is apparent, the formulation of ProVanax™ is aimed towards increasing dopamine and γ-aminobutyric acid levels in brain and to oppose the pathophysiological effects of stress, chronic inflammation and oxidative stress. Thus, ProVanax™, as our findings suggest, may be an effective therapy for treating depression and associated conditions like anxiety and panic attacks. Additionally, this formulation in the long run may also help in tackling metabolic diseases, let alone depression.
CONCLUSION

Findings of the study – prima facie – suggest that the herbal contents of ProVanax™ may be effective at countering depression and related symptoms like anxiety, panic attacks, insomnia, apprehension and stress. In effect, ProVanax™ has the potential to improve quality of life, productivity and general well-being in an individual with depression. Additionally, in all likelihood, it may also help prevent or control the symptoms of metabolic diseases – obesity, diabetes and cardiovascular events.

FURTHER RESEARCH

This clinical trial was instrumental in proving the efficacy and safety of the herbal commercial preparation on a short-term basis.

We suggest a larger and longer duration clinical study to back up the results obtained here and to ascertain the safety (on long term use) – especially to investigate if the supplement has an inherent addiction potentiality on a longer-term use.

ACKNOWLEDGMENTS

The authors wish to thank the subjects for their invaluable contribution to the study.
APPENDIX

Hamilton Depression Rating Scale (HAM-D)

This is a practitioner-rate form. Please rate and select a number 0, 1, 2, 3 or 4 which indicates symptoms severity over the past week. This assessment is not intended to be a diagnosis.

Instructions: To rate the severity of depression in patients who are already diagnosed as depressed, administer this questionnaire. The higher the score, the more severe the depression. For each item, circle the number next to the correct item (only one response per item).

4-item 0 = Absent 1 = Mild  2 = Moderate, 3 = Severe, 4 = Very severe
2-item 0 = Absent 1 = Mild  2 = Definite

1 Depressed Mood
0 = Absent
1 = Gloomy attitude, pessimism, hopelessness
2 = Occasional weeping
3 = Frequent weeping
4 = Patient reports virtually only those feeling states in his / her spontaneous verbal or non-verbal communication

2 Feeling of guilt
0 = Absent
1 = Self-reproach, feels he / she has let people down
2 = Ideas of guilt or rumination over past errors or sinful deeds
3 = Present illness is punishment
4 = Hears accusatory or denunciatory voices and / or experiences, threatening visual accusations and delusions of guilt

3 Suicide
0 = Absent
1 = Feels life is not worth living
2 = Wishes he / she were dead or any thoughts of possible death to self
3 = Suicide, ideas or half-hearted attempt
4 = Attempts at suicide (any serious attempt rates 4)

4 Insomnia (early)
0 = No difficulty falling asleep
1 = Complaints of occasional difficulty falling asleep; i.e. more than ½ hour
2 = Complains of nightly difficulty falling asleep

5 Insomnia (middle)
0 = No difficulty
1 = Patient complains of being restless and disturbed during the night
2 = Waking during the night: any getting out of bed rates 2 (except for voiding)

6 Insomnia (late)
0 = No difficulty

7 Work and Activities
0 = No difficulties
1 = Thoughts and feelings of incapacity related to activities, work and hobbies
2 = Loss of interest in activity, hobbies or work either directly reported by patient, or indirectly seen in listlessness, indecision and vacillation (feels he / she has to push self to work or activities)

8 Retardation
Slowness of thought and speech; impaired ability to concentrate
0 = Normal speech and thought
1 = Slight retardation at interview
2 = Obvious retardation at interview
3 = Interview difficult
4 = Interview impossible

9 Agitation
0 = None
1 = Fidgeting
2 = Playing with hands, hair, obvious restlessness
3 = Moving about, can’t sit still
4 = Hand wringing, nail biting, hair pulling, biting of lips, patient is ‘on the run’

10 Anxiety (Psychic)
Demonstrated by: Subjective tension and irritability, loss of concentration, worrying about minor matters, apprehension, fear expressed without questioning, feelings of panic, feeling
0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

11 Anxiety (Somatic)
Physiological concomitants of anxiety, e.g. dry mouth, wind, indigestion, diarrhea, cramps, belching, palpitations, headaches, hyperventilation, sighing, urinary frequency, sweating, giddiness, blurred vision, tinnitus
0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

12 Somatic Symptoms (Gastrointestinal)
0 = None
1 = Loss of appetite but eating without staff encouragement
2 = Difficulty eating without staff urging. Requests or requires laxatives or medication for GI symptoms

13 Somatic symptoms (General)
0 = None
1 = Heaviness in limbs, back or head, backaches, headaches, muscle aches, loss of energy, fatigability
2 = Any clear-cut symptom rates

14 Genital symptoms
Symptoms such as libido / menstrual disturbances
0 = Absent
1 = Mild
2 = Severe

15 Hypochondriasis
0 = Not present
1 = Self-absorption (bodily)
2 = Preoccupation with health
3 = Strong conviction of some bodily illness
4 = Hypochondriacal delusions

16 Loss of weight
0 = No weight loss
1 = Probable weight loss associated with present illness
2 = Definite (according to patient) weight loss

17 Insight
0 = Acknowledges being depressed and ill
1 = Acknowledges illness but attributes cause to bad food, overwork, virus, need for rest. Etc.
2 = Denies being ill at all

18 Diurnal Variation
18(a) Note whether symptoms are worse in morning or evening. If no diurnal variation, mark ‘none’
0 = No variation
1 = Worse in AM
2 = Worse in PM
18(b) When present, mark the severity of the variation. Mark ‘non’ if no variation
0 = None
1 = Mild
2 = Severe

19 Depersonalization and Derealization (e.g. feelings of unreality; nihilistic ideas)
0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

20 Obsessional and compulsive symptoms
0 = Absent
1 = Mild
2 = Severe

Total Score (total of circled responses): _____

Source: (Hamilton, 1960)
Hamilton Anxiety Rating Scale (HAM-D)

Below is a list of phrases that describe certain feelings that people have. Rate the patients by the answer which best describes the extent to which he/she has these conditions. Select one of the five responses for each of the fourteen questions.

0 = Absent 1 = Mild 2 = Moderate, 3 = Severe, 4 = Very severe

1. **Anxious mood**: worries anticipation of the worst, fearful anticipation, irritability 1 /2 /3 /4
2. **Tension**: Feelings of tension, fatigability, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax 1 /2 /3 /4
3. **Fears**: of dark, of strangers, of being left alone, of animals, of traffic, of crowds 1 /2 /3 /4
4. **Insomnia**: difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors 1 /2 /3 /4
5. **Intellectual**: difficulty in concentrating, poor memory 1 /2 /3 /4
6. **Depressed mood**: loss of interest, lack of pleasure in hobbies, depression, early waking, diurnal swing 1 /2 /3 /4
7. **Somatic (muscular)**: pain and aches, twitching, stiffness, myoclonic jerks, grinding of teeth, unsteady voice, increased muscular tone 1 /2 /3 /4
8. **Somatic (sensory)**: tinnitus, blurring of vision, hot and cold flushes, feelings of weakness, pricking sensation 1 /2 /3 /4
9. **Cardiovascular symptoms**: tachycardia, palpitations, pain in chest, throbbing of vessels, fainting feelings, missing beat 1 /2 /3 /4
10. **Respiratory Symptoms**: pressure or constriction in chest, choking feelings, sighing, dyspnea 1 /2 /3 /4
11. **Gastrointestinal symptoms**: Difficulty in swallowing, wind abdominal pain, burning sensations, abdominal fullness, nausea, vomiting, borborygmi, looseness of bowels, loss of weight, constipation 1 /2 /3 /4
12. **Genitourinary symptoms**: frequency of micturition, urgency of micturition, amenorrhea, menorrhagia, development of frigidity, premature ejaculation, loss of libido, impotence 1 /2 /3 /4
13. **Autonomic Symptoms**: dry mouth, flushing, pallor, tendency to sweat, giddiness, tension headache, raising of hair 1 /2 /3 /4
14. **Behavior at interview**: fidgeting, restlessness or pacing, tremor of hands, furrowed brow, strained face, sighing or rapid respiration, facial pallor, swallowing, etc. 1 /2 /3 /4

REFERENCES


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