A Comparative Evaluation of StressCare Capsules in Mild and Occasional Anxiousness with Special Reference to Cortisol and Well-being

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ABSTRACT

Anxiousness is related to autonomic stimuli. The aim of this study was to evaluate the clinical efficacy and safety of StressCare Capsules in mild and occasional anxiousness with special reference to cortisol and wellbeing. This study was a prospective, randomized, double blind, placebo-controlled clinical trial conducted on fifty consecutive people of mild and occasional anxiousness attending the Outpatient Department of Medicine, Patna Medical College Hospital, after getting an approval of the Institutional ethical committee. On entry, a detailed medical history was obtained to ascertain the presence of anxiousness followed by complete physical and psychological examination. All the people were randomly divided into StressCare and placebo groups, and people from both the groups received StressCare or placebo for a period of 4 weeks, in a dose of 2 capsules twice daily, orally. Those involved in the study were evaluated clinically on entry and at the end of the study period, i.e. 4 weeks. Plasma cortisol levels were measured on entry and at the end of the study. The adverse effects as volunteered by the people involved were noted in the case record forms. Between the group analysis has shown that StressCare group was found to be effective compared to placebo and was beneficial in supporting to bear mild and occasional anxiousness.

Keywords: StressCare, Anxiousness, placebo.

INTRODUCTION

Anxiousness is regarded as a subjective response to any stressor which may present as displeasing feeling of fear, uncertainty, restlessness, sleep disturbances and fatigue. Mild anxiety is a normal human emotion¹.

The term anxiousness covers four aspects of experiences an individual may have: mental apprehension, physical tension, physical symptoms and mild anxiety²⁻³. It becomes a disorder when it is of greater intensity or duration that would be normally expected. People with mild anxiety are often frequent users of supplements. Even though there is a lack of agreement regarding the nature of anxiety, most researchers have developed their measures based on Freudian theory, though recently there has been an increasing discussion of physiological theories.

Anxiety is a common disorder, possibly occurring in 5% of the population.⁴ In Europe, Africa and Asia, lifetime rates of anxiety disorders are between 9 and 16%, and yearly rates are between 4 and 7% ⁵. In the United States, the lifetime prevalence of anxiety disorders is about 29% and between 11 and 18% of adults have the condition in a given year. ⁵ Anxiety can arise in response to life stresses such as worries. Somewhere between 4% and 10% of older adults are identified to have mild anxiety, a figure that is probably an underestimate due to the tendency of adults to minimize problems or to focus on their physical manifestations. Anxiety is also common among older people who have forgetfulness.⁷,⁸

Low mood or loss of interest, usually accompanied by one or more of the following-low energy, change in appetite, change in weight or sleep pattern, poor concentration, is common in people with mild anxiety.⁹,¹⁰
Based on Freudian theory, objective anxiety involves a complex internal reaction to anticipated injury or harm from some external danger. With objective anxiety, the intensity of the anxiety reaction is proportional to the magnitude of the external danger that evokes it, the greater the external danger, the stronger the perceived threat, the more intense the resulting reaction.

According to May, the particular events or stimuli which evoked anxiety are largely determined by learning rather than impulses. An anxiety reaction is normal if it is proportionate to the objective danger and does not involve repression or other defense mechanisms.

Anxiety is also viewed as an intensely unpleasant state of tension arising from experiencing disapproval in interpersonal relations.

Once aroused, anxiety distorts the individual’s perception of reality and limits the ranges of stimuli that are perceived. Today, anxiety is viewed as an unpleasant emotional state, which is characterized by subjective feelings of tension, apprehension, and worry, and by activation or arousal of the autonomic nervous system mostly consistent with Freud’s conceptualization.

Recently, there has been increasing discussion of physiological theories behind anxiety. These theories explain that individuals with mild anxiety may experience stressful situations in their social set up. Anderson and Hope also noted that such an interpretation of physiological arousal leads to increased symptoms of anxiety (e.g. racing heart or blushing) among individuals with mild anxiety. Furthermore, perceptions about the dangerousness of such physiological arousal may maintain anxiety symptoms as individuals learn to avoid threatening or stressful situations in order to evade such physiological arousal.

While competing conceptualizations about anxiety exist, most anxiety measures seem to be based on the theoretical conception proposed by Freud, who viewed anxiety as an unpleasant emotional state or condition characterized by subjective feelings of tension, apprehension, and worry.

Low levels of Gamma-aminobutyric acid (GABA), a neurotransmitter that reduces activity in the central nervous system, contribute to anxiety. A number of anxiolytics achieve their effect by modulating the GABA receptors, specifically reducing the intensity of anxiety. These include drugs like diazepam, alprazolam, and clonazepam. While these drugs are effective, they can also have side effects and may become habit-forming.

For some people, anxiety can be very much reduced by coming off caffeine. Anxiety can temporarily increase during caffeine withdrawal.

For some people, anxiety can be very much reduced by coming off caffeine. Anxiety can temporarily increase during caffeine withdrawal. There are also many traditional herbal remedies and essential oils that have been used for centuries to help alleviate anxiety. These include valerian root, chamomile, passionflower, and lavender. These herbs are known to promote relaxation and help calm the mind.

AIM OF THE STUDY
To evaluate the safety and efficacy of StressCare Capsules in mild and occasional anxiety with special reference to cortisol and well-being.

MATERIALS AND METHODS
This study was a prospective, randomized, double blind, placebo-controlled clinical trial conducted on fifty consecutive people of mild and occasional anxiousness attending the Outpatient Department of Medicine, Patna Medical College Hospital, after getting an approval of the Institutional ethical committee. Those who opted for treatment were informed of voluntary nature of trial and written consent was obtained. Only those cases were included in the study they fulfilled the inclusion and exclusion criteria. They were randomized using a random table in to StressCare group and placebo group comprising of 25 people each. Both the groups were comparable at entry. People in StressCare
group received StressCare Capsules in dose of 2 capsules twice a day, while people in placebo group received identical looking placebo in the same dose, for the period of 4 weeks. Those involved in the study were evaluated clinically on entry and at the end of the study period, i.e. 4 weeks. Plasma cortisol levels were measured on entry and at the end of the study to assess changes following StressCare therapy using Enzyme linked fluorescent assay. Adverse effects, if any, were noted. The study was initiated only after getting informed consent from the people involved. All study people were free to withdraw from the study, if they desired.

**STUDY PROCEDURE**

Fifty consecutive people belonging to the age group of 41-58 years with mild and occasional anxiousness were included in the study as per the subject selection criteria. People were arbitrarily grouped into StressCare group and placebo group comprising 25 people each. People characteristics on entry are given in Table 1. Both the groups were comparable.

People in StressCare group received StressCare Capsules in dose of 2 capsules twice a day, while people in placebo group received identical looking placebo in the same dose, for the period of 4 weeks. People were evaluated clinically on entry and at the end of the study period, i.e. 4 weeks. Plasma cortisol levels were measured on entry and at the end of the study to assess changes following StressCare therapy. Adverse effects, if any, were noted. The study was initiated only after getting informed consent from the people. People involved were free to withdraw from the study, if they desired.

All the enrolled subjects were monitored for 4 weeks, for any reported or observed adverse effects. In case any adverse effects were reported, or observed by the subjects were recorded with information about severity, date of onset, duration and action taken regarding StressCare. Subjects were allowed to voluntarily withdraw from the study, if they had experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For subjects withdrawing from the study, efforts were made to ascertain the reason for dropout. Non-compliance (defined as failure to take less than 80% of the StressCare) was not regarded as failure and reasons for non-compliance were noted.

**Follow-up and assessment**

Subjects were evaluated clinically on entry and at the end of the study period, i.e. 4 weeks. Plasma cortisol levels were measured on entry and at the end of the study to assess changes following StressCare therapy.

**Inclusion criteria**

Male or female individuals above 18 years of age with mild occasional anxiousness.

**Exclusion criteria**

Aggressive people, seizure disorders, any psychiatric condition that would require inpatient admission, current abuse of alcohol or other substance, clinically judged by the investigator to be at risk for suicide, suffering from liver, kidney, and heart diseases and pregnant or lactating women and cases with known history of allergy to medications.

**Statistical Analysis**

Results were analysed statistically for comparison between the groups using Fisher’s exact test to find out the statistical significance. Analysis was performed using Graphpad Prism software Version 4.03, San Diego, California, USA.

**RESULTS**

Demographic data are shown in Table 1 and indicates that both the groups are comparable. Significant improvement in support of mild and occasional anxiousness was noted in people in the StressCare group. Between the groups analysis has shown that StressCare group was found to be effective compared to placebo. StressCare group was found to be effective compared to placebo in various parameters. Treatment with StressCare capsule showed significant improvement in the symptoms of anxiousness at the end of 4 weeks like restlessness (p<0.0005), Emotional discouragement (p<0.0005), Occasional Mental confusion (p<0.0374), Sweating (p<0.0001), Occasional sleep disturbances (p<0.0019), Occasional mild fatigue (p<0.0106) are shown in Table 2 Plasma cortisol level evaluated in StressCare and placebo group was evident in table 3. The level of plasma cortisol was found to be 33.45 ± 6.41 µg/ml in StressCare group on entry. After treatment with StressCare, the level of plasma cortisol reduced to 25.70 ± 7.50 µg/ml at 4 weeks. Whereas, in the placebo group, the level of plasma cortisol which was 29.83 ± 6.25 µg/ml on entry changed to 25.70 ± 6.25 µg/ml at the end of 4 weeks of treatment with placebo. The statistical analysis conducted between the group has shown that, the level of significance was found to be p<0.0397 in StressCare group as compared to placebo after 4 weeks of treatment. All the people completed the study protocol and none withdrew.

**DISCUSSION**

Stress and anxiety may affect the normal physiological functioning of the nervous and cardiovascular systems. In addition, acetylcholine and plasma cortisol level are also known to increase following continued stress and anxiety.
In this double blind, placebo-controlled study, the efficacy of StressCare in anxiousness was investigated. 4 weeks of StressCare treatment in comparison with placebo was noted. StressCare decreased plasma cortisol. StressCare has antioxidant and adaptogenic properties and supports cellular regeneration and repair. It supports physical capacity, normal levels of fatigue, and promotes well-being. StressCare’s support properties could be due to the sum total of its ingredients.

**Chyavanprash**
Chyavanprash is a classical preparation of 40 ingredients that holds an important traditional application in Indian Medicine. It is a common, historically-used tonic famous for its rejuvenating and adaptogenic reputation.

**Capparis spinosa**
*Capparis spinosa* is an antioxidant shown to prevent the free radical-induced oxidative damage to various organs and systems. It provides support to liver, spleen, and kidney; thus helping to maintain well being.

**Cichorium intybus**
*Cichorium intybus* contain escutetin and its glycosides. Trials suggest that extract of *Cichorium intybus* has Fe2+ chelating, and free radical scavenging activity towards the DDPH showing effective antioxidant activity; thus helping to maintain well being.

**Solanum nigrum**
Berries contain solasonine and sapogenins. They support normal microcirculation. Phenolic compounds present in *Solanum nigrum* extract show antioxidant activity that may be helpful in support of normal health.

**Cassia occidentalis**
Anthroquinone derived from *Cassia occidentalis* has support the normal structure-function of the colon, as regular bowel movements promote normal health. *Cassia occidentalis* is used as a general tonic.

**Terminalia arjuna**
Experimental studies have revealed the bark of *Terminalia arjuna* to support normal coronary artery flow. It has also been detected to have a supportive effect on prostaglandin E(2) activity. *Terminalia arjuna* mainly contain plant sterols (β-sitosterol) and arjunic acid, respectively whereas ethanolic fraction was enriched with derivatives of arjunic acid like arjunoglycoside (I, II, II and IV), arjunenin, arjunolone, arjutenin, tanins, and ellagic acid. Some pure compounds namely Arjunolic acid, Terminoside, Ellagic acid and Tanins have been found to possess antioxidant activity, helping maintain normal health.

**Achillea millefolium**
Selenium as present in *Achillea millefolium* has antioxidant activity.

**Tamarix gallica**
Galls of *Tamarix gallica* contain the polyphenols, gallic acids, ellagic acid, which support various health promoting activities. The extract also shows antioxidant activity.

**Crocus sativus**
The richness of total phenolic content along with other values shows antioxidant activity. Safranal, isolated from Crocus sativus shows supportive effects on different markers of oxidative damage in hippocampal tissue, again showing its antioxidant activity.

**Curculigo orchioides**
Rhizomes contain glycosides, curculigoside and alkaloid lycorine. The rhizomes exhibit tonic activities. Use of the extract has shown support of normal humoral antibody (HA) titre level, delayed type hypersensitivity (DTH) and levels of WBC, which indicate support of a normal immune system.

**Caesalpinia digyna**
The extract of *Caesalpinia digyna* root exhibited increase in the levels of catalase (CAT) and superoxide dismutase (SOD) and significant decrease in the levels of lipidperoxidation (LPO) in serum, liver and kidney; indicating antioxidant activities.

**Asparagus racemosus**
The minerals, which are biochemically important for the human system, are present in significant concentrations in different parts of *Asparagus racemosus*. Traditionally it is used as health tonic and used as a rejuvenator and promoter of strength. *Asparagus racemosus* has also been reported to have adaptogenic activity.

**Withania somnifera**
Roots contain the alkaloids withanine and withasomnine.

**Glycyrrhiza glabra**
The major constituents are triterpene saponins along with others reported are Glycyrrhizin.

**Centella asiatica**
*Centella asiatica* shows antioxidant activities.

**Terminalia chebula**
*Terminalia chebula* shows antioxidant activities.
Mucuna pruriens
The antioxidant activity of Mucuna pruriens was demonstrated by its ability to scavenge DPPH radicals, ABTS radicals and reactive oxygen species.

Myristica fragrans
Recent research carried out on Myristica fragrans indicates its antioxidant activity.

Piper longum
Alcoholic extract of the fruits of the plant Piper longum and its component piperine has noted for its support of a normal immune system. It is also reported to enhance the bioavailability that potentiates action of other ingredients.

Elettaria cardamomum
Elettaria cardamomum seed extract which mainly contains the essential oils have potential applications as a general health supplement.

Curcuma longa
Preliminary report in experimental studies says extract of Curcuma longa is supportive in the normal function of the liver, heart, and immune system due to its richness of phytoconstituents.

Adhatoda vasica
Support of normal acid phosphatase level points out the role of the extracts of Adhatoda vasica in promoting normal organelle membrane structure. The extracts contain several alkaloids such as vasicine, vasicinone and a quinazoline-alkaloid, and peganin.

Eclipta alba
Eclipta alba has been reported to inhibit the oxidation of DMSO indicating hydroxyl radical scavenging activity; and support of normal levels of free radical DPPH, indicating its effect as an antioxidant.

CONCLUSION
This clinical study clearly indicates clinical efficacy of StressCare Capsules in support of mild and occasional anxiousness. There was a clinically significant improvement in the StressCare group as compared to the placebo by between the group analyses. The cortisol levels significantly reduced with StressCare treatment as compared to placebo. There were no adverse effects either observed or reported in the clinical study. All the subjects completed the study and the compliance to the study is good. Therefore it may be concluded as StressCare capsule is found to be beneficial in supporting those suffering from mild and occasional anxiousness.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>StressCare (n=25)</th>
<th>Placebo (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (Mean ± SD)</td>
<td>41.8 ± 9.4</td>
<td>43.3 ± 10.6</td>
</tr>
<tr>
<td>Weight (Kg) (Mean ± SD)</td>
<td>56.8 ± 12.1</td>
<td>58 ± 9.8</td>
</tr>
<tr>
<td>Sex ratio (M:F)</td>
<td>18.7</td>
<td>20.5</td>
</tr>
<tr>
<td>Restlessness</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td>Emotional discouragement</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Occasional Mental confusion</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Sweating</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Occasional sleep disturbances</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Occasional mild fatigue</td>
<td>13</td>
<td>12</td>
</tr>
</tbody>
</table>

Table 2: Effect of StressCare and Placebo on anxiousness

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameter</th>
<th>Duration</th>
<th>No. of people showing incidence</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Restlessness</td>
<td>On entry</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Week 4</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>2.</td>
<td>Emotional discouragement</td>
<td>On entry</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Week 4</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>3.</td>
<td>Occasional Mental confusion</td>
<td>On entry</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Week 4</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>4.</td>
<td>Sweating</td>
<td>On entry</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Week 4</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>5.</td>
<td>Occasional sleep disturbances</td>
<td>On entry</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Week 4</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>6.</td>
<td>Occasional mild fatigue</td>
<td>On entry</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Week 4</td>
<td>1</td>
<td>9</td>
</tr>
</tbody>
</table>

Statistical analysis: Fisher’s exact test. Analysis was performed between the groups for “on entry” and “week 4” values. NS: Not significant.
Table 3: Effect of StressCare on plasma cortisol level (Mean ± SD)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Plasma cortisol (µg/ml)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>StressCare (µg/ml)</td>
<td>Placebo (µg/ml)</td>
</tr>
<tr>
<td>On entry</td>
<td>33.45 ± 6.41</td>
<td>32.95 ± 5.68</td>
</tr>
<tr>
<td>Week 4</td>
<td>25.70 ± 7.50</td>
<td>29.83 ± 6.25</td>
</tr>
</tbody>
</table>

Statistical analysis: Unpaired t-test. Analysis was performed between the groups for “on entry” and “week 4” values.

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