Comparing the Effectiveness of Paroxetine, Attention Modification Program and Combination of both on Improving Social Anxiety Symptoms

Hosein Khedmatgozar¹, Behrooz Birashk¹, Hassan Ashayeri², Aliasghar Asgharnejad Farid⁴

Introduction: Although the effectiveness of paroxetine and Attention Modification Program has been studied separately in treating social anxiety disorder, there has been no research comparing them according to the literature. The aim of this study was to compare the effectiveness of paroxetine, Attention Modification Program (AMP) and combination of both on improving the Social Anxiety Symptoms.

Methods: 33 patients meeting DSM-IV-TR criteria for social anxiety disorder were randomly assigned in 3 groups: 11 in paroxetine group, 11 in AMP group and 11 in combined group. Treatment intervention was done during 8 weeks period. Social Phobia Inventory (SPIN), Beck Depression Inventory (BDI-II) and Sheehan Disability Scale (SDS) were administered before and after treatment intervention. One-way Analysis of Covariance (ANCOVA) was used to determine the differences and efficacy of treatment interventions between groups. Data analysis was done by SPSS-16 software.

Results: 28 participants completed the treatment period. One-way ANCOVA results showed statistically significant differences in post-treatment scores of social phobia (p=0.007), depressive symptoms (p=0.007) and daily life functioning (p=0.011) between three groups. Bonferroni correction showed that combined treatment is significantly more effective than AMP in reducing social phobia symptoms (p=0.007), depressive symptoms (p=0.022) and enhancing daily life functioning (0.019). Yet, there were no significant differences between Paroxetine and combined treatment in all post-treatment scores (p=0.890, p=1.000, p=1.000 for social phobia, depressive symptoms and daily life functioning respectively). Paroxetine showed more significant improvement of depressive symptoms (p=0.016) and enhancing daily life functioning (p=0.045) than AMP. Also, there were no significant differences between paroxetine and AMP in reducing social anxiety symptoms.

Discussion: It seems that paroxetine has wider effect in reducing social anxiety symptoms, depressive symptoms and enhancing daily life functioning than AMP and adding the AMP to paroxetine does not make significant changes than medicating with paroxetine alone.

Key Words: Paroxetine, Attention Modification Program, Social Anxiety, Social phobia.

ABSTRACT

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1. Introduction

Social phobia or social anxiety disorder is defined as the fear of social situations such as criticism and being in touch with strangers and becoming embarrassed in social meetings or verbal presentation in front of others. They may also experience specific fears when they are doing certain activities such as writing, speaking in front of others or unspecific fears in social situations (McClure, 2009). Compared with matched unaffected controls, individuals with SAD report impaired social functioning, diminished social support, lower levels of educational attainment, poorer occupational function, and decreased rates of marriage (Comer & Olfson, 2010).

The National Comorbidity Survey Replication Study (NCS-R), which assessed over 9,000 non-institutionalized individuals throughout the United States, found that 12.1% of people have social anxiety disorder at some point during their lives. In this survey, social anxiety disorder was the fourth most common psychiatric disorder, with only major depressive disorder, alcohol abuse, and specific phobia being more prevalent. More conservative lifetime prevalence estimates suggest that clinically significant social anxiety affects a compelling but more modest (4%) of the population (Turk et al., 2008).

Existing literature supports the link between attentional bias towards negative emotional information and emotional disorders (Amir & Taylor, 2010). There is general support for the notion of attention bias in SAD. Individuals with SAD exhibit increased attention to potentially threatening social information. Findings on attentional bias support the assumption that the stimulus-driven attentional system is more affected by threat-related stimuli in anxious individuals than in non-anxious individuals (Craig et al., 2009).

The attention-based treatments aim to modify pathological cognitive operations characteristic of emotional dysregulation rather than targeting the content of those cognitive processes that may be more specific to particular psychological disorders. For example, whereas cognitive restructuring techniques typically target disorder-specific cognitive misappraisals (e.g., fear of bodily sensations in panic disorder; fear of negative evaluation in SAD; inflated appraisals of responsibility in obsessive-compulsive disorder), attention interventions are intended to target basic underlying cognitive functions (e.g., attention control) hypothesized to play a role in the persistence of psychopathology. Thus, attention-based interventions may more directly target fundamental psychopathological vulnerabilities, while the maladaptive cognitions and behaviors characteristic of emotional disorders may be viewed as more distal expressions of those basic vulnerabilities (Amir & Taylor, 2010). Therefore, emphasizing on unconscious aspects of mental disorders in psychotherapy and research means that verbal intervention is not the only way of intervention and many other therapeutic methods such as exposure can impact unconscious information processing (David, Ellis & Lynn, 2010; Dobson, 2010).

According to the Schematic Propositional Analogical Associative Representation Systems (SPAARS) model of emotion, the so called basic emotions have an innate prewired component and certain emotions may come to be elicited directly, without any apparent “on-line” interpretation or appraisal (Power & Dalgleish, 2008). Some types of information processing (including both perceptual and semantic processing), by their nature, cannot be made conscious because they are represented in our memory in a format (e.g., non-verbal associations) that is not consciously accessible (Schacter & Tulving, 1994). Few workers in the field have assimilated this line of cognitive unconscious research in psychotherapy.

Indirect evidence for the causal role of attentional bias to threat in SAD has been evaluated in the context of treatment outcome studies. That is, if attentional bias to threat is a necessary condition for SAD, amelioration of the disorder should be associated with a reduction of attentional bias to threat. Empirical investigations have generally supported this hypothesis in socially anxious individuals using both the emotional Stroop paradigm and the dot probe paradigm (Amir & Boymea, 2010).

Several randomized, controlled trials have established the efficacy of both Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRI) in the treatment of generalized social anxiety disorder. The fact that SSRIs and SNRIs share similar pharmacological properties and safety profiles has supported their role as the first-line pharmacological agents. None of these medications has been established as superior to another, in efficacy or acceptability. But, paroxetine in its immediate-release and controlled-release forms is one of the SSRIs most studied in randomized, controlled trials for the treatment of social anxiety disorder, and it was the first drug to receive US Food and Drug Administration (FDA) approval for this indication. Findings on the effectiveness of pharmaco-
therapy and psychotherapy are not consistent and each one has been shown to have successes in treating SAD (Blanco et al., 2010).

Our knowledge and understanding of basic attentional processes in generating and regulating emotion and of how attentional deviation could cause emotional disorder is developing. Also, in regard to a causal role of the attentional bias in emotional disorders (Amir & Bomyea, 2010), we face some questions: “could changes in attention be effective in reducing the symptoms of emotional disorders (especially in social anxiety disorder)? Are there any differences between Attention Modification Program and paroxetine in treating social anxiety disorder?”

2. Methods

33 patients with social anxiety disorder referring to outpatient clinics in Tehran were recruited and randomly assigned in 3 groups in a semi-experimental research design. Independent variable was a 3-typed treatment intervention including Attention Modification Program, pharmacotherapy (Treatment As Usual to stand as a control group) and a combination of both. Dependent variable was the possibility of some therapeutic changes in social anxiety disorder, depression and daily life functioning.

Participants were diagnosed by psychiatrists, on the basis of Diagnostic and Statistical Manual of mental disorders (DSM-IV-TR) criteria (American Psychiatric Association, 2000), who then signed the consent sheet. All participants were informed that their information will be kept confidential and will be used for the research purpose. Structured Clinical Interview for axis I Disorders (SCID-I, First et al., 1996) and axis II Disorders (SCID-II, First et al., 1997) was administered to finalize the diagnosis. Participants with SAD who were under psychotherapy and pharmacotherapy prior to this research, also participants with suicidal ideation, substance abuse and other axis I and II disorders were all excluded from this study. Participants with SAD, who had 18 to 50 years of age and middle school or higher levels of education, were included in this study.

Participants were randomly assigned in 3 groups: 11 patients in paroxetine group, 11 patients in Attention Modification Program group and 11 patients in combined group. 2 patients in the paroxetine group and 2 others in the combined group left the study because of the drug side effects. 1 patient in the Attention Modification Program group also left the study. They received, however, alternative therapies. Therefore, this study was done by 28 participants in 3 groups. Demographic characteristic of participants have been presented in table1.

A software known as the Probe Detection Task had been applied by McLeod (1986) for the first time for detecting attentional biases. Amir and his colleagues (2009) used modified version of this software for treating some mental disorders especially social anxiety disorder. A computer based program adopted from Amir and his colleagues’ work was written by a computer programmer (Saeed Khavandizadeh Aghdam) and the corresponding author of this article in Visual Basic language. This program has the possibility of presenting words and pictures. 14 socio-emotionally neutral words and 14 socially emotion evoking words were adopted from Ostvar (2006) and were used as stimulus in this program. Patients would be sitting in front of a 17 inches monitor at a 30 centimeter distance. All randomly paired words (emotional and neutral) were presented in a white Arial 12 font inside two rectangles on the center of monitor with a black background and 1.5 centimeter space between two rectangles. Therefore, all emotional words were accompanied by neutral words. All randomly paired words were presented in 500 milliseconds. A + sign were appeared in the center of the monitor about 1650 millisecond before presenting words to attract the patient’s attention. In 100 percent of trials a • sign known as the probe sign was replaced with the neutral word. The patient’s task was to press the corresponding arrow key on the keyboard immediately after observing the probe sign. In the total trials, 50 percent of emotional and neutral words were appeared on the right side and 50 percent on the left side. Thus, 196 trials were formed and by repeating the trials we had 392 trials for each session per week. To make the participants acquainted with the program, 10 trials were preplanned for rehearsal at the beginning of the first session. Usually, the therapeutic period of social anxiety disorder with paroxetine is 6-12 months, with the highest therapeutic effectiveness in 8-12 weeks (Blanco et al., 2009). Our total Paroxetine sample received the daily, oral dosage of 20 mg of the generic Paroxetine prescribed by psychiatrist. Participants in the combined group received both paroxetine and Attention Modification Program as defined earlier. Treatment interventions in all 3 groups were done during 8 weeks period in this study. The limitations of this study are the lack of placebo for the paroxetine and sham intervention for the Attention Modification Program and not blinding the investigators.
2.1. Measurement Tools

Structured Clinical Interview (SCID), Social Phobia Inventory (SPIN), Beck Depression Inventory (BDI-II) and Sheehan Disability Scale (SDS) were administered before and after intervention.

Structured Clinical Interview (SCID-I and II): In a study on 299 individuals, 18 to 65 years old who had been referred to inpatient or outpatient clinics in Tehran, psychometric properties of SCID were assessed. In this study the results of psychiatrist interviews and SCID were compared. The validity of SCIDS was high, measured by the diagnosis made by independent psychiatric interviews. On the other hand, the diagnostic agreements between test and retest SCID administration were fair to good for most diagnostic categories. Overall weighted k was 0.52 for current diagnoses and 0.55 for lifetime diagnoses. Specificity values for most psychiatric disorders were high (>0.85) (Sharifi, 2009).

Social Phobia Inventory (SPIN): Connor and his colleagues (2000) made this inventory for assessing social anxiety. SPIN consists of 17 items rated on a scale from 0 to 4 (not at all, a little bit, somewhat, very much and extremely). The full scale score thus ranges from 0 to 68. The result of Connor study indicates that SPIN exhibits acceptable psychometric properties. It demonstrates both good test-retest reliability (0.78-0.89) and internal cohesion (α=0.94). The SPIN also shows a substantial difference between people with social phobia and people without, when compared with a gold standard clinical interview. In a study in Iran, Abdi (2007) reported acceptable internal consistency (α=0.86) and good test-retest reliability (0.83).

Beck Depression Inventory (BDI-II) is a 21 item self-reporting scale for assessing severity of depression. Each item has a score of 0 to 3 and 0 to 63 for the whole scale. Research studies focusing on the psychometric properties of the Beck Depression Inventory (BDI) with psychiatric and non-psychiatric samples were reviewed from 1961 to June, 1986. A meta-analysis of the BDI’s internal consistency estimates, yielded a mean coefficient alpha of 0.86 for psychiatric patients and 0.81 for non-psychiatric subjects. The concurrent validities of the BDI, with respect to clinical ratings, and the Hamilton Psychiatric Rating Scale for Depression (HRSD) were also high. The mean correlations of the BDI samples with clinical ratings and the HRSD were 0.72 and 0.73, respectively for psychiatric patients. With non-psychiatric subjects, the mean correlations of the BDI with clinical ratings and the HRSD were 0.60 and 0.74, respectively. Recent evidence indicates that the BDI discriminates subtypes of depression and differentiates depression from anxiety (Beck et al., 1988). A study on 94 Iranian samples has reported good test-retest reliability (0.94) and alpha coefficient (0.91) (Fata et al., 2005).

The Sheehan Disability Scale (SDS) is a self-reporting visual analog scale and measures impairment in daily life functioning. The scale generates 3 scores in 3 items: a work disability score, a social life disability score, a family life disability score and a total score. Scores for each item range from 0 to 10 on a Likert scale. The 3 items can also be summed into a single dimensional measure of global functional impairment, ranging from 0 (unimpaired) to 30 (highly impaired). Elevated score (≥5) on each item has been shown to be related to high risk in psychiatric disorders. There are also evidences that show SDS is sensitive to therapeutic changes (Sheehan, 1983). In a study on 54 Spanish patients with social phobia (based on DSM-IV criteria) and 53 healthy individuals, convergent validity of SDS with Global Assessment of Functioning was 0.39. Internal consistency for SDS subscale was 0.75 (Cronbach’s alpha) and test-retest reliability was 0.88 (Gonzalez et al., 2009).

3. Results

Analysis on demographic data and pre-treatment scores statistically showed no significant difference between the 3 groups. As the table 1 presents there were statistically no significant differences between the 3 groups in sex (p>0.05), age (p>0.05), job (p>0.05) and educational level (p>0.05) of participants. Results of the Analysis of Variance (ANOVA) on pre-treatment scores of SPIN (p>0.05), BDI-II (p>0.05) and SDS (p>0.05) presented in table 2 also showed no statistically significant difference between the 3 groups. One-way Analysis of Covariance (ANCOVA) on SPIN, BDI-II and SDS post-treatment scores showed statistically significant differences between the 3 groups. The results of ANCOVA have been shown in table 3. As table 3 shows, the effect of groups on SPIN (F=6.09, df=2, p=0.007), BDI-II (F=6.09, df=2, p=0.007) and SDS (F=5.44, df=2, p=0.011) post-treatment is significant. Bonferroni correction revealed that differences between the mean of social anxiety post-treatment scores in combined group and AMP group was statistically significant (p=0.007). However, there were statistically no significant differences between the mean of social anxiety post-treatment scores in paroxetine and combined group (p=0.887) and also between paroxetine and the AMP group (p=0.085). As a result, it was shown that combined treatment was
more effective than AMP in reducing social anxiety symptoms. Bonferroni correction on the mean of SDS (p=1.000) and depression (p=1.000) scores suggested that there is no significant difference between paroxetine and the combined group, but there are significant differences between paroxetine and AMP group on the mean of BDI (p=0.016) and SDS (p=0.045) scores. Also, there were significant differences between combined and AMP group on the mean of SDS, DBI-II (p=0.022) and SDS (p=0.019) post-treatment scores. The results of p values of pair wise posthoc comparisons have been shown in table 4. The results suggested that paroxetine and combined treatment were more effective than AMP in reducing depressive symptoms and enhancing daily life functioning. Therefore, adding the AMP to paroxetine does not make any significant changes compared to medicating with paroxetine alone. These results and modified means of SPIN, BDI-II and SDS post-treatment scores have been presented in Graph 1.

Table 1. Demographic properties of participants in 3 groups: (proportions, ANOVA results, χ², F results, Standard Deviations and p values). SDs are in brackets

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>χ²</th>
<th>F</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (%women)</td>
<td>Paroxetine</td>
<td>AMP</td>
<td>Combined</td>
<td></td>
</tr>
<tr>
<td></td>
<td>44</td>
<td>30</td>
<td>33</td>
<td>χ</td>
</tr>
<tr>
<td>Age (years)</td>
<td>30.44(7.68)</td>
<td>25.20(4.44)</td>
<td>27.22(5.40)</td>
<td>0.185</td>
</tr>
<tr>
<td>Education</td>
<td>15.44(2.51)</td>
<td>14.40(2.33)</td>
<td>14.89(2.71)</td>
<td>0.000</td>
</tr>
<tr>
<td>Marital status (%married)</td>
<td>44</td>
<td>30</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Job (%unemployed, %student)</td>
<td>33,11</td>
<td>50,20</td>
<td>33,22</td>
<td>χ²=1.01</td>
</tr>
</tbody>
</table>

Table 2. Means, Standard Deviations and ANOVA results of pre-treatment scores of measures

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>F</th>
<th>sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPIN</td>
<td>36.67 (14.08)</td>
<td>35.70 (14.70)</td>
<td>30.89 (9.25)</td>
</tr>
<tr>
<td>BDI-II</td>
<td>22.56 (8.79)</td>
<td>22.70 (12.64)</td>
<td>24.56 (10.90)</td>
</tr>
<tr>
<td>SDS</td>
<td>17.56 (5.70)</td>
<td>18.20 (4.64)</td>
<td>19.47 (4.47)</td>
</tr>
</tbody>
</table>

Table 3. Results of ANCOVA on post-treatment scores of measures

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sum of Square</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>Sig</th>
<th>Partial eta Square</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPIN</td>
<td>830.26</td>
<td>2</td>
<td>415.13</td>
<td>6.09</td>
<td>0.007</td>
<td>0.34</td>
</tr>
<tr>
<td>BDI-II</td>
<td>305.91</td>
<td>2</td>
<td>152.96</td>
<td>6.09</td>
<td>0.007</td>
<td>0.34</td>
</tr>
<tr>
<td>SDS</td>
<td>122.51</td>
<td>2</td>
<td>61.26</td>
<td>5.44</td>
<td>0.011</td>
<td>0.31</td>
</tr>
</tbody>
</table>
### Table 4. P values of pair wise posthoc comparisons

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group Paroxetine vs. Combined</th>
<th>AMP vs. Combined</th>
<th>Paroxetine vs. Amp</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPIN</td>
<td>0.890</td>
<td>0.007</td>
<td>0.090</td>
</tr>
<tr>
<td>BDI-II</td>
<td>1.000</td>
<td>0.022</td>
<td>0.016</td>
</tr>
<tr>
<td>SDS</td>
<td>1.000</td>
<td>0.019</td>
<td>0.045</td>
</tr>
</tbody>
</table>

#### Graph 1. Modified means of SPIN, BDI-II and SDS post-treatment scores

#### 4. Discussion

The results of this study showed that paroxetine and the combined treatment (paroxetine and AMP) are more effective than the AMP in reducing social anxiety symptoms and enhancing the total daily life functioning. A Meta-analysis of a series of AMP effectiveness studies has revealed very diverse results. Treating psychological disorders by modifying attention bias is in its initial stages and results of effectiveness of this method are different in literature (Hakamata et al., 2010). Studies on the effectiveness of the paroxetine, however, have always showed consistent positive findings (e.g. Stein et al., 1996; Allgulander, 1999; Leibowitz et al., 2002).

Effectiveness of paroxetine in this study is consistent with other investigations on the effectiveness of Selective Serotonin Reuptake Inhibitors (SSRI) in reducing social anxiety symptoms (e.g. Gould et al., 1997; Stein et al., 1996; Leibowitz et al., 2002). Therefore, it was not out of expectation that paroxetine could be effective in this study too. However, the smaller effectiveness of AMP could be a matter of discussion in the present research. As mentioned above this method is in its initial stages and there are many variables that their impacts on modifying attention biases are not yet completely investigated. According to the attention bias theory, targeting mechanisms of attention control related to bias to threat could directly impact social anxiety symptoms in affected people. Based on this hypothesis, attention bias modification training targets information processing linked to threat and is related to functioning in brain systems sensitive to threat in anxious individuals (March, 2010). In a meta-analysis study from 1995 to 2010,
Hakamata and his colleagues (2010) suggested that therapeutic outcomes of AMP were not similar because of inconsistency in controlling some variables such as word or picture, left-right or top-down presentation of stimulus, number of stimulus, etc. These variables have to be investigated to determine their exact impacts on modifying the attention bias leading to therapeutic effectiveness.

Reduction in depression scores in this study is consistent with other investigations that emphasize on relation between depression and social anxiety disorder. For example, in a study Moscovitch and his colleagues (2005) reported that paroxetine causes changes in social anxiety symptoms and accordingly changes in depressive symptoms. In another research, Dempsey (2009) found that paroxetine leads to reduction in social anxiety symptoms during time, along with reduction in depressive symptoms. In regard to less reduction in depressive symptoms of AMP group versus the two other groups, it seems that there would be direct correlation between changes in social anxiety symptoms and depressive symptoms. Therefore, less reduction in depressive symptoms is because of the fact that there is less reduction in social anxiety symptoms in AMP group than in two other groups. This result is consistent with Kocabasoglu and his colleagues (2003), who suggested that there are correlations between improvement of anxiety and depressive symptoms. In addition, it seems that there are common factors between social anxiety and depression that paroxetine also targets; factors such as neurochemical links between depression and anxiety (Iny et al., 1994; Zaninelli, 1999), interpersonal sensitivity (Vidyamidhi et al., 2009) and dysfunctional attitudes (Reiter et al., 1991).

Consistent with other studies (e.g. McCafferty, 2000; Baldwin et al., 1999; Sheehan et al., 2003) this research showed that paroxetine leads to daily life functioning improvement in patients with social anxiety disorder. Sheehan and his colleagues (2000) suggest that presence of mood and anxiety disorders strongly cause impairment in daily life functions. As a result, it is natural that daily life functioning improves in accordance with social anxiety symptoms reduction. Therefore, it seems that the smaller amount of functional improvement in AMP group versus two other groups could be the result of lesser improvement in social anxiety symptoms of this group.

In general, it seems that the limitation in sample size of the present study on one hand, and the lack of identification of more detailed determinants of the possible effective factors in attention bias modification training procedure in literature (Hakamata, 2010) on the other hand, have affected the results of this study. This could partially explain the smaller effectiveness of AMP in treating social anxiety symptoms in comparison to the other two methods. Another reason for less effectiveness of AMP could be unfamiliarity of the participants with computer-based treatments. Patients are familiar with standard treatments and it might have been difficult for them to accept that computer could treat psychological disorders. It seems that paroxetine has wider effect in reducing social anxiety symptoms, depressive symptoms and enhancing daily life functioning than AMP. Therefore, it seems that paroxetine could be a better choice for treating social anxiety, depressive symptoms and enhancing daily life functioning than AMP and more research need to be done to prove that AMP can replace it.

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