Available online at www.sciencedirect.com
SCIENCE DIRECT®
European Psychiatry 21 (2006) 174–179
EUROPEAN PSYCHIATRY
http://france.elsevier.com/direct/EURPSY/

Original report

A comparative study of fluoxetine, moclobemide, and tianeptine in the treatment of posttraumatic stress disorder following an earthquake

E. Önder [b], Ü. Tural [a,*], T. Aker [b]

[a] *Department of Psychiatry, Medical School of Kocaeli University, Kocaeli, Turkey*
[b] *Center for Psychological Trauma, Medical School of Kocaeli University, Kocaeli, Turkey*

Received 30 October 2003; accepted 24 March 2005

Available online 17 June 2005

Abstract

***Purpose.* –** Although antidepressant drugs have been proven as an effective treatment for posttraumatic stress disorder (PTSD), there are few comparative studies of antidepressants that are acting on different neurotransmitters. The main aim of this study is to compare the efficacy of different class of antidepressant drugs on the PTSD.

***Subjects/materials and methods.* –** In this open label study, the patients who met DSM-IV criteria for PTSD were randomly assigned to flexible doses of fluoxetine, moclobemide, or tianeptine. After the first assessment, consecutive assessments were performed at the end of weeks 2, 4, 8, and 12 using clinician administered PTSD scale (CAPS) and Clinical Global Impression of Severity (CGI-S). Changes in the total score of CAPS and sub-scale scores of symptom clusters (re-experience, avoidance, and hyperarousal) were the main output of efficacy. All statistics were based on intention-to-treat and last-observation-carried-forward (LOCF) principles.

***Results.* –** Thirty-eight patients were assigned to fluoxetine, 35 patients were assigned to moclobemide, and 30 patients were assigned to tianeptine group. Gender distributions and mean ages of the treatment groups were not significantly different. Drop-out rates due to an adverse events or unknown reasons were not significantly different among fluoxetine (18.4%), moclobemide (14.3%), and tianeptine (20.0%) groups. All three treatments has led to a significant improvement in PTSD severity assessed with CAPS total score (ANOVA $P < 0.001$). Similarly, total scores of re-experiencing, avoidance, and hyperarousal clusters that are subscales of CAPS were significantly reduced by all three treatments (with ANOVA all P values < 0.001). There was not significant difference in terms of treatment effect between three groups.

***Discussion.* –** Treatment groups showed very similar improvement on all ratings scales. The findings support that fluoxetine, moclobemide, and tianeptine are all effective in the treatment of PTSD. Different mechanisms of action for these antidepressant drugs might result in the same common neurochemical end point. However, further studies using different classes of antidepressant drugs are needed.

Keywords: Posttraumatic stress disorder; Natural disasters; Fluoxetine; Moclobemide; Tianeptine; Treatment

1. Introduction

Posttraumatic stress disorder (PTSD) is characterized by the development of characteristic symptoms following exposure to a markedly distressing traumatic event [3]. The person's response to the traumatic event must involve intense fear, helplessness, or horror, while the characteristic symptoms resulting from the exposure to the extreme trauma include persistent re-experiencing of the traumatic event (Criterion B; intrusive thoughts, nightmares, flashbacks, images or memories), persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (Criterion C; flattened affect or detachment and/or loss of interest and motivation), and persistent symptoms of increased arousal (Criterion D; startle reactions, poor concentration, irritability and jumpiness, insomnia, and hypervigilance). Natural disasters, such as earthquakes, hurricanes and cyclones, floods, and tornadoes are traumatic events that can also cause PTSD [3].

Because of high prevalence, comorbidity and disability of PTSD, it is important to alleviate the symptoms of this disorder [2,6,10,14]. There is clear evidence for effective pharma-

* Corresponding author. Present address: Kocaeli Üniversitesi Tıp Fakültesi Psikiyatri Bölümü, Derince-İzmit, Kocaeli 41900, Turkey. Tel.: +90 262 233 5981x1708; fax: +90 262 233 5461.
E-mail addresses: turalu@kou.edu.tr (Ü. Tural), turalu@hotmail.com (Ü. Tural).

0924-9338/$ - see front matter © 2005 Elsevier SAS. All rights reserved.
doi:10.1016/j.eurpsy.2005.03.007

cotherapy of PTSD [2,6,10]. Currently, antidepressants are the primary choice of pharmacotherapy for PTSD [2,6,10,14]. Antidepressants with empirical support include monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs). However, the research literature examining SSRIs in the treatment of PTSD already exceeds that of the tricylic antidepressants and MAOIs, and there are several large, double-blind, placebo-controlled studies. Thus, considering reported overall efficacy and side effect profiles, SSRIs emerge as the preferred first line treatment for PTSD [2,6,10]. Among the SSRIs, fluoxetine has been found as effective in the pharmacological treatment of PTSD. At least four positive double-blind, placebo-controlled studies exploring the efficacy of fluoxetine in PTSD were reported [7,19,20,25]. In mentioned studies, reported changes were most marked in the intrusive [19] hyperarousal [19,25], avoidance [20] and numbing symptom subcategories [25]. On the other hand, moclobemide and tianeptine have not been proven as effective and safe in long-term treatment of PTSD. Traditional MAOIs have shown efficacy in the treatment of PTSD, but their use is limited by some serious drug and food interactions. The development of reversible MAOIs which are associated with a lower risk of hypertensive reactions has renewed interest in this class of antidepressants. There is one study reporting promising results for moclobemide, which is a reversible inhibitor of MAO-A [22]. MAO-A degrades serotonin and norepinephrine preferentially [17,24]. One of the metabolites of moclobemide does inhibit MAO-B; however, this action is minimally significant in humans [17]. In that 12-week open trial of moclobemide, Neal et al. [22] reported that among their 20 patients with PTSD due to diverse traumas, moclobemide significantly reduced intrusions, avoidance, and hyperarousal symptoms of PTSD as well as depression, with improvement being most marked for avoidance/numbing symptoms.

The investigation of tianeptine in PTSD is also not sufficient to prove its efficacy in the treatment of PTSD although it has been shown that tianeptine could prevent and reverse the damage of hippocampal neurons which are triggered by stress in animal studies [8,9]. Tianeptine stimulates serotonin uptake in the brain, which seems an opposite mechanism of functioning to SSRIs, however, results in enhanced serotoninergic activity [24,26]. In an open label study, 44 veterans suffering from PTSD were treated with either tianeptine or fluoxetine for 5 months. Results showed no significant differences between two antidepressants in the reduction of symptom severity and anxiety level; however, tianeptin group needed less additional anxiolitic or hypnotic drugs than fluoxetine group [13]. In another study, the anxiolytic effect of tianeptine 25–50 mg/day for 6 weeks was similar to that of the anxiolytic alprazolam 1–2 mg/day for 6 weeks in patients with adjustment disorder and mixed anxio-depressive features [4].

However, studies comparing the efficacy of different antidepressants on the symptom clusters of PTSD are limited in number. Most of the studies are comparing an active drug with placebo. Therefore, there is less evidence presented by comparative studies of superiority of any antidepressant on certain symptoms or symptom clusters of PTSD. We selected three different types antidepressant with different mechanisms: fluoxetine blocks reuptake of serotonin in the synaptic cleft, tianeptine is a serotonin reuptake enhancer, and moclobemide inhibits monoamine oxidase, the degrading enzyme of serotonin and noradrenalin. The aim of this study is to compare the efficacy of fluoxetine, moclobemide and tianeptine on severity of global and symptom clusters (re-experiencing, emotional numbness and avoidance, hyperarousal) of PTSD.

2. Subjects and methods

2.1. Subjects

The entire sample experienced to the 1999 Marmara earthquake that measured 7.4 on the Richter scale at 3:01 AM on August 17, 1999. Marmara, which is located in the north west of Turkey, is the most crowded and industrial region of the country. The earthquake resulted in 15,226 death, 23,983 wounded, and caused approximately US$9–13 billion of property damage. 27,634 of households were collapsed totally or heavily, and 27,428 of households were damaged moderately. 14,444,298 inhabitants living in the Marmara region are thought to be affected by the event totally [15]. Patients were enrolled between 4th and 12th months after the disaster. After an oral and written explanation of the study's aim, all subjects gave written informed consent for their participation. The patients were male and female outpatients 18 years and older, who met DSM-IV criteria [3] for a primary diagnosis of PTSD as determined by SCID [12]. They were recruited using local outpatient psychiatric unit of the University ($n = 56$) and Psychological Trauma Center ($n = 47$). Only patients with PTSD due to the earthquake were included in the study. All patients were screened for general medical health, including medical history, routine blood and urine tests to assess general medical conditions, which can interact with the metabolism of the drugs or mimic the psychiatric symptoms. Subjects with clinically significant medical illness, including diabetes mellitus, any cardiac condition causing documented hemodynamic compromise, epilepsy or pregnancy were excluded. Other exclusion criteria included (1) current or past history of bipolar disorder, schizophrenic, or other psychotic disorder, (2) alcohol or substance abuse or dependence in the past 6 months, (3) primary diagnosis of major depression assessed with SCID or a score of 12 points or higher on 17-item Hamilton Depression Scale [18].

2.2. Procedure

This study was an open label, flexible-dose randomized comparison of three different classes of antidepressants, fluoxetine, moclobemide, and tianeptine. Tianeptin and moclobe-