



Pharmacotherapy for Reducing the Grieving Process of Romantic Relationship Breakup: A Clinical Trial

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Abstract

The breakup of a romantic relationship imposes considerable grief to individuals and is actually a psychological and psychiatric challenge. The current study is a clinical trial of a pharmacologic agent reducing post-relationship grief. 90 female patients with the mean age of 29.55 ± 4.65 years were divided into two groups as an intervention group ($n = 45$) and the control group ($n = 45$). All patients were experiencing a diagnosed depression due to a romantic breakup during the last six months. The control group received a standard pharmacotherapy for depression, which was 50 mg sertraline daily. The intervention group received an additional 0.05 mg Clonidine daily. The treatment was continued for 8 weeks, and the visual analog scale evaluated the subjective report of the patients for grief and intensity of love. Comparison of pre-treatment and post-treatment grief and intensity of love were analyzed using ANOVA. Clonidine induced a significant decrease in the post-breakup grief with no significant change in the intensity of love. This pharmacotherapy is suggested for better management of romantic breakup.

Keywords: Detachment Suffering, Grieving Romantic Breakup, Heartbreak, Romantic Love

1. Background

Romantic love is a universal experience and life milestone (1). From Eric Erickson's point of view, the most critical concern in the age range of 40 to 20 years is intimacy versus isolation, meaning that development in this period of life revolves around the ability to make love and the formation of deep and secure emotional relationships while failure in this area will lead to isolation (2). However, love poses consequences, one of the most important of which is the likelihood of emotional breakup. The end of a romantic relationship leads to physical disturbances and emotional stress (3), and separation from a loved one can trigger the grieving responses, sometimes leading to major depressive disorder (4).

The level of attachment in emotional relationships could be various. One of the issues affecting this attachment is the specific personality temperament of individuals. Among the four factors of harm avoidance, novelty seeking, reward dependency, persistence, the third one, "reward dependence," plays a major role in attachment and its depth and intensity. People with higher reward

dependence, show greater and deeper processing of interpersonal symptoms, enter into romantic relationships more intensely, and experience more disturbance due to the breakdown of the relationship (2). Neurobiologically, the reward dependence is related to serotonin and norepinephrine neurotransmitters (5-7). Some studies indicated the role of the noradrenergic system in anxiety disorders thereupon drugs such as clonidine has been successfully used to modulate the arousal of this system and to control anxiety (4). However, to the best of our knowledge, there is no previous report about modifying the "reward dependence" trait, which is closely linked to the noradrenergic system, to management of romantic breakup.

One of the outstanding limitations of current approaches for the treatment of depression is that little attention is paid to the related causes. As in classical psychiatry, diseases are diagnosed and treated according to certain criteria and not according to causes. But in modern psychiatrist, the individualization is of importance (8).

2. Objectives

Considering the fact that a particular interpersonal loss (love failure) can cause depression and given the fact that the love is a neurobiological eruption closely interwoven with reward dependence, we formulated the novel approach of reducing noradrenergic arousal by low dose clonidine, along with anti-depressant therapy with SSRIs, for this specific condition. We postulated that this pharmacotherapy approach could reduce suffering from a romantic relationship breakup.

3. Methods

3.1. Setting and Participants

Patients were randomly selected from women living in Tabriz city, who referred to the Psychiatric Clinic of Tabriz Razi Educational and Medical Center from 2017 May to 2018 March.

3.2. Sample Size

Since no similar study had been done before, the formula of comparison of two ratios, type I error 0.05, power of 80%, was used, and 30% difference in the severity of suffering from detachment was considered as the primary outcome. Thus, considering the probability of sample drop (1% increase in sample size), 90 samples were studied.

90 women with a mean age of 29.55 ± 4.65 years were enrolled in the study. Patients were between 20 and 40 years old. The intervention group consisted of 45 patients with a mean age of 30.2 ± 4.96 and control group 45, with a mean of 28.91 ± 4.35 .

3.3. Randomization

Samples were randomly selected and divided into two groups of 45 individuals using Rand list (version 1.2) software.

Patients were referred to the relevant expert after diagnosis and included in the study as group A or B based on the list. The therapist was blind to these two groups.

3.4. Clinical Evaluation

Diagnosis of depression in patients was determined by a psychiatrist based on a structured interview-SCID and DSM-5 criteria.

Depression began after the romantic breakup reported in the last 6 months. Beck Depression Inventory was used to measure the severity of depression. Patients with one or more of the following (exclusion criteria) were also excluded from the study:

1. Concomitant anxiety disorder, obsessive-compulsive disorder, personality disorders, substance abuse, psychotic disorder, bipolar mood disorder

2. Take of antihypertensive medications
3. History of heart disease
4. Depression due to medical condition
5. The ego-dystonic cases, whose love is unreal and is the dependency that is more obsessional
6. Severe depression with a score of 35 in the Beck inventory
7. Cases that break up has caused major changes in their lives, such as divorce.

3.5. Ethical Considerations

After a brief description of the project, the informed consent of all participants was obtained, and their company was voluntary. The voluntary codes of ethics for subjects during the study were considered, including the fact that the registration of data with encoding and without identity information, at any time from the study, one could withdraw from the study without any reason. Also, the company did not have an impact on healthcare services.

3.6. Measuring Tools

The visual analog scale (VSA) was used to measure the intensity of love and suffering from separation and their changes. This scale is used to measure emotions that cannot be measured physically, such as mental qualities and pain. The use of VSA to measure the severity of pain is a well-known clinical and research application and is used as a subjective criterion (as stated by the patient himself) in reports and assessments (Kindler, Harms, Amsler, Ihde-Scholl, & Scheidegger, 2000). In this study, the subjective severity of love and suffering both in the time of diagnosis and after treatment was recorded based upon this scale. Ultimately, the two intensities were compared as a pre- and post-treatment comparison.

3.7. Therapeutic Intervention

In this study all participants received 50 mg Sertraline as standard treatment of depression. We rounded the control group off with this treatment. In the intervention group, 0.05 mg of clonidine was added daily to standard treatment. The duration of treatment for all participants was 8 weeks.

We prescribe low dosage of clonidine due to the prevention of adverse effects of drugs because there was no known dosage from previous studies.

3.8. Statistical Methods

Data were entered into SPSS statistical software. Descriptive analyzes such as mean, standard deviation, etc. were used. Analysis of covariance ANCOVA was used as a comparison before and after pre-treatment/post-treatment, and the change in the severity of suffering and love before and after treatment was compared. The significance level was considered $P < 0.05$.

4. Results

90 subjects were participated in this study; the minimum age was 21 and maximum 40 years. The mean age of the subjects in the intervention group was 30.2 (SD = 4.96) and the control group was 28.91 (SD = 4.35), respectively.

The evaluated outcomes were: the intensity of love and severity of suffering from detachment before treatment and 8 weeks after treatment, which was measured as visual analog scale (VSA) scores from zero to 100.

In terms of educational level, in the intervention group, 2 were diplomas, 15 were bachelors, 10 were masters, and 17 were doctoral. In the control group, 4 were diplomas, 14 were bachelor, 12 were masters, and 15 were doctoral.

In the evaluation of love intensity before treatment, in the intervention group, the minimum and maximum scores were 40 and 100, with an average of 93.92 (SD = 13.26) and in the control group, 40 and 100, respectively, with a mean of 22.29 (SD = 13.03).

In the measure of love after 8 weeks of treatment, in the intervention group, the minimum and maximum scores were zero and 100 with a mean of 50/67 (SD = 29.30) and in the control group, respectively, 10 and 100 with a mean of 93.9 (SD = 22.67).

In the measure of suffering from detachment before treatment, in the intervention group, the minimum and maximum scores were 50 and 100, with an average of 26.29 (SD = 12.97), and in the control group, 50 and 100, with a mean of 26.28 (SD = 14.87).

In the measure of suffering from detachment after 8 weeks of treatment, in the intervention group, the minimum and maximum scores were 20 and 100, with an average of 43.45 (SD = 23.32) and in the control group, 10 and 100, with an average of 41/71 (SD = 23.18)

In the mean comparison, there was a significant difference between the two groups in reducing the severity of suffering ($P < 0.001$) before and after treatment and in subjects treated with combination therapy with sertraline and clonidine severity of suffering decreased significantly compared to the group receiving sertraline alone.

The intensity of love decreased in both groups after treatment, but there was no significant difference between the two groups in the mean intensity of love before and after treatment ($P = 0.5$). Thus, the intervention did not show a significant effect on this variable. (Figure 1)

5. Discussion

This study showed that the addition of clonidine to standard antidepressant therapy in those who were depressed after a romantic breakup significantly reduced the severity of suffering from detachment, but it had no effect

on the intensity of love. There was a decrease in love intensity in both groups, but no significant difference between the two groups.

The findings of the present study, which demonstrate the efficacy of clonidine in people experiencing emotional breakup, testifies to the fact that love as a primary component of itself includes a significant arousal, probably due to the eruption of the noradrenergic system and affect most of the intrapsychic structures and behavioral and social life and also leads to a profound psychic pain.

The temperamental trait that deals with human interactions and attachment is "reward dependence". This component is neurobiologically relevant to the noradrenergic system (6). The effect of clonidine on reducing the suffering from a romantic breakup in the present study can be a reflection of the relationship of love with this temperamental trait that can pave the way for many future hypotheses and researches.

On the other hand, love is a rewarding experience, and breaking off a love affair actually means a withdrawal of a rewarding behavior. As we know, dopamine and norepinephrine play important roles in rewarding activities and one of the important regions of the brain that is associated with reward is *Lucus Coeruleus*. Clonidine is used to treat addiction withdrawal by affecting this area. Therefore, if love is also a reward-related behavior, as addiction, it can be argued that clonidine may have played a role in reducing the suffering of emotional separation.

Moreover, the effect of clonidine has been significant in reducing suffering, but it has not changed the intensity of love. This result can suggest the substantial concepts: First, love as it is considered as only an instinct for the continuation of the generation, is not only included in human temperament but also has other dimensions, and it may include aspects of a higher level of cognition. In fact, while the experience of love has physical and neurobiological aspects, there is affection, perception, and cognition behind it, which, despite the removal of the physical aspect with medicine, remains. Therefore, love is not a kind of escape from suffering or merely rewarding, although it may include them, but it also has a wider dimension.

The duration of follow-up in this study was 8 weeks, and it is unclear whether the intensity of love also changed with increasing treatment duration or dose.

Decreasing the intensity of love in both groups can be due to the effect of sertraline. Sertraline is a drug that has known effects in psychiatric disorders such as depression, anxiety and obsessive-compulsive disorder (2). The decrease in the intensity of love in this study can be due to the effect of sertraline on obsessive-compulsive aspects of love so far studied not set.

From the positive psychiatric approach (8, 9), the use of the therapeutic effect of clonidine in those experiencing suffering from emotional breakup can actually help them

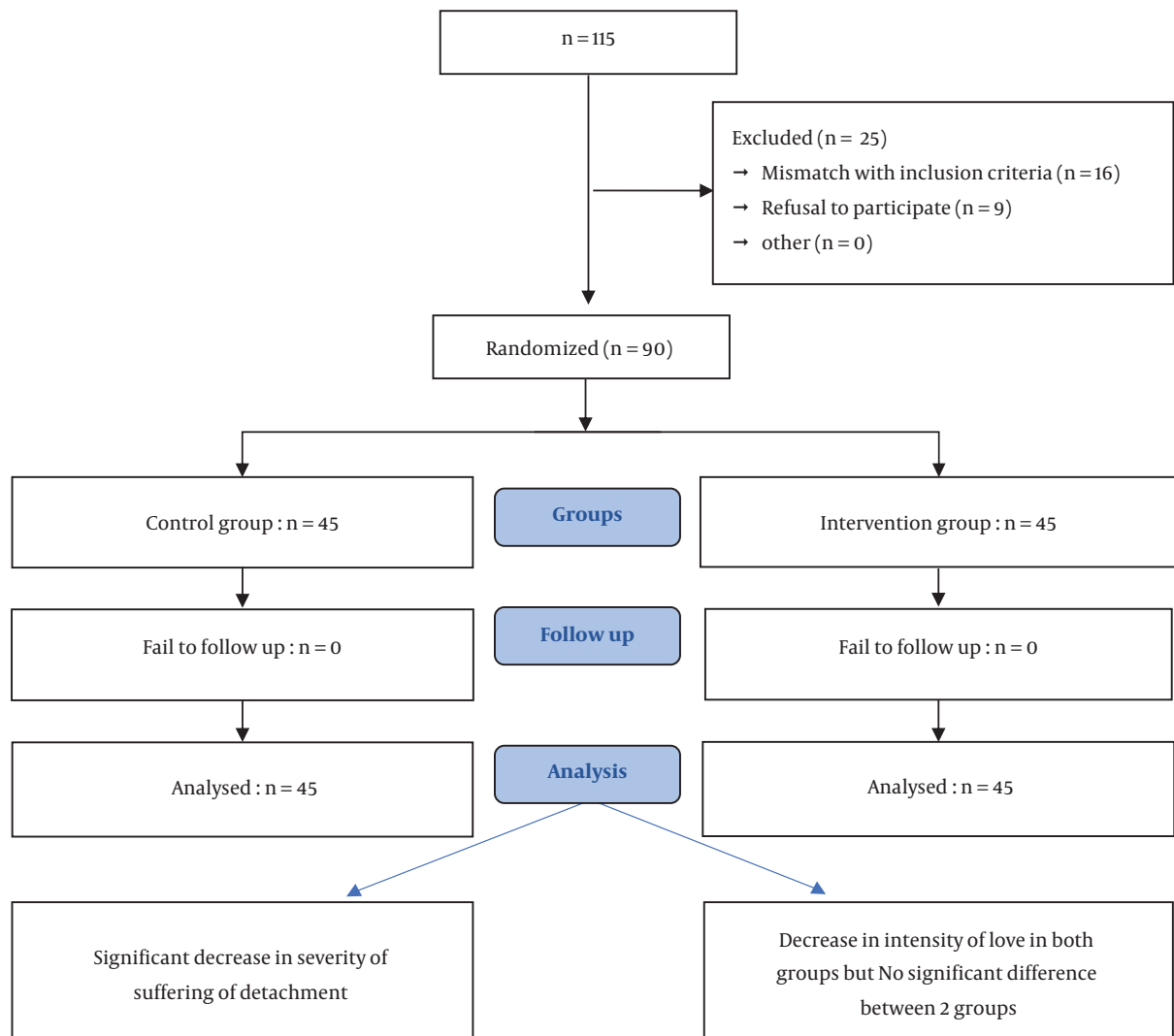


Figure 1. Clinical trial diagram

to take advantage of the developmental aspects of love.

On the whole, it must be concluded that love is not merely a painful excitation caused by a neurodegenerative system and not merely physical and physical structures. However, the suffering caused by this aspect of love is, by the way, discriminatory with medicine.

The emotional and cognitive effects of love with no distressing suffering will probably not be psychologically pathologic, and with upgraded approaches, there is no need for discounts with treatment. It does not seem that a pervasive experience like love cannot be just a sickly experience in all cases.

5.1. Limitations

Since no similar study has been conducted, it was decided to conduct this study with a sample size of 90 to obtain initial information and use it in future studies. To eliminate some confounding factors, including physiological and cultural factors, participants were selected only from women. Therefore, the inclusion of men in future research can provide more information. Patients were followed up for 8 weeks after the intervention, which is recommended to be extended in subsequent studies and the results evaluated. The dose of clonidine was not increased during treatment to prevent complications and due to time limitation.

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Footnotes

Authors' Contribution: Alireza Farnam designed the study. Azar Heidarzadeh gathered the data. Alireza Farnam and Ali Reza Shafiee-Kandjani analyzed and interpreted the results. Azar Heidarzadeh and Alireza Farnam drafted the manuscript. It was revised by Masume Zamanlu and Morteza Gojazadeh. All read and finalized the paper.

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Patient Consent: After a brief description of the project, the informed consent of all participants was obtained and their company was fully voluntary.

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