ORIGINAL RESEARCH

Comparison of efficacy of Crocus sativus L. with fluoxetine for improving depression among patients with cardiovascular diseases

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ABSTRACT
Background: The predominant contributor to psychiatric disability across the globe is depression. Hence; the present study was conducted for comparing the efficacy of Crocus sativus L. with fluoxetine for improving depression among patients with cardiovascular diseases. **Materials & methods:** A cohort of 40 patients aged between 20 and 60 years was recruited for the study. Inclusion criteria mandated that participants had a diagnosis of any form of cardiovascular disease and fulfilled the DSM IV-TR criteria for depression. The Hamilton Depression Rating Scale (HDRS), established by Hamilton in 1960, was employed to evaluate the severity of depressive symptoms.The patients were randomly assigned. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software. **Results:** Mean age of the patients of saffron group and fluoxetine group was 41.9 years and 44.7 years respectively. Baseline to 6 weeks change of HDRS score among patients of the saffron group and fluoxetine group was 11.7 and 12.1 respectively. Among saffron group, dry mouth and constipation was seen in 5 percent of the patients each. Among the Fluoxetine group, drowsiness, dry mouth and constipation was seen in 5 percent, 10 percent, and 20 percent of the patients respectively. **Conclusion:** Both the drugs showed similar efficacy in terms of improvement and incidence of adverse events in managing depression among patients with cardiovascular diseases.

Key words: Depression, Fluoxetine, Saffron

INTRODUCTION

Psychiatric disorders represent 22.8% of the global disease burden. The predominant contributor to this disability is depression, which has seen a significant rise since 1990, primarily due to population growth and an aging demographic. Approximately 350 million individuals are affected worldwide, with the economic impact of depressive disorders in the United States alone exceeding $210 billion. This figure includes around 45% related to direct costs, 5% associated with suicide-related expenses, and 50% linked to workplace costs. Such trends present considerable challenges for healthcare systems in both developed and developing nations, necessitating effective patient treatment, resource optimization, and enhancements in mental health care delivery.[1- 3]

Antidepressants, categorized into various classes with distinct mechanisms of action, are commonly prescribed for major depressive disorder and are accessible globally. Nonetheless, there remains an ongoing debate regarding their efficacy and effectiveness, as short-term benefits tend to be modest on average, and the long-term balance of benefits versus harms is frequently under-researched. Consequently, advancements in psychopharmacology are essential, yet identifying new molecular targets poses significant challenges due to the limited understanding of the mechanisms by which antidepressants exert their effects. In clinical practice, healthcare providers have a broad selection of medications at their disposal and require robust evidence to make informed decisions tailored to each

patient's needs.[4- 6] Hence; the present study was conducted for comparing the efficacy of Crocus sativus L. with fluoxetine for improving depression among patients with cardiovascular diseases.

MATERIALS & METHODS

The present study was conducted for comparing the efficacy of Crocus sativus L. with fluoxetine for improving depression among patients with cardiovascular diseases. A cohort of 40 patients aged between 20 and 60 years was recruited for the study. Inclusion criteria mandated that participants had a diagnosis of any form of cardiovascular disease and fulfilled the DSM IV-TR criteria for depression. The Hamilton Depression Rating Scale (HDRS), established by Hamilton in 1960, was employed to evaluate the severity of depressive symptoms, with scores ranging from 14 to 22 indicating the presence of depression. The patients were randomly assigned to one of two treatment groups, receiving either fluoxetine or saffron (IMPIRAN) over a six-week period. The treatment regimen involved administering one capsule every other day during the first week, followed by one capsule daily in the second week, and increasing to two capsules daily for the remainder of the study. Participants were prohibited from using any other antidepressant medications or engaging in behavioral therapy throughout the trial. The saffron capsules utilized in this research were prepared by extracting 120 grams of dried and milled C. sativus L. stigma with 1800 milliliters of 80% ethanol through a percolation method. The HDRS served as the primary measure for assessing treatment efficacy, with each patient evaluated at baseline, as well as at three and six weeks, to determine changes in depressive symptom severity. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

RESULTS

Mean age of the patients of saffron group and fluoxetine group was 41.9 years and 44.7 years respectively. Majority proportion of patients of both the study groups were males. Mean baseline HDRS score among patients of the saffron group and fluoxetine group was 17.3 and 16.7 respectively. Baseline to 3 weeks change of HDRS score among patients of the saffron group and fluoxetine group was 8.9 and 9.1 respectively. Baseline to 6 weeks change of HDRS score among patients of the saffron group and fluoxetine group was 11.7 and 12.1 respectively. Among saffron group, dry mouth and constipation was seen in 5 percent of the patients each. Among the Fluoxetine group, drowsiness, dry mouth and constipation was seen in 5 percent, 10 percent, and 20 percent of the patients respectively.

Table 1: Demographic data

Variable	Saffron group	Fluoxetine group
Mean age (years)	41.9	44.7
Males (%)	60	70
Females (%)	40	30
Baseline HDRS score (mean)	17.3	16.7
Stable angina (%)	20	30
Unstable angina (%)	40	30
NSTEMI (%)	20	20
STEMI (%)	10	20

Table 2: Comparison of change in HDRS score changes

HDRS score	Saffron group	Fluoxetine group	p-value
Baseline to 3 weeks change	8.9	9.1	0.12
Baseline to 6 weeks change	11.7	12.1	0.28

Table 3: Adverse events

Adverse events	Saffron group	Fluoxetine group
Drowsiness (%)	0	5
Dry mouth (%)	5	10
Constipation (%)	5	20

DISCUSSION

The release of fluoxetine was the beginning of a new era of safe and effective treatment for patients with depression. Fluoxetine was introduced into clinical use for the treatment of patients with depression in 1988. Since then, fluoxetine has become the most widely prescribed antidepressant drug in the world. In the following years, it was approved for use in the treatment of patients with OCD and bulimia nervosa. Other indications for its use, outside of Italy, are Premenstrual Dysphoric Disorder (PMDD) and major depression in children and adolescents.Fluoxetine is a selective inhibitor of serotonin re-uptake; it has little effect on other neurotransmitters. It is well absorbed after oral administration, with peak plasma concentrations observed after 6 to 8 hours. The parent

compound, fluoxetine, has an elimination half-life of 1 to 4 days, whereas the active metabolite, norfluoxetine, has an half-life of 7 to 10 days. This extended half-life appears to protect against sporadic noncompliance and against the occurrence of withdrawal phenomena.[6- 9]Hence; the present study was conducted for comparing the efficacy of Crocus sativus L. with fluoxetine for improving depression among patients with cardiovascular diseases.

Mean age of the patients of saffron group and fluoxetine group was 41.9 years and 44.7 years respectively. Baseline to 3 weeks change of HDRS score among patients of the saffron group and fluoxetine group was 8.9 and 9.1 respectively. Baseline to 6 weeks change of HDRS score among patients of the saffron group and fluoxetine group was 11.7 and 12.1 respectively. Among saffron group, dry mouth and constipation was seen in 5 percent of the patients each. Among the Fluoxetine group, drowsiness, dry mouth and constipation was seen in 5 percent, 10 percent, and 20 percent of the patients respectively.Cipriani A et al determined the efficacy of fluoxetine, compared with other ADs, in alleviating the acute symptoms of depression, and to review its acceptability.Relevant studies were located by searching the Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR), the Cochrane Central Register of Controlled Trials (CENTRAL), Medline (1966-2004) and Embase (1974-2004). Non-English language articles were included.On a dichotomous outcome fluoxetine was less effective than dothiepin (Peto OR: 2.09, 95% CI 1.08 to 4.05), sertraline (Peto OR: 1.40, 95% CI 1.11 to 1.76), mirtazapine (Peto OR: 1.64, 95% CI 1.01 to 2.65) and venlafaxine (Peto OR: 1.40, 95% CI 1.15 to 1.70). On a continuous outcome, fluoxetine was more effective than ABT-200 (Standardised Mean Difference (SMD) random effects: - 1.85, 95% CI - 2.25 to - 1.45) and milnacipran (SMD random effects: - 0.38, 95% CI - 0.71 to - 0.06); conversely, it was less effective than venlafaxine (SMD random effect: 0.11, 95% CI 0.00 to 0.23), however these figures were of borderline statistical significance.Fluoxetine was better tolerated than TCAs considered as a group (Peto OR: 0.78, 95% CI 0.68 to 0.89), and was better tolerated in comparison with individual ADs, in particular than amitriptyline (Peto OR: 0.64, 95% CI 0.47 to 0.85) and imipramine (Peto OR: 0.79, 95% CI 0.63 to 0.99), and among newer ADs than ABT-200 (Peto OR: 0.21, 95% CI 0.10 to 0.41), pramipexole and reboxetine.There are statistically significant differences in terms of efficacy and tolerability between fluoxetine and certain ADs, but the clinical meaning of these differences is uncertain.[10]Feiger AD et al, in another study, examined response and remission rates in outpatients treated with sertraline or fluoxetine who were suffering from two depression subtypes: anxious-depression and severe depression. Data were pooled from five double-blind studies comparing fluoxetine versus sertraline for the treatment of DSM-III-R or IV major depression. Clinical outcome was assessed using the Hamilton Depression Rating Scale (HAM-D) and the Clinical Global Impression-Improvement scale (CGI-I). One thousand and eighty-eight patients were randomized, with 654 (60%) meeting criteria for anxious depression and 212 (19%) meeting criteria for high severity depression. For the total sample, treatment response was similar for both sertraline and fluoxetine. In the high severity subgroup, the mean (+/-SD) HAM-D score at week 12 was 8.9+/-5.7 for sertraline and 10.8+/-6.9 for fluoxetine (P=0.07), and the mean (+/-SD) CGI-I score was 1.5+/-0.7 for sertraline and 2.0+/-1.1 for fluoxetine (P=0.005). CGI-I responder rates were 88% versus 71% (P=0.03) in the high severity subgroup, and 84% versus 79% (P=0.16) in the anxious-depression subgroup. Overall, sertraline and fluoxetine showed comparable antidepressant efficacy, although sertraline may offer an advantage in those patients with severe depression.[4]

CONCLUSION

Both the drugs showed similar efficacy in terms of improvement and incidence of adverse events in managing depression among patients with cardiovascular diseases.

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