



TO COMPARE EFFICACY OF PROBIOTIC NUTRACEUTICALS AND PROBIOTIC FOOD (CURD) ALONG WITH ANTIDEPRESSANT IN SUBJECTS SUFFERING FROM DEPRESSION

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ABSTRACT **INTRODUCTION:** Approximately 280 million people are currently living in the world with depression and in India, approximately around 57 lack people are affected by depression. There are various antidepressants available for major depressive disorder but there is a need also emerging for novel approaches to treatment for depression that not only reduce the cost of intervention but also the associated side effects of these antidepressants. Since ancient times there has been an old saying that all diseases start in the gut. Hence scientists and researchers in this century started working on a special bidirectional pathway called —the gut-brain axis. Depression is characterized by a low level of serotonin, dopamine, and noradrenaline and as with most of these neurohormones, up to 90 percent of production occurs in the gut by microbiota hence gut-brain axis was found to be a very important link in searching for alternate novel depression treatments. **AIM:** To compare efficacy of probiotic nutraceuticals and probiotic food (curd) along with antidepressant in subjects suffering from depression. **MATERIAL AND METHODS:** This Prospective Observational Study was conducted at the department of psychiatry, MGMMC Indore India. A purposive sampling technique was used. The study sample consists of 90 subjects with depression in the age group 18-60. Diagnosis of depression was done as per the ICD-10 and Hamilton depression rating scale. The duration of the study was 4 weeks with two follow-ups on day 14 and day 28. Among subjects with depression thirty subjects were given tablet Escitalopram 10mg, thirty subjects were given tablet Escitalopram 10 mg and 120 ml curd, and the remaining thirty subjects were given tablet escitalopram 10 mg and probiotic capsule. Hamilton depression rating scale was applied after each follow-up. Different statistical methods such as comparative analysis through the Chi-square (χ^2) test and Tukey's Honest Significance Difference Test were employed by using the SPSS tool (version 20) with significance at 1 % level ($P < .01$). **RESULTS:** On analyzing the results it was found that the comparison of mean HDRS on patients between days of treatment and each treatment type was statistically significant ($P < 0.001$). It was also observed that between day 0 and day 28 there was a slightly greater reduction in mean HDRS values by one or two points in the probiotic group from day 0 value of $12.50 \pm 0.50a$ to $5.50 \pm 0.84c$ on day 28 when compared to a reduction in HDRS values in curd group from day 0 value of $12.43 \pm 0.43a$ to $6.70 \pm 0.90c$ on day 28 and reduction in HDRS value in escitalopram group from day 0 value of $12.67 \pm 0.42a$ to $7.07 \pm 0.94b$ on day 28. **CONCLUSION:** Present study provide valuable evidence of the efficacy of probiotics nutraceuticals and probiotic food (Curd) when used with the anti-depressive drug Escitalopram. Among other issues such as the potential to produce a visible effect, antidepressant medication is frequently accompanied by intolerable side effects that cause a significant proportion of patients to discontinue their medication but the lower dose of the anti-depressive drug when given with probiotic supplementation and curd and also reduced side effects due to better gut health might be beneficial for the depression patients

KEYWORDS :

INTRODUCTION

Depression is a major health problem, contributing to significant morbidity, disability, and even mortality along with significant socioeconomic losses. Approximately around 280 million people are currently living in the world with depression and in India, approximately around 57 lack people are affected by depression[1]. There are various antidepressants available for major depressive disorder but there is an emerging need for novel approaches to treatment for depression that not only reduce the cost of intervention but also the associated side effects of these antidepressants. Since ancient times there has been an old saying that all diseases start in the gut. Hence scientists and researchers in this century started working on a special bidirectional pathway called —the gut-brain axis [2].

Depression is characterized by a low level of serotonin, dopamine, and noradrenaline and as with most of these neurohormones up to 90 percent of production occurs in the gut by microbiota [3] hence gut brain axis was found to be a very important link in searching for alternate novel depression treatments[4]. Dysbiosis (decrease in good or beneficial bacteria and increase in pathogenic bacteria) secondary to stress and gastrointestinal inflammation due to depression caused lesser activation of the Hypothalamic-pituitary axis properly through the vagus nerve and also lesser serotonin production hence stress was not relieved [5] [6]. Stressors in life or persistent stress or bad dietary habits and eating unhygienic food can cause dysbiosis[7]. All these factors lead to a decrease in good bacteria in our gut and hence the bacteria is not able to activate the Hypothalamic-pituitary axis properly through the vagus nerve hence stress is not relieved.

Hence lies the importance of our gut microbiota in the gut-brain axis and depression. Researchers have used natural means to provide these beneficial microorganisms like dietary curd and probiotics to increase serotonin production and treat depression. Probiotics are nutraceuticals containing live microorganisms given by the oral route to correct dysbiosis in the gut[8]. They were found to have fewer or nil side effects and were studied for their role in the gut-brain axis[9]. Gut

microbiota are microorganisms like bacteria, and fungi and are also as good or beneficial bacteria as they have a role in the metabolism of food, defense against pathogens, and their role in behavioral problems in the neuropsychiatric domain by regulating and synthesizing neurotransmitters. Some of the microorganisms lining the gut like *Escherichia coli*, *Lactobacillus*, *Bifidobacterium*, *Streptococcus*, *Bacillus*, etc. are known to produce serotonin, noradrenaline, dopamine, GABA, etc. hence their role in psychiatry[10]. Some of the probiotic foods are curd, fermented milk, pickle, vegetables, yogurt, and fermented cheese. Probiotic capsules and Curd which is prepared in our home or found in dairy contain several species of the *Lactobacillus* like *L. acidophilus*, *L. Confusus*, *L. Fermentum* and *Leuconostoc lactis* and also *Bifidobacterium* are known to produce serotonin and other neurotransmitters thus playing a role in depression through gut-brain axis [11][12]

MATERIAL AND METHODS

Present study was conducted in the Department of Psychiatry, MGM Medical College and associated Mental Hospital, Indore, Madhya Pradesh, India. Ethics committee approval was obtained. Subjects were recruited as per specified inclusion and exclusion criterias.

Inclusion Criteria

1. Subjects who were diagnosed with mild or moderate depression as per ICD-10.
2. Subjects who were diagnosed with mild or moderate depression by senior consultant psychiatrists and are being prescribed ESCITALOPRAM as monotherapy were eligible for the study.
3. Subjects or LAR (living with subject sharing same house and kitchen) who were minimum primary educated.
4. Subjects of depression in the age group from 18 to 60 years old.
5. Subjects who were antidepressant-free for the last 4 weeks.
6. Criteria of selection of mild to moderately depressed subjects were according to the Hamilton depression rating scale.
7. Subjects willing to give informed consent

Exclusion Criteria

1. Subjects of depression suffering from inflammatory bowel

- disease, and short bowel syndrome.
- 2. Subjects of depression suffering from diarrhea or constipation in the last two weeks.
- 3. Subjects of depression who were consuming antibiotics or have consumed antibiotics in the last 4 weeks.
- 4. Subjects with depression who are having immunodeficiency syndromes
- 5. Subjects suffering from bipolar depression and psychotic depression.
- 6. Subjects of depression not providing informed consent.
- 7. Subjects of depression who were pregnant or lactating.
- 8. Subjects diagnosed with severe depression and suicidal depression.
- 9. Subjects of depression who are taking anti-inflammatory, antitubercular, antiviral, antiprotozoal, and antifungal drugs in the last 4 weeks.
- 10. Subjects of depression with organic brain pathology.
- 11. Subjects of depression presenting with a history of lactose intolerance

The present study was a Prospective Observational Study. A purposive sampling technique was used. The study sample consisted of 90 subjects with depression in the age group 18-60. Diagnosis of depression was done as per the ICD-10 and Hamilton depression rating scale. The duration of the study was 4 weeks with two follow-ups on day14 and day28. Among subjects of depression thirty subjects were given tablet Escitalopram 10mg, thirty subjects were given tablet Escitalopram 10 mg and 120 ml curd, and the remaining thirty subjects were given tablet escitalopram 10 mg and probiotic capsule (1od for 1 week and 1bd for remaining 3 weeks). Hamilton depression rating scale was applied after each follow-up. Different statistical methods such as comparative analysis through the Chi-square (χ^2) test and Tukey's Honest Significance Difference Test were employed by using the SPSS tool (version 20) with significance at 1 % level ($P < .01$).

RESULTS

On analyzing the results it was found that the comparison of mean HDRS on patients between days of treatment and each treatment type was statistically significant ($P < 0.001$) but the comparison of mean HDRS on patients between each day of treatment and each treatment type did not show a statistically significant difference ($P > 0.001$). It was also observed that between day 0 and day 28 there was a slightly greater reduction in mean HDRS values by one or two points in the probiotic group from day 0 value of $12.50 \pm 0.50a$ to $5.50 \pm 0.84c$ on day 28 when compared to a reduction in HDRS values in curd group from day 0 value of $12.43 \pm 0.43a$ to $6.70 \pm 0.90c$ on day 28 and reduction in HDRS value in escitalopram group from day 0 value of $12.67 \pm 0.42a$ to $7.07 \pm 0.94b$ on day 28.

Table 1.0 and Fig 1.0 evaluates the comparison of mean HDRS on patient between days of treatment and each treatment type was statistically significant ($P < 0.001$) while between each day of treatment and each treatment type did not show a statistically significant difference ($P = 0.933$, $P = 0.486$ and $P = 0.437$).

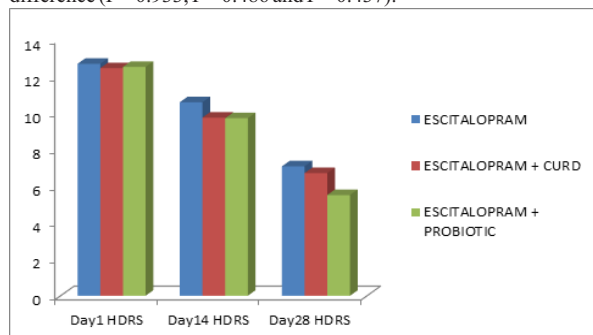


Fig 1.0: Comparison of Mean HDRS of different treatment groups in different days

1.0 Comparative analysis of Mean HDRS on different treatment groups in different days

Table 1.0: Comparison of Mean HDRS on different treatment groups in different days

Days Treatment Group	Day0 HDRS	Day14 HDRS	Day28 HDRS	P-Value (within Group)
ESCITALOPRAM	12.67 ± 0.42a	7.07 ± 0.94b	7.07 ± 0.94b	<.001**
ESCITALOPRAM + CURD	12.43 ± 0.43a	6.70 ± 0.90c	6.70 ± 0.90c	<.001**
ESCITALOPRAM + PROBIOTIC	12.50 ± 0.50a	5.50 ± 0.84c	5.50 ± 0.84c	<.001**
P-Value (Between group)	.933	.486	.437	N = 90

ESCITALOPRAM	12.67 ± 0.42a	10.57 ± 0.65a	7.07 ± 0.94b	<.001**
ESCITALOPRAM + CURD	12.43 ± 0.43a	9.70 ± 0.57b	6.70 ± 0.90c	<.001**
ESCITALOPRAM + PROBIOTIC	12.50 ± 0.50a	9.73 ± 0.50b	5.50 ± 0.84c	<.001**
P-Value (Between group)	.933	.486	.437	N = 90

** Significant at 1 % level ($P < .01$)

DISCUSSION

In the present study, it was found that the comparison of mean HDRS on patients between days of treatment and each treatment type was statistically significant ($P < 0.001$) but the comparison of mean HDRS on patients between each day of treatment and each treatment type did not show a statistically significant difference ($P > 0.001$). It was also observed that between day 0 and day 28 there was a slightly greater reduction in mean HDRS values by one or two points in the probiotic group from day 0 value of $12.50 \pm 0.50a$ to $5.50 \pm 0.84c$ on day 28 when compared to a reduction in HDRS values in curd group from day 0 value of $12.43 \pm 0.43a$ to $6.70 \pm 0.90c$ on day 28 and reduction in HDRS value in escitalopram group from day 0 value of $12.67 \pm 0.42a$ to $7.07 \pm 0.94b$ on day 28. Similar findings were seen in earlier studies by Ghorbani et al., Kazemi et al., and Nikolova El et al. An earlier study by Ghorbani et al. reported that major depressive disorder patients who were given symbiotic capsule (probiotic capsule plus fluoxetine) led to a greater reduction in HAM-D scores compared to placebo (placebo plus fluoxetine) [39]. Our study found similar results with a slightly greater reduction in HDRS scores in subjects of depression given escitalopram plus probiotics than those patients given escitalopram alone. Though in our study antidepressant used was escitalopram both escitalopram and fluoxetine belong to the SSRI family. A previous study by Kazemi et al. reported that probiotic supplementation containing lactobacillus and Bifidobacterium strains led to significant improvement in Beck depression inventory scores compared to placebo in major depressive disorder [13]. This is similar to our present study where there was an improvement in depressive symptoms in patients receiving probiotics. The probiotic used in our study also contained lactobacillus and Bifidobacterium strains similar to the study by Kazemi et al. Though in our study HDRS was used to access depression instead of Beck depression inventory. An earlier meta-analysis done by Nikolova EL et al. obtained a beneficial effect of probiotics in patients with MDD receiving antidepressants but not with probiotic monotherapy[14] which is in agreement with the present study. Although in our study probiotic was not given as monotherapy to depressive patients but subjects receiving probiotics and escitalopram had a slightly greater reduction in HDRS scores which is in agreement with the meta-analysis. Some of the likely causes for the improvement in depressive symptoms and slightly greater reduction in HDRS scores in the probiotic plus escitalopram group could be that besides escitalopram which is a proven treatment for major depressive disorder management, probiotics has also a role in correcting dysbiosis in our gut by providing artificial means of beneficial bacteria which are deficient in depression subjects. These bacteria in probiotics also correct the disturbed bidirectional pathway of the gut-brain axis and also synthesize serotonin, and GABA in the gut, and also increase serotonin production indirectly in our brain through the gut-brain axis. Also as depression is an inflammatory disease, these probiotics can reduce pathogenic bacteria in the gut and reduce inflammation of the gut leading to better gut health and improving serotonin production [15],[16].

LIMITATIONS

The present study had a small sample size. Hence for the results to be a better representative of the whole population a larger sample size could have been taken. Further, we used purposive sampling for selecting patients in each treatment group. Randomized sampling could have been used to reduce researcher bias. Further, the present study lacked a placebo group, having a placebo group in the present study could have led to a better comparison of results in all the 3 treatment groups. In all the 3 treatment groups escitalopram was given so significant results in depression response in all the groups were seen. So the study could have been done by using probiotics and curd as monotherapy instead of as an adjuvant to escitalopram. This would have led to the better observation of treatment response by using probiotic and curd in depression subjects.

CONCLUSION

Findings in the present study provide valuable evidence of the efficacy of probiotic nutraceuticals and probiotic food (Curd) when used with anti-depressive drug Escitalopram, known as selective serotonin reuptake inhibitor. The present investigation could have a major impact on many patients looking for relief from depressive disorder. Among other issues such as potential to produce a visible effect, antidepressant medication is frequently accompanied by intolerable side effects that cause a significant proportion of patients to discontinue their medication but the lower dose of anti-depressive drug along with probiotic supplementation and curd and also reduced side effects due to better gut health might be beneficial to the society.

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