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Review Article

Pharmacotherapy of Anorexia Nervosa and Bulimia Nervosa Using SSRIs, MAOIs and TCAs

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ABSTRACT

Anorexia nervosa and bulimia nervosa are mental disorders categorised under eating and feeding disorders (American Psychiatric Association). While psychotherapy is the main form of treatment, pharmacotherapy can also be used for these disorders. This paper discusses the use of Selective Serotonin Reuptake Inhibitors (SSRIs), Monoamine Oxidase Inhibitors (MAOIs) and Tricyclic Antidepressants (TCAs) in treating anorexia nervosa and bulimia nervosa. Studies found in the database provided by Web of Science were reviewed and relevant English language and translated studies were considered. SSRIs have limited effect on anorexia nervosa and require further research to ascertain their efficacy. SSRIs such as fluoxetine, sertraline, citalopram, and fluvoxamine are effective in treating bulimia nervosa. Monoamine oxidase inhibitors and tricyclic antidepressants cannot be used to treat anorexia nervosa since they are not safe to use for this specific eating disorder. In some cases, a number of MAOIs (moclobemide, phenelzine, tranylcypromine and isocarboxazid) are effective in treating bulimia nervosa alongside some TCAs (nortriptyline, imipramine, desipramine and amitriptyline). Anorexia nervosa and bulimia nervosa are both conditions with high mortality rates and it is vital to understand more about the different forms of treatment that can be employed to cure these disorders. SSRIs are to be used as the first treatment but there is a possibility of response to MAOIs and TCAs from treatment resistant patients.

Keywords: Anorexia Nervosa, Bulimia Nervosa, Selective Serotonin Reuptake Inhibitors, Monoamine Oxidase Inhibitors, Tricyclic Antidepressants.

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INTRODUCTION

Anorexia Nervosa and Bulimia Nervosa are eating disorders according to DSM-5-TR.[1] Anorexia nervosa is characterised by overvaluation of one's body shape and weight.[2] It is most common in women, with around 80-90% of the individuals with anorexia nervosa being female.[2] People with anorexia nervosa tend to have great capacity for weight loss as they engage in various practices to achieve weight loss such as food restriction, overexercising and exerting oneself too much, purging etc.[2] Anorexia nervosa also makes an individual overly conscious with their body and that results in body checking, which can be described as "repeated weighing, measuring, mirror gazing, and other obsessive behaviour to reassure themselves that [the individual with anorexia nervosa] are still thin".[2] Along with weight loss, anorexia nervosa may present itself in symptoms of depression, obsessive behaviour, amenorrhea, insomnia, abnormal blood counts and infertility.[2] Anorexia nervosa is also the psychiatric disorder with the highest mortality rate,[2] which makes the need to understand effective treatment for the disorder more imminent. Bulimia nervosa is similar to anorexia nervosa as they both involve a preoccupation with one's weight and body shape; however, bulimia nervosa differs in its characteristic of patterned binge eating and then extreme measures of purging to counteract the previous binge eating.[3] Bulimia nervosa, similar to anorexia nervosa, also has a high mortality rate; however, in both the cases, fatality occurs from medical complications which arose due to the two disorders.[4] Additionally, during the course of the two illnesses, it is noted that the endocrine changes and altered neurotransmitter metabolism (both arising from a calorie deprivation) cause an association of anorexia nervosa and bulimia nervosa with other comorbid mental disorders.[4] This makes it important to study various modes of treatments for these two disorders.

Psychotherapy alongside pharmacotherapy have been used to treat both anorexia nervosa and bulimia nervosa. Pharmacotherapy of both bulimia nervosa and anorexia nervosa involves the use of various classes of drugs ranging from antidepressants to mood stabilisers. The aim of this paper is to review the use of three classes of antidepressants, which are Selective Serotonin Reuptake Inhibitors (SSRIs), Monoamine Oxidase Inhibitors

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(MAOIs) and Tricyclic Antidepressants (TCAs), in the treatment of both anorexia nervosa and bulimia nervosa.

Selective Serotonin Reuptake Inhibitors (SSRIs) are the first line of treatment for many psychiatric disorders including anorexia nervosa and bulimia nervosa.[5] The mechanism of action of SSRI medications is by inhibiting the reuptake of the neurotransmitter serotonin which thereby increases the concentration of serotonin; they have very little effect on other neurotransmitters like dopamine and norepinephrine.[5] As SSRIs have little effect on adrenergic, cholinergic, and histaminergic receptors, they have very few side effects, making them very safe and preferred over other antidepressants such as MAOIs and TCAs.[5] Monoamine Oxidase Inhibitors (MAOIs) were the first class of antidepressants introduced; however, they are not the first line of treatment and are often used to treat other forms of depression and other nervous system disorders.[6] They are used as a secondary option due to the various adverse side effects, safety concerns and dietary restrictions.[6] The severe dietary restrictions accompanying MAOIs are due to the adverse reaction with the amino acid tyramine which is present in various foods.[6] MAOI works by inhibiting the enzyme monoamine oxidase; this enzyme breaks down norepinephrine, serotonin, dopamine, and tyramine, hence the inhibition of monoamine oxidase by MAOIs lead to higher concentration of these neurotransmitters.[6]

Tricyclic Antidepressants (TCAs) are a class of drugs used to treat major depressive disorder and other illnesses as a second line of treatment after SSRIs due to its anticholinergic properties as well as a lower threshold for overdose.[7] However, it is found that TCAs are very effective and equivocal with SSRIs in terms of efficacy.[7] The mechanism of action of TCAs involves modulating around five different neurotransmitter pathways: they inhibit the reuptake of serotonin and norepinephrine, thereby increasing the concentration of these two neurotransmitters, and also are competitive antagonists for postsynaptic cholinergic (alpha-1 and alpha-2), muscarinic, and histamine receptors (H1).[7]

METHODOLOGY

The database offered by Web of Science by Clarivate was used to find the studies for the various drugs in relation to either anorexia nervosa or bulimia nervosa. English language or translated articles and articles that were relevant to the subject were considered. They were selected based on relevance to the topic as well as impact score. One article each for each one of the drugs per condition were chosen (in many cases there were only one such article available), except in the cases of fluoxetine, sertraline, tranylcypromine and desipramine's efficacy on bulimia nervosa. The selected articles surmised the key concepts of the efficacy and safety of the myriads of drugs on anorexia nervosa and bulimia nervosa.

RESULTS

Use of SSRIs in Anorexia Nervosa Treatment

The American Psychiatric Association Practice Guidelines' recommendations for anorexia nervosa involves the use of antidepressants to combat relapse and to fight off depressive and obsessive-compulsive symptoms; the aforementioned recommendations specifically prefer the use of SSRIs in treating anorexia nervosa.[8] The efficacy of SSRIs in specific in the treatment of anorexia is heavily debated, with studies conducted on both sides. Commonly, it is suggested that there is an inordinate amount of evidence that the use of SSRIs is not effective in anorexia nervosa, even if the patients report comorbid depression.[9] The depressive state accompanied with anorexia nervosa is most commonly seen to settle when the individual regains weight and reaches the healthy level.[9] In the study led by Garner *et al*., it was found that antidepressants are the most commonly prescribed medication for patients with anorexia nervosa. While a very small percentage were prescribed Tricyclic Amitriptyline (which is a TCA), the most used antidepressant category was SSRIs (79%), with the most commonly used SSRI being fluoxetine. While this study focuses on the number of individuals administered various kinds of psychotropic drugs for anorexia nervosa, there are specific studies which research the actual efficacy of SSRIs in treating anorexia nervosa. Ferguson *et al*. studied two groups of individuals who were all diagnosed with anorexia nervosa.[10] One group was administered SSRIs during their treatment while the other group was not given any medication and were solely treated through psychotherapy. At the end of the study, it was noted that the body weights and the measures used to quantify symptoms of depression and distorted thinking were similar in both the groups. This study has been replicated and it has been observed that there are no major benefits of administering SSRIs to patients with anorexia nervosa. It is also hypothesised that anorexia nervosa may impact serotonin receptors due to the extreme weight loss, which may affect the efficiency of SSRIs in treating the illness. However, multiple drugs are commonly prescribed for anorexia nervosa, the most common of them being fluoxetine, sertraline, paroxetine and citalopram.

Fluoxetine in Anorexia Nervosa Treatment

Fluoxetine is an SSRI commonly prescribed for a variety of reasons. It has great advantage over tricyclic antidepressants mainly due to its safety i.e. minimal adverse side effects as well as unwanted drug events.[11] Fluoxetine is the most common SSRI administered to individuals with anorexia nervosa. However, its efficacy is under question. A study led by Attia *et al.* has been commonly referred to when discussing the efficacy of fluoxetine. It is a double-blind, placebo-controlled trial in which 31 patients with ages ranging from 16 to 45 were studied and they all had anorexia nervosa for 8±5.8 years.[12] These patients were put in two groups, control and experimental group. The control group

consisted of 16 patients who were given placebo treatment and the experimental group consisted of 15 patients who were given fluoxetine (starting at 20 mg/d and increased to 60 mg/d over 1 week). There was no noteworthy improvement noted from the experimental group over the control group. Both groups showed significant improvements, but the levels were similar to each other. Both the groups were also provided with intensive psychotherapy as well, which may have led to the improvements noted. The use of fluoxetine in anorexia nervosa, therefore, may not be beneficial to the extent as it is currently believed to be.

Sertraline in Anorexia Nervosa Treatment Sertraline is another SSRI which is used to treat anorexia nervosa. Its mechanism mainly operates on inhibitory effects on presynaptic serotonin reuptake.[13] Santonastaso *et al*., conducted a study researching the use of sertraline in treating anorexia nervosa.[14] A sample of 11 individuals with anorexia nervosa was taken to conduct this study, with one group being the control group and the other group given sertraline. They were all assessed through a structured interview and a self-reported questionnaire after 14 weeks of treatment. After 64 weeks, they were assessed again regarding their psychological state as well as their body weight. At the 14 week follow up, there was a similar report in regain of weight from both the groups but the psychological state was better improved in the group provided with sertraline. At the end of 64 weeks, only one patient from the experimental group reported still having an eating disorder whereas 5 patients of the control group reported a diagnosis of an eating disorder. This study leads one to believe that sertraline is an effective drug to treat anorexia nervosa. However, it must be kept in mind that the sample group used was extremely small and the study has not been replicated. Therefore, it is vital to conduct further research to ascertain the efficacy of sertraline in treating anorexia nervosa.

Paroxetine in Anorexia Nervosa Treatment

Paroxetine is another SSRI used to treat anorexia nervosa. Paroxetine, alongside being an SSRI, has been noted to have a noradrenergic effect by inhibiting the reuptake of norepinephrine and also activating it, making it ideal for patients with depression to combat symptoms of lethargy.[15] Paroxetine was particularly common in the 1990s; however, a negative relation between the drug and oncogenesis of breast cancer was found.[15] Strobel *et al.* conducted a study consisting of 83 female patients in the Department of Child and Adolescent Psychiatry and Psychotherapy at the University of Wuerzburg, Germany.[16] The study examined the efficacy of SSRIs and TCAs in treating anorexia nervosa; paroxetine and clomipramine, which is a TCA. The criteria used to diagnose anorexia nervosa in this study was on the basis of The International Classification of Diseases (ICD)-10. The results of the study proved that paroxetine is more effective than clomipramine in treating anorexia nervosa; however, the efficacy of paroxetine itself is under question. Therefore, similar to other drugs, it is necessary that more studies are conducted analysing the effects of paroxetine when administered to individuals with anorexia nervosa.

Citalopram in Anorexia Nervosa Treatment

Citalopram is another SSRI which was studied for its effects in treating anorexia nervosa. Citalopram is quite safe in terms of side effects as well as drug interactions, and is effective in treating depression.[17] Bezchlibnyk *et al*. conducted a critical review of the pharmacological and clinical effects of citalopram.[18] There were no sex related differences noted, it was observed through *in vitro* cytochrome P-450 enzyme studies and *in vivo* observation that citalopram had much less drug interactions as compared to other SSRIs, adverse hepatical, renal and haematological side effects were found to be extremely rare and there is no association between citalopram and serious cardiovascular toxicity. Nevertheless, its effectiveness in treating anorexia nervosa is still unclear. A pilot study was conducted by Fassino *et al*., specifically to study the efficacy of citalopram in anorexia nervosa.[19] The study started with 52 patients with anorexia nervosa as the subjects, with 26 given citalopram and the rest in the control group. The weight gain was the same between both groups; however, the group provided with citalopram showed significant improvement in various categories, including a decrease on the Beck Depression Inventory scale and Symptom Checklist-90 subscale as well as an improvement on the Eating Disorder Inventory-2 scale and State-Trait Anger Expression Inventory scale. It is to be noted that 13 participants dropped out of the study, reducing the sample size, hence, further research is required to ascertain the effectiveness of citalopram in treating anorexia nervosa.

Use of SSRIs in Bulimia Nervosa Treatment

Similar to anorexia nervosa, bulimia nervosa entails symptoms of severe body image distortions, extreme fear of weight gain as well as heightened focus on one's appearance.[20] There is more information available about pharmacotherapy for bulimia nervosa as compared to anorexia nervosa, which is understandable due to the fact that bulimia nervosa is much more common than anorexia nervosa.[20] There are various studies showing improvement in the symptoms of bulimia nervosa through the use of different kinds of drugs such as Tricyclic Antidepressants (TCAs), Monoamine Oxidase-Inhibitors (MAOIs), atypical antidepressants and and Selective Serotonin Reuptake Inhibitors (SSRIs). Serotonin in particular is a neurotransmitter that plays a role in impacting appetite. Reduced serotonin activity has been observed as the cause for the cognitive and mood disturbances associated with bulimia nervosa.[20] Therefore, it can be inferred that SSRIs will have a positive impact on individuals with bulimia nervosa. There is extensive research done on the effects of SSRIs on bulimia nervosa and a positive correlation has been established. Fluoxetine is the first SSRI to be studied for its effects on bulimia nervosa and it was found to be a great success in treating bulimia nervosa according to various studies conducted.[21-24] Other SSRIs

also studied for their effects in treating bulimia nervosa include sertraline, fluvoxamine and citalopram.

Fluoxetine in Bulimia Nervosa Treatment

As mentioned before, fluoxetine was the first SSRI used to treat bulimia nervosa. A study conducted in 1993 to study the effectiveness of fluoxetine in pharmacotherapy of bulimia nervosa.[25] This study was prominent and exceptional when compared to other studies relating to the same subject matter as a large test group was used for two trials (n = 387 and 398, respectively). The results of both the trials showed that the use of 60 mg of fluoxetine derived positive impacts as there was a reduction in both behavioural and attitudinal symptoms of bulimia nervosa. It has been noted since that the dosage of fluoxetine which is beneficial for those with bulimia nervosa is 60 mg. Goldstein *et al.* conducted a study to study the long-term effects of fluoxetine on individuals with bulimia nervosa. A large trial group of 483 individuals took part in the study with a 3:1 ration of being administered fluoxetine 60 mg or placebo. The study observed the efficacy of fluoxetine over 16 weeks and it was surmised that fluoxetine is beneficial and safe in the long term for individuals with bulimia nervosa.[23]

Sertraline in Bulimia Nervosa Treatment

Another SSRI used to treat bulimia nervosa is sertraline. Sertraline is not as widely studied as fluoxetine when it comes to its efficacy in treating bulimia nervosa. There was a study conducted by Sloan *et al*. in 2004 where 18 women diagnosed with bulimia nervosa were observed under treatment on sertraline.[26] After 8 weeks, these women were assessed through the means of self-report questionnaires and semi structured interviews, according to which it was noted that sertraline is effective in treating bulimia nervosa. Sabatino *et al*. conducted another randomised trial to study the effectiveness of sertraline in which 20 female patients who were diagnosed with bulimia nervosa, as per Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV), were studied.[27] They were split into two groups; one was administered 100 mg of sertraline per day and the others were given placebo. It was surmised at the end of the study that sertraline has a positive impact on those with bulimia nervosa as the group that was administered sertraline demonstrated higher improvement than those in the control group.

Fluvoxamine in Bulimia Nervosa Treatment

Fluvoxamine is an SSRI that can also be used to treat bulimia nervosa. Fluvoxamine differs structurally from other SSRIs but has the same mechanism of action where it inhibits Central Nervous System (CNS) neuronal uptake of serotonin.[28] A study conducted by Siano *et al*. in 2005 tested the efficacy fluvoxamine in treatment of bulimia nervosa by observing 20 women who were diagnosed with bulimia nervosa under DSM-IV.[29] They were placed into two groups where one group was given 150-300 mg of fluvoxamine daily and the other group was given placebo. The first group that was administered fluvoxamine showed great improvement in regards to symptoms associated with bulimia nervosa after the observation period. Therefore, it can be noted that fluvoxamine has a beneficial impact on individuals with bulimia nervosa and is well tolerated as well; however, further research is necessary to determine the complete efficacy of fluvoxamine.

Citalopram in Bulimia Nervosa Treatment

Another SSRI that will be discussed in regard to its efficacy in treating bulimia nervosa is citalopram. Siano *et al*. conducted another study following the same methods as the study conducted to examine the effectiveness of fluvoxamine, except the experimental group was given 20-40 mg of citalopram every day while the control group was given placebo.[30] After the 12-week observation period, it was noted that once again, the experimental group has significant reduction of symptoms associated with bulimia nervosa. Hence, it was inferred that citalopram is well tolerated and useful for those with bulimia nervosa; however, further research is required as the sample pool consisted of only 20 people, all female and in the age group of 24-36.

Use of Monoamine Oxidase Inhibitor (MAOI) in Anorexia Nervosa Treatment

It is not recommended that monoamine oxidase inhibitors be used for treatment of anorexia nervosa.[31] This is due to the lack of efficacy of MAOIs in treating anorexia nervosa alongside the safety issues accompanying this class of drugs. Suicide and suicide ideation is common among patients with anorexia, therefore it is dangerous to prescribe them medication that can easily lead to a lethal overdose.[31]

Use of Monoamine Oxidase Inhibitor (MAOI) in Bulimia Nervosa Treatment

Monoamine oxidase inhibitors (MAOIs) are another class of antidepressants however they are one of the least commonly prescribed antidepressants as there are concerns regarding their interactions with food and other drugs. The mechanism of action of monoamine oxidase inhibitors involves stopping the enzyme monoamine oxidase from affecting neurotransmitters such as serotonin, norepinephrine and dopamine. There is a high risk of negative interactions of MAOIs with certain kinds of food, particularly those containing the amino acid tyramine, and certain types of drugs. While it is not recommended to use MAOIs in treating anorexia nervosa, there are a few MAOIs that are administered to individuals with bulimia nervosa. This paper will discuss the MAOIs used to treat bulimia nervosa, which are moclobemide, phenelzine, tranylcypromine, and isocarboxazid.

Moclobemide in Bulimia Nervosa Treatment

Although not commonly, moclobemide is an MAOI which can be used to treat bulimia nervosa. Moclobemide is commonly used to treat major depressive disorder and bipolar disorder.[32] Moclobemide is a reversible inhibitor of monoamine oxidase A, or a RIMA.[32] The efficacy of moclobemide as well as its tolerance was tested in a study conducted by Carruba *et al*. in 2001.[33] It was a six-week, double blind, placebo-controlled trial. 52 women who were diagnosed with bulimia nervosa (according to DSM-IV) were selected for the study. They were put in two groups; one group was administered 600 mg of moclobemide every day while the other group received placebo. It was noted that there was no significant improvement in the group that was prescribed moclobemide, hence, it is surmised that moclobemide at the dosage of 600 mg per day has no significant benefit for those with bulimia nervosa.

Phenelzine in Bulimia Nervosa Treatment

Phenelzine is another MAOI that is used to treat depression; however, it is usually used as a last resort as it is only given to those individuals for whom other medications have not proved useful.[34] It is also used as an anxiolytic in adults.[34] It is a part of the class of non-selective MAOIs, which are no longer commonly used with the advent of SSRIs.[34] Walsh *et al*. conducted a study in 1984 testing the efficacy of phenelzine in treating bulimia nervosa.[35] There were twenty women selected for a double blind trial. Nine of them were given phenelzine sulphate and 11 were given placebo. The results of the study pointed to the fact that phenelzine sulphate is beneficial when given to those with bulimia nervosa as long as the individual is on a tyramine free diet.

Tranylcypromine in Bulimia Nervosa Treatment

Tranylcypromine is another MAOI which, like phenelzine, is only used for patients with depression who are not responding to other medications.[36] It is a non-selective and irreversible inhibitor of monoamine oxidase.[36] There are no studies specific to tranylcypromine and its efficacy in treating individuals with bulimia nervosa. However, there is a study conducted by McElroy *et al*. in 1989, studying the pharmacological treatments of kleptomania and bulimia nervosa which concluded that tranylcypromine, while having a positive result in treatment of kleptomania, needs further research to understand its efficacy in treating bulimia nervosa.[37]

Isocarboxazid in Bulimia Nervosa Treatment

Isocarboxazid is an MAOI which is usually used to treat cases of severe depression.[38] Unlike moclobemide, isocarboxazid is an irreversible inhibitor of monoamine oxidase.[38] A double blind, placebo-controlled trial took place in 1988, conducted by Kennedy *et al*. in which eighteen women diagnosed with bulimia nervosa were studied. After being administered isocarboxazid, they improved significantly with symptoms of vomiting and binge eating.[39]

However, a majority of the subjects chose to discontinue the use of isocarboxazid after a year of taking it. Therefore, further research is required to study the efficacy of isocarboxazid in treating bulimia nervosa.

Use of Tricyclic Antidepressants (TCA) in Anorexia Nervosa Treatment

It is not recommended that tricyclic antidepressants be used for treatment of anorexia nervosa.[40] Similar to the reasons for the disuse of MAOIs in Anorexia Nervosa treatment, TCAs also have a low threshold for lethal overdose.[31] Furthermore, TCAs have various adverse side effects such as "decreased seizure threshold, QT interval prolongation, orthostatic hypotension, and gastrointestinal symptoms."[31] These side effects are especially dangerous for those with anorexia nervosa as it can worsen their preexisting gastrointestinal and cardiovascular issues.[31]

Use of Tricyclic Antidepressants (TCA) in Bulimia Nervosa Treatment

Tricyclic antidepressants are one of the earliest developed classes of antidepressants.[7] The mechanism of action of tricyclic antidepressants involves inhibiting the reuptake of the neurotransmitters serotonin and norepinephrine.[7] Most guidelines recommend that TCAs be used as a second line treatment after SSRIs despite them having equivalent efficacy; this is due to the adverse side effects that are associated with TCAs, especially cardiotoxicity, and make them less safe than SSRIs.[7] Much like MAOIs, TCAs are rarely used to treat bulimia nervosa as SSRIs have an advantage over other classes of drugs when it comes to pharmacotherapy of bulimia nervosa. However, there are instances of tricyclic antidepressants used to treat bulimia nervosa. 8 patients who were diagnosed with bulimia nervosa were given desipramine, imipramine, nortriptyline, phenelzine, amoxapine, maprotiline and lithium carbonate in a study.[41] Out of the eight patients, six showed remarkable improvement.[41] The next sections of this paper will review the efficacy of nortriptyline, imipramine, desipramine and amitriptyline in treating bulimia nervosa.

Nortriptyline in Bulimia Nervosa Treatment

Nortriptyline is a tricyclic antidepressant that is commonly used to treat depression, but also for "chronic pain, diabetic neuropathy, myofascial pain, orofacial pain, and postherpetic neuralgia."[42] It is also used for smoking cessation and migraine prophylaxis.[42] Nortriptyline works by inhibiting the reuptake of serotonin and norepinephrine by the presynaptic neuronal membrane, which then increases the concentration of serotonin and norepinephrine. Furthermore, nortriptyline inhibits histamine, 5-hydroxytryptamine, and acetylcholine. There is not

much literature on the specific effects of nortriptyline on bulimic patients. However, in 1988, Newman, Schlefer and Abraham published a brief report on their recordings of

treatment of a bulimic and diabetic patient with nortriptyline.[43] A combination of both bulimia nervosa and diabetes can be fatal. Newman, Schlefer and Abraham's report found that nortriptyline, alongside atenolol (to treat high blood pressure), were successful in treating the patient with bulimia nervosa and diabetes.

Imipramine in Bulimia Nervosa Treatment

Imipramine is a tertiary amine tricyclic antidepressant which is commonly used to treat depression and anxiety.[44] Imipramine also works by blocking the reuptake of the neurotransmitters serotonin and norepinephrine.[44] It has a great affinity for serotonin and works against the neurotransmitter acetylcholine. It is also used off-label to treat chronic pain, similar to nortriptyline.[44] Pope and Hudson studied the effectiveness of imipramine in treating bulimia nervosa.[41] They conducted a double blind, placebo controlled study to test imipramine's efficacy. The subjects were 22 women diagnosed with bulimia nervosa. They all showed reduction in symptoms of binge eating and other disordered eating. After an eight month follow up, 90% of the subjects continued to respond positively to imipramine or other antidepressants. This shows there is scope for further research to test the efficacy of imipramine on bulimia nervosa.

Desipramine in Bulimia Nervosa Treatment

Desipramine is a secondary amine tricyclic antidepressant that is commonly used to treat depression. It is also used off-label to treat "bulimia nervosa, irritable bowel syndrome, neuropathic pain, overactive bladder, post-herpetic neuralgia, and ADHD."[45] Desipramine works by blocking the reuptake of serotonin and norepinephrine in the presynaptic neuronal membrane and it is said that secondary amine tricyclic antidepressants such as desipramine are better at blocking norepinephrine than tertiary amine tricyclic antidepressants. To test the efficacy of desipramine in treating bulimia nervosa, McCann and Agras led a study involving a 12 week long, double blind, placebo controlled trial.[46] 12 women diagnosed with bulimia nervosa were a part of this trial. The results showed the success of desipramine as the group of women who were administered desipramine reduced the frequency of their binge eating by 63%, whereas the same of the group of women given placebo increased by 16%. At the end of the trial, 60% of the experimental group had stopped binge eating as compared to the 15% in the placebo group. While this trial demonstrates the successful treatment of bulimia nervosa with the use of desipramine, there was a study conducted by Leitenberg *et al*. in 1994 which it was concluded that there was no benefit of desipramine even combined with psychotherapy in treating bulimia nervosa.[47] However, this study had a high dropout rate and only seven subjects per condition. Therefore, further research is necessary to determine the efficacy of desipramine.

Amitriptyline in Bulimia Nervosa Treatment

Amitriptyline is a tertiary amine tricyclic antidepressant which works by blocking the reuptake of serotonin and norepinephrine. It is commonly used to treat depression but can also be used to treat "anxiety, post-traumatic stress disorder, insomnia, chronic pain (diabetic neuropathy, fibromyalgia), irritable bowel syndrome, interstitial cystitis (bladder pain syndrome), migraine prophylaxis, postherpetic neuralgia, and sialorrhea."[48] The use of amitriptyline in treating bulimia nervosa was studied by Mitchell and Groat in 1984 by conducting a double blind, placebo controlled trial consisting of 32 women who were diagnosed with bulimia nervosa according to DSM III.[49] The experimental group was given 150 mg of amitriptyline and the other group was given placebo. The results of the study indicated a dramatic improvement in the group that was provided with amitriptyline in depressive symptoms. The drug was also very well tolerated and led to no weight gain or carbohydrate craving. Further study of amitriptyline may lead to similar results, proving its efficacy.

DISCUSSION

Anorexia nervosa is the mental disorder with the highest fatality rate.[2] The number of fatalities is quite high in the case of bulimia nervosa as well.[4] And in cases of both anorexia nervosa and bulimia nervosa, its treatment remains an enigma as it is still not ascertained which is the best method of treating these two disorders.[50] This makes it imperative to find a form of treatment suitable for all who are facing these disorders. In the case of anorexia nervosa, it is crucial that the patient engages with psychotherapy as psychotropic medication do not seem to have a clear benefit for individuals with anorexia nervosa. Whereas, in the case of bulimia nervosa, while SSRIs are effective for most and are recommended to be used as the front-line treatment, MAOIs and TCAs can help in cases where the patient is treatment resistant. They can also help in cases where there are other issues coinciding with the eating disorder as in the case of Newman, Schlefer and Abraham's research in 1988 about a diabetic and bulimic young woman who was treated using both nortriptyline and atenolol.[43]

CONCLUSION

Anorexia nervosa and bulimia nervosa both respond to different kinds of treatment, especially in terms of pharmacotherapy. SSRIs show limited efficacy in treating anorexia nervosa as there are various limitations in the studies which conclude that SSRIs are efficient in treating anorexia nervosa. On the other hand, it is proven that SSRIs are very effective when administered to individuals with bulimia nervosa. MAOIs and TCAs both are extremely unsafe for those with anorexia nervosa, whereas they have some success in treating bulimia nervosa. While some drugs, especially SSRIs, like fluoxetine have an extensive amount of research regarding its use for anorexia nervosa and bulimia

nervosa, this is not the case for most of the drugs discussed in this paper. Even when studies are conducted, they are often subject to small sample sizes and high dropout rates as in the case of the study conducted by McCann and Agras to test the efficacy of desipramine. There is scope for future research with bigger experimental and control groups, more substantial reports on the well-being of the individuals at the end of the study, and multiple trials. As of now, SSRIs, in particular fluoxetine, are the safest and most effective method of pharmacotherapy of anorexia nervosa and bulimia nervosa. However, it can be proved that there is a chance of effective treatment for anorexia nervosa and bulimia nervosa using MAOIs and TCAs.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ADHD: Attention Deficit Hyperactivity Disorder; **CNS:** Central Nervous System; **DSM-III:** Diagnostic and Statistical Manual of Mental Disorders-III; **DSM-IV:** Diagnostic and Statistical Manual of Mental Disorders-IV; **DSM-5-TR:** Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision; **MAOI:** Monoamine Oxidase Inhibitor; **OCD:** Obsessive Compulsive Disorder; **PTSD:** Post Traumatic Stress Disorder; **RIMA:** Reversible Inhibitor of Monoamine Oxidase A; **SSRI:** Selective Serotonin Reuptake Inhibitor; **TCA:** Tricyclic Antidepressant.

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