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Does lisdexamfetamine dimesylate (Vyvanse) reduce the weekly incidence of binge eating in adults with binge eating disorder?

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Does lisdexamfetamine dimesylate (Vyvanse) reduce the weekly incidence of binge eating in adults with binge eating disorder?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

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ABSTRACT

Objective: The objective of this selective EBM review is to determine whether or not "Does lisdexamfetamine dimesylate (Vyvanse) reduce the weekly incidence of binge eating in adults with binge eating disorder?"

Study Design: A systematic review of three double-blind, randomized, placebo-controlled trials published between 2015 and 2017.

Data Sources: All articles were obtained from PubMed and were published in peer-reviewed journals, in the English language. They were selected based on their applicability to the clinical question, credibility, and if the researched outcomes were patient oriented.

Outcomes Measured: The number of binge eating days per week was the outcome measured, with the data compiled from self-reported diaries and clinical interviews. The mean value of binge eating days per week $\pm$ standard deviation for both the placebo and intervention group was calculated at two time points, before the trial started and at the end of the trial. The mean change from baseline was then calculated.

Results: The study conducted by McElroy et al. demonstrated a statistically significant reduction (p-value < 0.001) in the number of binge eating days per week with lisdexamfetamine dimesylate 70mg, with a mean change from baseline of 4.1. In the study conducted by Hudson et al., lisdexamfetamine dimesylate 70mg led to a statistically significant reduction (p-value < 0.001) in the number of binge eating days per week, indicated by a mean change from baseline of 4.72. The study conducted by Guerdjikova et al. revealed a statistically significant reduction (p-value $= 0.03$) in the number of binge eating days per week with lisdexamfetamine dimesylate 70mg, with a mean change from baseline of 3.4.

Conclusion: The results of these three studies demonstrated that the use of lisdexamfetamine dimesylate 70mg led to a statistically significant reduction in the number of binge eating days per week in adults diagnosed with binge eating disorder.

Key Words: binge eating disorder, lisdexamfetamine

INTRODUCTION

Binge eating disorder (BED) is defined as recurrent episodes of uncontrolled eating, in which an individual consumes large amounts of food within short periods of time. BED is the most common eating disorder in the United States, with a lifetime prevalence of 3.6% for women and 2.1% for men.[1] While the etiology of BED is unknown, it is believed to be multifactorial. Factors that are thought to put an individual at a higher risk for developing BED include childhood obesity and negative family dynamics and upbringings.[1] To establish a diagnosis of BED, an individual must meet the diagnostic criteria outlined by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*). An individual must have episodes of binge eating at least once a week for three months, plus at least three of the following associated behaviors: eating faster than normal, eating until uncomfortably full, eating despite not feeling hungry, eating alone to avoid embarrassment, feeling guilty after eating.[1] BED is clinically distinguishable from bulimia nervosa, as individuals with BED do not compensate for their excessive caloric intake with measures including laxative use or self-induced vomiting.[1] Furthermore, individuals with BED are often average weight or overweight and do not have goals revolving around obtaining extreme thinness, which are differentiating characteristics that are present in an individual with anorexia nervosa.[1]

With increasing prevalence and recognition of feeding and eating disorders in the United States, there is a need for applicable research involving these conditions. In 2018-2019, the total financial costs associated with eating disorders was an estimated $64.7 billion, with a total of $19.4 billion (30%) spent on BED specifically.[2] Additionally, from 2018-2019 there were approximately 8,000 emergency department visits, resulting in 5,600 inpatient admissions associated with eating disorders.[2] It is estimated that individuals diagnosed with eating disorders

saw a mental health professional 35.8 more times and a primary care provider 3.0 more times compared to the general population.[2] The role of physician assistants (PAs) in the care of individuals with psychiatric disorders is important to include in this discussion as 62% of PAs, in 2015, helped care for individuals with mental health conditions, with the highest percentage of these healthcare professionals working in psychiatry, followed by internal medicine, emergency medicine, and family medicine.[3] As of 2015, 1.6% of credentialed PAs worked in psychiatry.[3]

The existing approach for the treatment of binge eating disorder can be broken down into two distinct categories, cognitive behavioral therapy (CBT) and pharmacologic therapy. While CBT is currently the most researched and supported treatment method for BED, not all individuals have access to this therapy; additionally, not all patients will respond to this treatment method.[4] Examples of pharmacologic therapy that have been utilized in the treatment of BED, but are not FDA approved, include antidepressant medications and anticonvulsant medications.[1] Lisdexamfetamine dimesylate is an additional medication that has promising, ongoing research for its use in the treatment of binge eating disorder. Lisdexamfetamine dimesylate is a psychostimulant that inhibits the presynaptic neuronal reuptake of dopamine and norepinephrine, resulting in increased levels of these neurotransmitters in the brain.[5] Though most commonly recognized for its use in the treatment of attention deficit hyperactivity disorder, lisdexamfetamine dimesylate was approved by the FDA in 2015 for the treatment of BED.[1] While the exact mechanism of action in reducing binge eating episodes in those with BED is unknown, it is thought to improve impulse control.[4] This paper analyzes three randomized controlled trials that study the use of lisdexamfetamine dimesylate and its ability to reduce the number of binge eating days per week in those diagnosed with binge eating disorder.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not "Does lisdexamfetamine dimesylate (Vyvanse) reduce the weekly incidence of binge eating in adults with binge eating disorder?"

METHODS

The studies referenced in this EBM review were found on PubMed using the key words "lisdexamfetamine" and "binge eating disorder." Inclusion criteria comprised studies that were published in the past 10 years, were randomized controlled trials, were written in the English language, and included humans as the subjects of the study. Exclusion criteria eliminated studies that were published before 2011. It was required that the studies employed randomization and were published in peer-reviewed journals. Statistical analyses that were utilized in these selected randomized controlled trials included p-values and standard deviations. All studies were chosen based on credibility, applicability to the clinical question, and incorporation of patient-oriented outcomes.

This EBM review includes studies that have comparable populations, interventions, comparisons, and outcomes measured. The target population for this EBM review includes adults between the ages of 18 and 55 who were clinically diagnosed with binge eating disorder. The intervention being investigated is lisdexamfetamine dimesylate 70mg per day compared to a physically identical placebo. The outcome being measured in this review is the number of binge eating days per week. The demographics and characteristics of these studies can be found in Table 1.

Table 1 - Demographics & Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/ D	Interventions
McElroy (2015) [4]	Double Blind RCT	260	18-55	Adults (18-55 yo); met the DSM-IV-TR diagnostic criteria for BED; BMI 25 to 45	Current bulimia, anorexia, ADHD, other psychiatric disorder; psychological or weight loss interventions (past 3 months); psychostimulant use (past 6 months); total MADRS score of 18 or higher; personal or family hx of CVD; hx of substance abuse	58	lisdexamfetamine dimesylate 30mg, 50mg, or 70mg versus placebo
Hudson (2017) [6]	Double Blind RCT	275	18-55	Adults (18-55 yo); met the DSM-IV-TR diagnostic criteria for BED; protocol-defined moderate to severe BED (>3 BE days/ week x 2 weeks prior to study); BMI 18 to 45	Current bulimia, anorexia, suicidal ideation, other psychiatric disorder; past suicide attempt; psychotherapy or weight loss support for BED (past 3 months); psychostimulant use (past 6 months); hx of CVD; significant ECG abnormalities; hx of substance abuse	123	lisdexamfetamine dimesylate 70mg versus placebo
Guerdjikova (2016) [7]	Double Blind RCT	50	18-55	Adults (18-55 yo); met the DSM-IV-TR diagnostic criteria for BED; >3 BE days/week x 2 weeks prior to the study	Current bulimia, anorexia, suicidal ideation; suicide attempt (past year); psychological or weight loss intervention for BED (past 3 months); hx of substance use disorder; significant laboratory or ECG abnormalities	23	lisdexamfetamine dimesylate 70mg versus placebo

OUTCOME MEASURED

All three studies included in this EBM review utilized self-reported diaries and clinical interviews to obtain and verify the number of binge eating days per week for each individual participating in the study. The number of binge eating days per week for each subject was established before the study started and at the end of the study. The data was complied, calculated, and then reported as a mean value $\pm$ standard deviation for both the placebo and intervention groups. Additionally, a p-value was reported for the intervention group and the mean change from baseline was then calculated.

RESULTS

McElroy et al. conducted a randomized, double blind, placebo-controlled trial, with results of the study published in 2015.[4] A total of 260 participants were selected between the ages of 18 and 55 and met the diagnostic criteria for BED. Using a web-based system, subjects were randomized at a 1:1:1:1 ratio to receive the intervention of lisdexamfetamine dimesylate at a maintenance dose of 30mg, 50mg, or 70mg versus an identical placebo. Blinding was maintained throughout the trial by having the placebo and lisdexamfetamine dimesylate indistinguishable by size, shape, weight, and color. This study consisted of a three week dose titration phase followed by an eight week maintenance phase, for a total of an 11 week trial. The subjects that were receiving the active treatment were all started at 30mg and were titrated weekly, by 20mg, up to their assigned dose. In order to maintain consistency between all three studies discussed in this EBM review, the focus of this article will be the intervention group with a maintenance dose of 70mg. The intervention group, with a maintenance dose of 70mg, lost 13 participants total. Three subjects were lost due to adverse events, one being due to methamphetamine overdose (not related to the study drug), and the remaining 10 participants were lost due to protocol violations, lack of follow up, and withdrawal by the subject.[4] No

participants in the study were lost due to lack of efficacy. Though not leading to withdrawal from the study, both the placebo and intervention group experienced adverse events, the most commonly reported being dry mouth, decreased appetite, and insomnia.[4]

The primary outcome analyzed in this study was the number of binge eating days per week, measured as the mean number of binge eating days per week, and standard deviation, before treatment and at the end of the trial at week 11. The outcome was analyzed through clinical interviews and reviews of self-reported diaries. The results of this study are summarized in Table 2 below. The placebo group showed a decrease in binge eating days per week with a baseline of 4.3±1.38 to 1.1±1.45 at week 11, with a mean change from baseline calculated as 3.2.[4] The 70mg intervention group exhibited a statistically significant decrease in binge eating days per week with a baseline of 4.6±1.25 to 0.5±1.25 at week 11, with a mean change from baseline calculated as 4.1, and a p-value of < 0.001.[4]

Table 2. Mean Change in Binge Eating Days/Week from Baseline to Week 11

Group	Before Treatment (Mean ± Standard Deviation)	After Treatment (Mean ± Standard Deviation)	Mean Change from Baseline (calculated)	P value
Placebo	4.3±1.38	1.1±1.45	3.2	Not reported
lisdexamfetamine dimesylate 70mg	4.6±1.25	0.5±1.25	4.1	< 0.001

Hudson et al. conducted a two-phase trial consisting of a 12 week open label phase, followed by a 26 week randomized, double blind, placebo-controlled trial.[6] To maintain consistency between all three studies in this EBM review, the focus of this article will be on the findings reported from the randomized controlled trial. All 275 subjects that were selected to be in this study were between the ages of 18 and 55 and met the diagnostic criteria for BED.

Subjects were randomized using a web-based system, at a 1:1 ratio, to receive a placebo versus 70mg of lisdexamfetamine dimesylate. Blinding was maintained throughout the trial by having the placebo and lisdexamfetamine dimesylate identical in appearance. The intervention group lost 35 total participants: two to protocol violations, nine to withdrawal by the participant, six to loss of follow up, five to meeting relapse criteria, and seven to other reasons. Six subjects in the intervention group were lost due to adverse events, two of which were reported due to breast cancer and nerve root compression.[6] The top adverse events that did not lead to withdrawal from the study, that were reported by both the placebo and intervention group, included headache, nasopharyngitis, and fatigue.[6]

The outcome, the number of binge eating days per week, was analyzed through clinical interviews and reviews of self-reported diaries. The results of this study are summarized in Table 3 below. The placebo group showed a decrease in binge eating days per week with a baseline of 4.71 ± 1.23 to 0.26 ± 0.465 at week 38.[6] The intervention group demonstrated a decrease in binge eating days per week with a baseline of 4.80 ± 1.19 to 0.08 ± 0.239 at week 38, with a mean change from baseline of 4.72.[6] The p-value for the intervention group was reported as < 0.001, which is a statistically significant finding.[6]

Table 3. Mean Change in Binge Eating Days/Week from Baseline to Week 38

Group	Before Treatment (Mean ± Standard Deviation)	After Treatment (Mean ± Standard Deviation)	Mean Change from Baseline (calculated)	P value
Placebo	4.71 ± 1.23	0.26 ± 0.465	4.45	Not reported
lisdexamfetamine dimesylate 70mg	4.80 ± 1.19	0.08 ± 0.239	4.72	< 0.001

Published in 2016, Guerdjikova et al. conducted a 12 week, randomized, double blind, placebo-controlled trial.[7] All patients selected were between the ages of 18 and 55 and met the diagnostic criteria for BED. A total of 50 participants were randomized using a web-based system, at a 1:1 ratio, to receive lisdexamfetamine dimesylate or the identical placebo. The dosage of lisdexamfetamine dimesylate started at 30mg and was titrated up to 50mg during week two. During week three, lisdexamfetamine dimesylate was titrated up to the maintenance dose which was defined as 70mg. With a total of 23 participants not completing the trial, 19 subjects were lost due to scheduling difficulties and loss of follow up.[7] Furthermore, two subjects in both the treatment and placebo group experienced adverse events which led them to discontinue the trial. In the intervention group, one subject experienced severe chest pain and the other experienced insomnia.[7] In the placebo group, one subject was diagnosed with pneumonia and the other experienced exacerbation of past obsessions.[7] Other adverse events that were reported but did not result in withdrawal from the study included dry mouth, jitteriness, and headache.[7] These adverse events were reported by subjects in both groups; however, subjects in the intervention group reported them occurring more frequently.

The primary outcome measured in this trial was the number of binge eating days per week, reported as the mean number, including standard deviation, before treatment and at the end of the trial. Data directly related to the primary outcome was collected and analyzed through clinical interviews and self-reported diaries. The results of this study are summarized in Table 4 below. The placebo group demonstrated a decrease in binge eating days per week with a baseline of 4.1 ± 1.1 to 1.8 ± 1.8 at week 12, resulting in a mean change from baseline of 2.3.[7] The intervention group revealed a decrease in binge eating days per week with a baseline of 4.3 ± 1.3 to 0.9 ± 1.3 at week 12, resulting in a mean change from baseline of 3.4.[7] The data presented

represents a statistically significant change for intervention group, with a reported p-value of 0.03.[7]

Table 4. Mean Change in Binge Eating Days/Week from Baseline to Week 12

Group	Before Treatment (Mean ± Standard Deviation)	After Treatment (Mean ± Standard Deviation)	Mean Change from Baseline (calculated)	P value
Placebo	4.1±1.1	1.8±1.8	2.3	Not reported
lisdexamfetamine dimesylate 70mg	4.3±1.3	0.9±1.3	3.4	0.03

DISCUSSION

With binge eating disorder reported as the most common eating disorder in the United States, there is a need for safe and effective treatments. This EBM review assessed lisdexamfetamine dimesylate as a reliable treatment method for adults diagnosed with binge eating disorder. The findings reported from all three articles demonstrated a statistically significant reduction in the number of binge eating days per week in subjects receiving the intervention of lisdexamfetamine dimesylate 70mg. McElroy et al. reported a p-value of < 0.001 with a mean change from baseline of 4.1, Hudson et al. reported a p-value of < 0.001 with a mean change from baseline of 4.72, and Guerdjikova et al. reported a p-value of 0.03 with a mean change from baseline of 3.4 for the intervention group. These results aid in validating the efficacy of lisdexamfetamine dimesylate and support its role in treating binge eating disorder. With a decrease in the number of binge eating days per week in individuals taking this medication, there is a subsequent improvement in the quality of life of these individuals diagnosed with binge eating disorder.

While all three studies discussed in this EBM review were double blind, randomized, placebo-controlled trials, which increases the validity of the studies, there are some limitations that need to be addressed. The studies conducted by McElroy et al. and Guerdjikova et al. were short in duration, making it difficult to generalize the long-term efficacy and safety of the intervention. The study completed by Guerdjikova et al. also had a small sample size, making it difficult to generalize the results. Additionally, all three studies in this EBM review excluded subjects that had comorbid psychiatric disorders. Research shows that those diagnosed with binge eating disorder are likely to have comorbid psychiatric disorders, so excluding these individuals from the trials makes it difficult to draw conclusions regarding the efficacy and safety of the intervention in these populations.[1] Lastly, all three studies had the greatest percentage of subjects being Caucasian females, resulting in the inability to rationalize the findings of the intervention to other demographics including the male population and those of other races.

While the efficacy and benefit of lisdexamfetamine dimesylate in the treatment of binge eating disorder has been thoroughly discussed in this EBM review, this medication comes with barriers to its use. Per the medication website, the most common side effects experienced from the use of this medication include dry mouth, decreased appetite, insomnia, feeling jittery, headache, and increased heart rate.[8] Lisdexamfetamine dimesylate also presents with some abuse and addiction potential, as it is categorized as a schedule II controlled substance.[8] Lisdexamfetamine dimesylate is not a medication that every individual with binge eating disorder can take; therefore, its use should be thoroughly discussed with a healthcare professional before initiation.

CONCLUSION

This systemic review revealed lisdexamfetamine dimesylate to be effective in decreasing the number of binge eating days per week in individuals diagnosed with binge eating disorder; therefore, increasing quality of life in these individuals. McElroy et al., Hudson et al., and Guerdjikova et al. all found lisdexamfetamine dimesylate 70mg to produce a statistically significant mean decrease in the number of binge eating days per week from the beginning of the study to the end. In order to further determine a place in therapy for lisdexamfetamine dimesylate in the treatment of BED, additional trials should be performed with larger sample sizes and for longer durations of time to assess the long-term effectiveness and safety of this medication. Other future studies of benefit include those that incorporate subjects of all demographics and those with comorbid psychiatric conditions. It would also be of interest to explore the combination of both lisdexamfetamine dimesylate and CBT to further optimize treatment efficacy. A final consideration is to create future studies that compare the use of lisdexamfetamine dimesylate to the other pharmacologic treatments that have the potential to be effective but have not been studied yet in comparison. With the increasing incidence and recognition of binge eating disorder, these future studies are warranted to provide the best treatment regimen for those with binge eating disorder, resulting in the most beneficial patient oriented outcomes.

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