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USE OF BUPROPION ASSOCIATED WITH SEROTONIN REUPTAKE INHIBITORS IN THE TREATMENT OF DEPRESSION

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Abstract: Bupropion is an antidepressant that has noradrenergic and dopaminergic effects, being a weak dopamine reuptake inhibitor. increasingly used as an adjuvant for the treatment of depression, which is rarely used in monotherapy. In this context, the aim of this study was to compile the literature and compare the effectiveness of the norepinephrine-dopamine reuptake inhibitor bupropion with selective serotonin reuptake inhibitors in the treatment of major depressive disorder. Sungo the results, which was performed and 147 patients, with an average age of 41.7 years, dividing them into three groups randomly to be treated with a different drug, the first with bupropion with 51 patients, the second with sertraline with 58 patients and the third with venlafaxine 65 patients. Regarding the rate of remission of symptoms, there was no statistical difference between the groups at week 10 of treatment. This review corroborates that there is a benefit of bupropion as an adjuvant in the treatment of patients who have depressive disorder and bipolar affective disorder. However, bupropion showed excellent results associated with antidepressants compared to other treatments with monotherapy, which did not reduce 50% of the Montgomery-Asberg depression scale score.
Keywords: Bupropion; Depression; Antidepressant.

INTRODUCTION

According to the Diagnostic and Statistical Manual of Mental Disorders (DMS-5) major depressive disorder manifestations come as a decline in energy, appetite and sleep quality, depressive disorders also rob individuals of the pleasure they previously derived from activities. Feelings of guilt may also subside when confronted. The cumulative effects of these symptoms can impede daily functioning and lead to emotional distress. Making

decisions becomes an arduous task, making regular activities challenging and often compromising quality of life.(BORGES et al., 2022)

However, to treat depression, there are several drugs available that work by inhibiting selective serotonin reuptake (SSRI) or increasing the bioavailability of neurotransmitters in the central nervous system. (FANG et al., 2011). Bupropion is an antidepressant that has noradrenergic and dopaminergic effects, being a weak inhibitor of dopamine reuptake (DA). it has been increasingly used as an adjuvant for the treatment of depression, which is rarely used in monotherapy. (POST et al., 2006). It is evident that the number of prescriptions for these drugs in developed countries has been growing since 1990, has become abusive and irrational. According to the bulletin published by the National Controlled Products Management System (SNGPC). (FORNARO et al., 2014).

Worldwide, according to the World Health Organization (WHO) estimates that 121 million people are affected by depression, of which less than 25% have access to effective treatments. WHO projections indicate that depression will be the second leading cause of disability in 2020. Approximately 5.8% of the Brazilian population is currently depressed. This number is greater than 11.5 million cases in all, which is the highest rate in the Americas, second only to the United States. The survey also showed that Ukraine, Australia and Estonia had higher rates of depression than any other American country; 6.3%, 5.9% and 5.9%, respectively, were the results of these countries, which are home to 17.4%, 14.1% and 14.1% of all cases in American depression surveys. (BRASIL, 2022)

Recently, research on the mental health of the general population is at the heart. However, this review aims to highlight this process, as it subsidizes the development of more effective actions and treatments aimed at communities. In this context, the aim of this study was to compile the literature and compare the effectiveness of the norepinephrine-dopamine reuptake inhibitor bupropion with selective serotonin reuptake inhibitors (SSRIs) in the treatment of major depressive disorder (MDD).

METHODOLOGY

This is an integrative review study that was designed based on the criteria established in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guide, considering the flow diagram and the PRISMA checklist. Thus, from the guiding question: "Is the use of bupropion in combination with serotonin reuptake inhibitors effective in the treatment of depressive disorder?" the articles were searched.

Keywords were defined according to the PICOS model as follows:

1. Population: people with depression;

2. Intervention: use of bupropion and antidepressants;

3. Comparative: control (placebo or antidepressants);

4. Results (variables): improvement in the clinical picture of depression with remission of symptoms;

5. Study design: clinical trial studies.

LITERATURE SEARCH

The survey of articles was carried out in the following databases: Medline/BVS and Medline/Pubmed. The following descriptors and their combinations in Portuguese and English were used to search for articles: "Bupropion AND Antidepressants AND

Treatment AND Depression // Bupropion AND Antidepressants AND Treatment AND Depression".

INCLUSION AND EXCLUSION CRITERIA

The selection of articles was guided by inclusion and exclusion criteria. The inclusion criteria defined for the selection of articles were: articles published in Portuguese, English; original articles in full that portray the theme related to the review and articles published and indexed in the aforementioned databases in the last 20 years.

The exclusion criteria defined for the selection of articles were non-original articles, dissertations and theses, articles that addressed the subject, but from a different point of view.

IDENTIFICATION AND SELECTION OF STUDIES

After applying the inclusion and exclusion criteria, the articles were identified. The screening of studies was carried out by reading and analyzing the titles and abstracts of all articles identified in each database, guided by the adopted inclusion and exclusion criteria. In the eligibility phase, after defining the articles to be included in each database, duplicate articles were excluded.

RESULTS

A total of 458 studies were identified according to our search strategy. Among them, presented two duplicate. After applying the adopted inclusion and exclusion criteria, 128 studies in Medline/VHL reading and 217 studies in Medline/Pubmed were excluded, with a total of 345 articles. Then the titles and abstracts were read, 62 of the 84 references were excluded based on the eligibility criteria. Thus, 22 references were selected for full text evaluation. Finally, four articles were eligible for qualitative evaluation. The selection process for identifying eligible studies included in the review, shown in figure 1.

The main characteristics of the included studies are shown in Table 1. In the study by Post et al.[1] (2006), which was carried out and 147 patients, with an average age of 41.7 years, dividing them into three groups randomly to be treated with a different drug, the first with bupropion with 51 patients, the second with sertraline with 58 patients and the third with venlafaxine 65 patients. Regarding the rate of remission of symptoms, there was no statistical difference between the groups at week 10 of treatment.

It is also worth considering, in line with Michael's essay *et al.*[2] (2006), which involved 342 patients, divided into 168 who received bupropion and 174 who received venlafaxine, 40% of the total number of subjects were male. It was possible to notice at the 12th week in the bupropion group a statistical difference in relation to remission favorable to the symptoms.

Regarding Hewett et al.[3] (2009), involving 571 patients divided into three groups with a mean age of 41.8 and standard deviation of 11.56 the therapeutic proposal using bupropion evenlafaxine compared with the placebo group showed more efficacy with p less than 0.05, during 8 weeks of treatment.

Finally, it is noted, according to Gaurav et al.3 (2012), that it consisted of a sample of 60 people divided into two groups equally, with group A receiving antidepressants plus placebo while group B received antidepressants plus bupropion . It is evident that the group that received the intervention showed significance compared to the control group in three weeks by the Montgomery Asberg depression scale (MARDS).

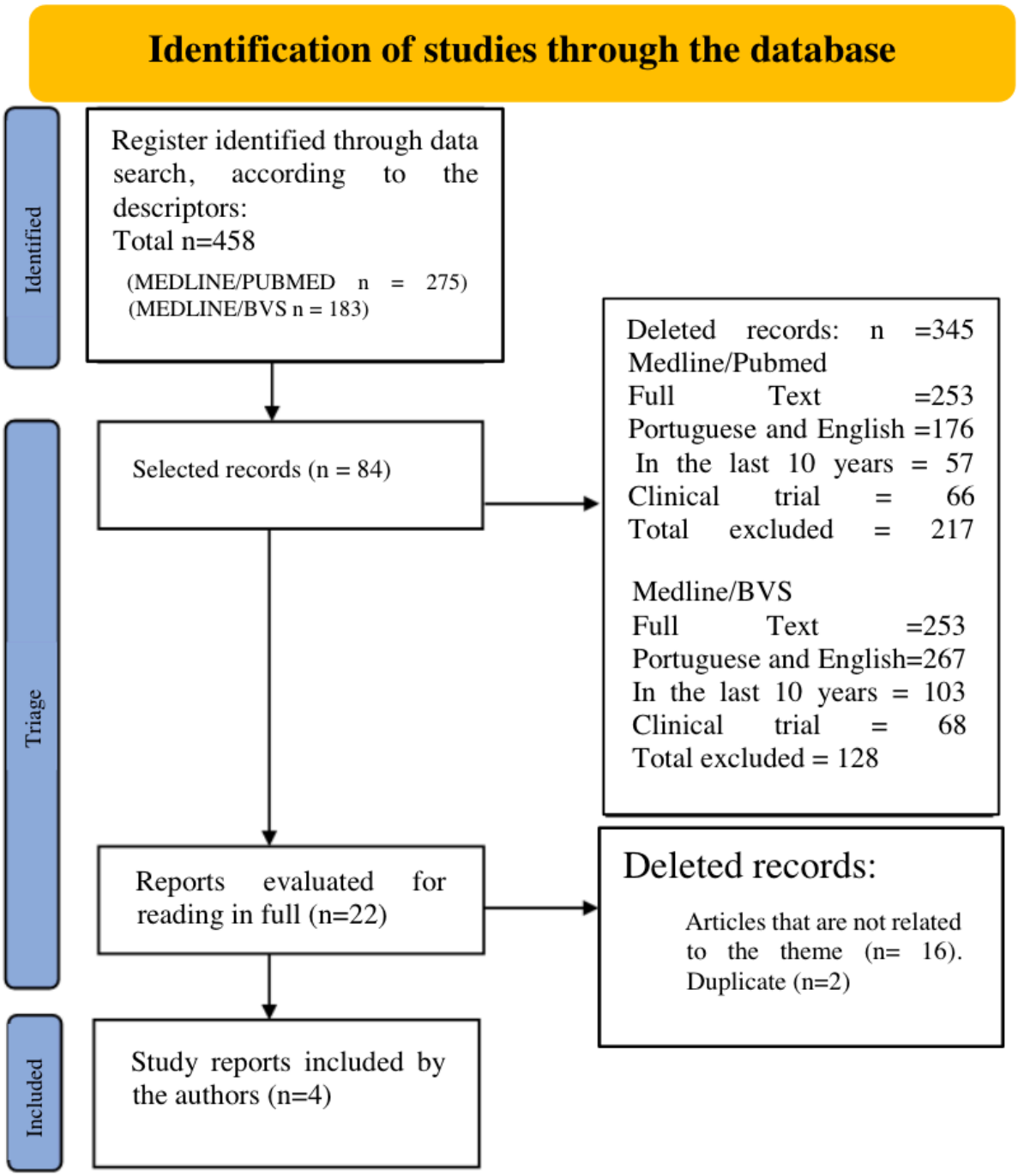

Figure 1: Flowchart for selection process, identification, screening, eligibility and included.

Title/Author	Publication year	Study design	Objectives	Methodology	Main results
Mood switch in bipolar depression: comparison of venlafaxine, bupropion and sertraline. Post RM	2006	Clinical Trial	Examine the relative acute effects of bupropion, sertraline, and venlafaxine as adjuncts to mood stabilizers.	In a 10-week study, participants receiving outpatient treatment for bipolar disorder (stratified for rapid cycling) were randomly treated with a flexible dose of one of the antidepressants, or their corresponding placebos, as an adjunct to the mood stabilizers.	All three antidepressants were associated with a similar range of acute response (49-53%) and remission (34-41%%). There was a significantly increased risk of changes in hypomania or mania in participants treated with venlafaxine compared with bupropion or sertraline.
A double-blind comparison between bupropion XL and venlafaxine XR: sexual functioning, antidepressant efficay, and tolerability. Michael E Thase	2006	Clinical Trial	Analyzing bupropion XL, a norepinephrine-dopamine reuptake inhibitor, and venlafaxine XR, a serotonin-norepinephrine reuptake inhibitor, were compared for sexual functioning, efficacy, and tolerability.	A total of 348 sexually active adult outpatients with depression were randomized to receive bupropion XL (titrated to a target dose of 300-450 mg/d) or venlafaxine XR (titrated to a target dose of 150-225 mg/d for 12 weeks.	The therapies resulted in similar changes on the 17-item Hamilton Rating Scale for Depression, remission rates were significantly higher among those treated with bupropion XL (46%) versus venlafaxine XR (33%) (radio odds, 193%; 95% confidence interval, 1.07-3.46).
Eight-Week, placebo-controlled, double-blind comparison of the antidepressant efficacy and tolerability of bupropion XR and venlafaxine XR. K Hewett	2009	Clinical Trial	The efficacy, safety, and tolerability of bupropion XR and venlafaxine XR were evaluated and compared with placebo in adult outpatients with major depressive disorder (MDD).	Adults meeting DSM-IV criteria for MDD with a minimum 17-item Hamilton Rating Scale for Depression (HAMD) total score > or = 18 were randomized to eight weeks of double-blind treatment with bupropion XR (150 mg/day), venlafaxine XR (75 mg/day) or placebo.	The mean changes from baseline at week 8 (LOCF) in the MADRS total score were statistically significant for patients on bupropion XR and venlafaxine XR compared to the placebo group: -16.0 for bupropion XR (P = 0.006 vs placebo) , -17.1 for venlafaxine XR (P<0.001 vs placebo) and -13.5 for placebo.
Bupropion as na augmenting agente in patientes of depression with partial response. Gaurav Guirez	2012	Clinical Trial	**The aim of this study is to evaluate the effects of bupropion as adjunctive therapy to selective serotonin reuptake inhibitor (SSRI) in patients with partial response major depressive disorder.**	**This prospective, randomized, controlled, single-blind study was conducted in sixty patients suffering from major depressive disorder according to Diagnostic and Statistical Manual (DSM)-IV TR criteria, who had a Hamilton Rating Scale (HDRS) score.) ≥16 after 4 weeks of SSRI treatment.**	**The percentage decrease in remitters was also significantly greater in group B (60% according to the HDRS score and 63% according to the MADRS score) compared to group A (24% according to the HDRS score and 27% according to the MADRS score)(p<0.05), at the end of treatment.**

Table 1: Description of the selected articles with the variables: Title of study/Author, year of publication, objectives, methodology and main results.

CONCLUSION

This review corroborates that there is a benefit of bupropion as an adjuvant in the treatment of patients who have depressive disorder and bipolar affective disorder. However, bupropion showed excellent results associated with antidepressants compared to other treatments with monotherapy, which did not reduce 50% of the Montgomery-Asberg depression scale score. Therefore, the risk factors associated with this class of drugs need to be investigated more closely in order to obtain a possible effective intervention.

REFERENCES

BRASIL. **Na américa latina, Brasil é o país com maior prevalência de depressão.** Ministério da saúde. 22 set. 2022.

BORGES, G. A. C.; COSTA, L. C. S.; GALHARDO, C. O.; BARBOSA, M. E.; COELHO, R. F.; CAETANO, M. C. G.; JULIO, B. R.; VASCONCELOS, G. F.; PEREIRA, U. B.; ARANTES, J. R.; MORATO, C. de O. N.; FARIA, A. S. IMPACT ON SEXUAL FUNCTION IN PATIENTS WITH DEPRESSIVE DISORDERS TREATED WITH ANTIDEPRESSANTS. **International Journal of Health Science**, [s. l.], v. 2, n. 76, p. 2–8, 2022. Disponível em: <https://atenaeditora.com.br/catalogo/artigo-revista/impacto-na-funcao-sexual-em-pacientes-transtornos-depressivos-tratados-com-antidepressivos>

FANG, Y.; YUAN, C.; XU, Y.; CHEN, J.; WU, Z.; CAO, L.; YI, Z.; HONG, W.; WANG, Y.; JIANG, K.; CUI, X.; CALABRESE, J. R.; GAO, K. A pilot study of the efficacy and safety of paroxetine augmented with risperidone, valproate, buspirone, trazodone, or thyroid hormone in adult chinese patients with treatment-resistant major depression. **Journal of Clinical Psychopharmacology**, [s. l.], v. 31, n. 5, p. 638–642, 2011.

FORNARO, M.; MARTINO, M.; MATTEI, C.; PRESTIA, D.; VINCIGUERRA, V.; DE BERARDIS, D.; DE PASQUALE, C.; IASEVOLI, F.; MUNGO, S.; FORNARO, P. Duloxetine-bupropion combination for treatment-resistant atypical depression: A double-blind, randomized, placebo-controlled trial. **European Neuropsychopharmacology**, [s. l.], v. 24, n. 8, p. 1269–1278, 2014. Disponível em: <http://dx.doi.org/10.1016/j.euroneuro.2014.04.004>

Gulrez G, Badyal DK, Deswal RS, Sharma A. **Bupropion as an augmenting agent in patients of depression with partial response**. Basic Clin Pharmacol Toxicol. 2012 Mar;110(3):227-30. doi: 10.1111/j.1742-7843.2011.00788.x. Epub 2011 Sep 28. PMID: 21895979.

Hewett K, Chrzanowski W, Schmitz M, Savela A, Milanova V, Gee M, Krishen A, Millen L, Leary MO, Modell J. **Eight-week, placebo-controlled, double-blind comparison of the antidepressant efficacy and tolerability of bupropion XR and venlafaxine XR. J Psychopharmacol.** 2009 Jul;23(5):531-8. doi: 10.1177/0269881108089602. Epub 2008 Jul 17. PMID: 18635695.

Manual diagnóstico e estatístico de transtornos mentais: **DSM-5 /** [American Psychiatric Association ; tradução: Maria Inês Corrêa Nascimento ... et al.] ; revisão técnica: Aristides Volpato Cordioli ... [et al.]. – 5. ed. – Porto Alegre : Artmed, 2014.

POST, R. M.; ALTSHULER, L. L.; LEVERICH, G. S.; FRYE, M. A.; NOLEN, W. A.; KUPKA, R. W.; SUPPES, T.; MCELROY, S.; DENICOFF, K. D.; GRUNZE, H.; KITCHEN, C. M. R.; MINTZ, J. Mood switch in bipolar depression: Comparison of adjunctive venlafaxine, bupropion and sertraline. **British Journal of Psychiatry**, [s. l.], v. 189, n. AUG., p. 124–131, 2006.

Thase ME, Clayton AH, Haight BR, Thompson AH, Modell JG, Johnston JA. **A double-blind comparison between bupropion XL and venlafaxine XR: sexual functioning, antidepressant efficacy, and tolerability.** J Clin Psychopharmacol. 2006 Oct;26(5):482-8. doi: 10.1097/01.jcp.0000239790.83707.ab. PMID: 16974189.