Review article

The Effectiveness of Bupropion in Cigarette Smoking Cessation – A Narrative Review

Matea Prenc [1], Frano Perić [2], Irena Petričić [3], Mirjana Flegarić Bradić [4], Robert Rončević [5]

[1] Department of Diagnostic and Interventional Radiology, Sestre milosrdnice University Hospital Center, Zagreb, Croatia
[2] Department of Radiology, Dubrovnik General Hospital, Croatia
[3] Department of Psychiatry, Sahlgrenska University Hospital, Gothenburg, Sweden
[4] Department of Diagnostic and Interventional Radiology, Sestre milosrdnice University Hospital Center, Zagreb, Croatia
[5] Department of Diagnostic and Interventional Radiology, University Hospital Center Osijek, Croatia

*Corresponding author: Matea Prenc, prenc.matea2@gmail.com

Abstract

Smoking is still a large indirect cause of premature death worldwide. The first line of treatment for smoking cessation is nicotine replacement therapy (NRT). Bupropion, a drug primarily developed as an antidepressant, in some countries is the first drug licensed for smoking cessation that is not associated with nicotine. The drug acts mostly through its inhibition of dopamine reuptake in the neuronal synapses, but other effects of bupropion may also have a role in smoking cessation. There have been many clinical studies of bupropion that have shown impressive results in helping patients with smoking cessation. Because of its antidepressant role, it is useful in smoking cessation in patients with depression. Through the years bupropion has proven to be a potential cost-effective alternative to NRT.

(Prenc M, Perić F, Petričić I, Flegarić Bradić M, Rončević R. The Effectiveness of Bupropion in Cigarette Smoking Cessation – A Narrative Review. SEEMEDJ 2023; 7(2); 76-86)

Received: Jun 4, 2024; revised version accepted: Jul 14, 2024; published: Jul 19, 2024

KEYWORDS: bupropion, nicotine replacement therapy, smoking cessation

Introduction

Although smoking prevalence among adults has been in decline for the last couple of decades (1) it is still a serious health issue associated with the death of around 8.7 million people every year of which 1.3 million were estimated non-smokers and it stands among the top preventable causes of premature deaths (2). It is estimated that a smoker attempts quitting 30 times or more before successfully quitting for at least 1 year (3). Nicotine exerts most of its effects by binding to neuronal nicotinic acetylcholine receptors (nAChRs) located on the presynaptic membrane and causing the release of neurotransmitters dopamine, noradrenaline, acetylcholine, glutamate, γ-aminobutyric acid (GABA), serotonin and endorphins. There are a lot of subtypes of these receptors and the most important one associated with nicotinic addiction is the $\alpha 4 \beta 2$ receptor (4,5). The first step in an attempt to quit smoking is always counseling and cognitive behavioral therapy which both promote smoking cessation by giving patients information, guidance and skills for the prevention of a relapse. For many smokers, this approach alone is not enough so pharmaceutical intervention aids in the process of quitting (5). The main principles by which pharmaceutical intervention can aid in smoking cessation are the reduction of nicotine withdrawal symptoms, reduction of the rewarding pathway of nicotine by blocking or desensitizing nicotine receptors and providing a substitute for smoking with an alternative source of nicotine in controlled doses (5). Nicotine replacement therapy (NRT) is recommended by many clinical guidelines as the first-line therapeutic drug for smoking cessation (6). NRT is available in forms of transdermal patches, gums, inhalers, lozenges and nasal sprays which are most effective in a combination and deliver nicotine in controlled doses to the neural synapses thus reducing the urge to smoke and exposure to dangerous substances found in cigarettes. These doses should be low enough to reduce symptoms associated with nicotine withdrawal syndrome while not high enough to sustain addiction (7,8,9). Since the development of NRT, there have been a lot of clinical trials trying to find a cost-effective and safe alternative. Today, bupropion and varenicline are also licensed as first-line treatment options in many countries, with clonidine and nortriptyline being second-line options (10,11,12). The goal of this study is to explain the effectiveness of bupropion as a first-line smoking cessation pharmaco-therapy intervention.

Methods

For this narrative review, a comprehensive literature search was conducted predominantly in the medical database PubMed. The search was restricted to papers written in English that contained the words "bupropion" and/or "smoking cessation" and/or "tobacco cessation" and/or "nicotine withdrawal" in the title, abstract or body of the article. The review included open-access articles published in peer-reviewed journals. No date limits were applied to the articles included in the search. Additionally, a hand search of the references of full-text papers was obtained. This paper is a non-systematic review of existing literature on the topic of our interest in which retrieved articles were analyzed and key results were discussed in summary.

Mechanism and pharmacology

Bupropion, previously known as amfebutamone, was synthesized in 1966 by Burroughs Wellcome as an atypical antidepressant chemically distinct from the tricyclics (TCAs) or the selective serotonin reuptake inhibitors (SSRIs) with similar efficacy but with lesser side-effects related to sympathomimetic, cholinolytic or monoamine oxidase inhibitory properties (13,14). Bupropion is a monocyclic phenylbutylamine of the amino ketone group with tertbutyl moiety attached to the amine group and a chlorine group attached to the position 3' of the aromatic ring (15). The synthesis includes the reaction of 3-chlorobenzonitrile with ethylmagnesium bromide to produce 3-chloropropiophenone. Bromination of 3-chloropropiophenone gives 3-chloro-α-bromopropiophenone which reacts with tert-

butylamine and finally produces bupropion (16). While structurally unrelated to TCAs or SSRIs, the core structure is similar to that of neurotransmitters dopamine and norepinephrine but also to psychoactive substances diethylpropion, cathinone and amphetamine. The psychostimulant activity and abuse potential are reduced by the phenyl ring substitution and the size and branching of the N-alkyl group. Bupropion is a weak base (pKa: 7.9 at 25) available as a racemic mixture of R-()-bupropion and S- (þ)-bupropion and dispensed as hydrochloride (HCl) salt (15,17). Bupropion comes in three different, bioequivalent forms: immediate release (IR), sustained release (SR) – bupropion incorporated in a methylcellulose matrix and the extended-release (XL) – bupropion incorporated by controlled-release and moisture-barrier coatings (15).

The development of slow-release formulations with prolonged absorption that can be taken once a day largely decreased the prevalence of seizure activity that appeared with immediate form (14). Bupropion sustained release used for treating nicotine craving (generically Zyban) should be initiated 1 to 2 weeks before the quit date (while the patient is still smoking), usually started at the lowest dose of 150 mg daily for 3 days and then increased and continued at 300 mg per day for the next 6 to 12 weeks. The maximum single dose is 150 mg and the time interval between successive doses should be at least 8 hours. The maximum daily dose is 450 mg (18). Because it is a small and highly lipophilic molecule, bupropion is rapidly absorbed and distributed throughout the body, followed by a slower elimination phase (biphasic distribution). However, its bioavailability is reduced due to the extensive, stereoselective metabolism that eliminates the majority of parent compounds with less than 1% of bupropion excreted unchanged in the urine (19). Hepatic enzymes produce three primary metabolites: (2S,3R)- and (2S,3S)-hydroxybupropion, (R,R)- and (S,S)-threo-bupropion, and (R,S)- and (S,R)-erythro-bupropion (20). Hydroxybupropion is formed through hydroxylation of the side chain tert-butyl group of bupropion by hepatic cytochrome P450 (CYP) 2B6, and diastereoisomers threohydrobupropion and erythrohydrobupropion through reduction of the side chain ketone group by carbonyl reductase (19). Compared to bupropion, its major active metabolites reach higher plasma concentrations and have 25–50% potency and therefore have a significant impact on its efficacy and pharmacological and toxicological effects (15,19). Since bupropion has an extensive metabolic pathway and CYP2B6 is a catalyst for many biotransformation reactions there is high potential for drug interactions. Both bupropion and its metabolites are inhibitors of CYP2D6, increasing the levels of drugs metabolized by this enzyme (21). Because it crosses the blood-brain barrier and human placenta and is also excreted in human breast milk, bupropion belongs to pregnancy class C and requires caution in breastfeeding (15).

Bupropion sustained-release (bupropion SR)

Bupropion was primarily licensed as an antidepressant but during its use in the treatment of major depressive disorders in the late 1980s, it has been noted that some of the patients who smoked coincidentally quit smoking. Later through clinical trials, it has proven to be an effective smoking cessation aid (22,23). As an antidepressant, it was first used in its IR form, but in the treatment of nicotine addiction, it is used in ER form which is further divided into the SR form administered in 2 doses daily and the XL form administered as a single daily dose (24). With its inhibition of the reuptake of dopamine and noradrenaline, it simulates the effect of nicotine by elevating the concentrations of these neurotransmitters in the synapse. It also acts as a nicotine antagonist on the $\alpha 4\beta 2$ subtype receptor and with this mechanism lowers the dependence on nicotine (5,25,26). Some studies have shown that continuous bupropion SR therapy is associated with a reduction in smoking and shorter periods between attempts to quit (27). Another first-line drug therapy for tobacco cessation is varenicline. Compared to bupropion, varenicline is a partial agonist of the $\alpha 4\beta 2$ subtype receptors which are responsible for the major

nicotinic effects and as such it acts as an agonist, having half the efficacy of nicotine and thus relieving the symptoms of nicotine withdrawal syndrome. Meanwhile, as an antagonist, it inhibits the nicotinic reward pathway (28). Many studies have shown that bupropion has similar effectiveness as single-use NRT, but less than varenicline in smoking cessation, which in most cases outperformed both but did not prove to be more effective than combination NRT, but further research is necessary for confirmation (29,30). Combined bupropion SR and NRT therapy have shown to have somewhat higher abstinence rates than bupropion SR solely but were statistically of no significance compared to single NRT, where efficacy was much higher in the combination therapy (31). Unlike NRT, bupropion SR treatment should be started while the person is still smoking, ideally 2 weeks before the patient begins abstinence. It is normally used in doses of 100 to 300 mg daily and bupropion SR in particular is given typically in 2 doses of 150 mg per day. It is administered only orally and the maximum dose is 450 mg a day (32). Using bupropion SR alone or in combination with NRT reduces the normal weight gain that happens in smoking cessation. These effects last even after the end of long-term treatment whereas for short-term treatment, they last only during the active treatment (31).

Bupropion SR in smokers with mental illnesses

Nicotine addiction is common among people diagnosed with mental illnesses such as major depression, anxiety disorder and schizophrenia. There may be a connection in genetic predisposition between nicotine addiction and mental illness. The self-medication hypothesis suggests that psychiatric patients smoke cigarettes to lessen their symptoms (33,34). Some substances in cigarettes other than nicotine inhibit the functions of monoamine oxidases (MAO), enzymes that facilitate the breakdown of certain neurotransmitters, thus leading to their higher concentrations and enhancing the nicotine effects (35). Since MAO inhibition is used for the treatment of depression, this suggests that in some patients smoking might have positive effects in the short-term management of symptoms. Some studies have shown that patients with a history of depression were at higher risk of developing depressive episodes after smoking cessation (36). Even though in the early stages of abstinence they tend to develop anxiety and other depressive symptoms, it was observed that in the long term, smoking cessation improves the mood, and reduces stress, depression symptoms and anxiety equally in smokers with and without mental illnesses (37). Smoking cessation may be as effective as antidepressant therapy in the management of anxiety disorders. Although smoking is common in these patients there is little information about the safety and effectiveness of smoking-cessation medicamentation and further research is necessary. In clinical trials, bupropion showed a short-term reduction in depressive symptoms but the effect was of no significance in the long term after ending the treatment. While heavy smokers with higher nicotine dependence showed a bigger reduction in depressive symptoms during the treatment, after the end of treatment they experienced more severe depression symptoms than the less dependent smokers (38). Bupropion SR may show equal efficacy in patients with anxiety disorders as in the general population but without any significant reduction in depressive symptoms (39). There were some concerns of increased psychosis when using bupropion for smoking cessation in patients with schizophrenia but some studies refute these concerns and show that bupropion is acceptable in the treatment and may even relieve depressive symptoms (40). One study which included a clinical trial and meta-analysis has shown contradictory results that bupropion SR did not have any effect during the clinical trial but did show efficacy in the meta-analysis in smoking cessation in patients with schizophrenia. However, the conclusion was that bupropion was effective and tolerable in smoking cessation in patients with schizophrenia (41). It is suggested that the same treatment for smoking cessation including pharmaceutical intervention in the general population is of the same efficacy in smokers

with mental illnesses without significant risk of worsening their mental disease (42).

Drug interactions

As already mentioned, bupropion is metabolized in the liver by CYP2B6. Bupropion moderately inhibits enzymes such as CYP2D6 which is responsible for its pharmacokinetic interactions with other drugs. As CYP2D6 is responsible for the metabolization of other antidepressants such as venlafaxine, if used in combination with bupropion the effects but also the risk of side effects associated with venlafaxine are increased. Most second-generation antipsychotics are in the same way as antidepressants metabolized by CYP2D6 and bupropion could have similar interactions (43,44). On the other hand, CYP2D6 metabolizes some other medications to their active forms like opiates or tamoxifen. Bupropion used concomitantly with opiates like codeine, oxycodone and tramadol may lower their efficacy in analgesia (45,46). With tamoxifen only some SSRIs have proven to lower the efficacy of the drug and further research is needed to evaluate the potential effect of bupropion. There is not enough information on whether bupropion should be used with tamoxifen, but it is advisable to avoid it (47). Anticonvulsants phenobarbital, carbamazepine and phenytoin are strong CYP inducers including the CYP2B6 which lowers the concentration of bupropion and may reduce its effects (48,49).

Contraindications

Bupropion is contraindicated in patients who are allergic or hypersensitive to it. Because of drug interaction, it should not be prescribed in combination with MAOIs (50). Bupropion should be avoided in smokers with a present seizure disorder, a history of seizures or any other increased risk for seizures, which includes patients with central nervous system tumors, patients undergoing acute abstinence from alcohol or discontinuation of benzodiazepines and patients diagnosed with bulimia or anorexia nervosa. The only indication to use bupropion in these patients is when the benefits of smoking cessation surpass the seizure risk. Bupropion should not be prescribed in patients on medications that lower the seizure threshold such as antipsychotics, antimalarials, tramadol, quinolones, some antidepressants, etc. Alcohol abuse or a previous head trauma also lowers the seizure threshold (51,52).

Side effects

Bupropion is mostly safe to use and tolerable in the dose of 100 to 300 mg a day in most smokers up to 45 weeks. The most common side effects observed when used for smoking cessation are insomnia and dry mouth which mostly resolve on their own and can be controlled with dose regulation. Other less common side effects include headache, nausea, anxiety, pruritus, constipation and pharyngitis. Compared to placebo, bupropion SR did not show any higher frequency rates of side effects associated with the cardiovascular system such as hypertension, tachycardia, postural hypotension and vasodilation. In patients with preexisting cardiovascular diseases, it has proven to be as safe as in the general population. The most feared side effects of bupropion are seizures and hypersensitivity reactions. These are serious complications with a rare occurrence, but mostly not life-threatening. As seizures seem to be dose-related, bupropion SR should not be prescribed in higher doses than allowed. It is also contraindicated in patients who use medication that lowers the seizure threshold, have any other kinds of predispositions for seizures or have a history of seizures. Even though there have not been any clinical comparisons between SR and IR forms, it was observed that bupropion SR may have lower seizure rates (24,31,53,54). One of the rare side effects of bupropion is angioedema, a potentially serious complication that normally affects the head and neck and should be further studied (55). While most antidepressants are associated with sexual dysfunction as a side effect, bupropion is one of the exceptions (32). Some smokers tend to develop depression after the use of bupropion SR for smoking cessation which could be caused by bupropion itself or as part of nicotine withdrawal syndrome (51).

Discussion

To summarize, tobacco smoking is a global public health challenge with profound implications for individuals and societies. It stands at the top among preventable causes of death in the world. Beyond its direct health consequences, smoking exerts a substantial economic burden and carries significant social implications. The societal costs extend to secondhand smoke exposure, affecting non-smokers and exacerbating health disparities. Understanding the multifaceted nature of smoking provides a foundation for exploring interventions aimed at reducing its prevalence and mitigating its impact on health and society. Behavioral interventions form a cornerstone of smoking cessation efforts. These approaches target the psychological and behavioral aspects of smoking addiction. Cognitive-behavioral therapy, for example, focuses on identifying and modifying thought patterns and behaviors associated with smoking. Support groups, counseling sessions and motivational interviewing are additional examples of behavioral therapies that aim to empower individuals in their journey towards tobacco-free living. Pharmacological interventions play a pivotal role in smoking cessation, aiding individuals by addressing the physiological aspects of addiction. NRT, such as patches, gum, lozenges and nasal sprays, provide controlled doses of nicotine to alleviate withdrawal symptoms. Additionally, prescription medications, including varenicline and bupropion, have been developed to target nicotine receptors in the brain, reducing cravings and withdrawal symptoms. Bupropion, originally approved as an antidepressant, has found a prominent role in smoking cessation since its approval. Bupropion, an aminoketone antidepressant, exhibits a mechanism of action not fully elucidated. Although its impact on monoamine uptake is limited, it inhibits the reuptake of norepinephrine and dopamine, particularly affecting the latter. The heightened dopamine reuptake inhibition contributes to its clinical manifestations. Bupropion also acts on nicotinic receptors to a lesser extent as an antagonist. The onset of therapeutic effects varies based on the formulation (immediate, sustained or extended-release). Bupropion is administered orally as a hydrochloride salt. The recommended dosage for smoking cessation usually starts at 150 mg daily, with careful titration to a maintenance dose of 300 mg per day. The maximum daily dose is 450 mg, administered in divided doses. The most significant adverse effects include a lowered seizure threshold and potential hypersensitivity. Seizures, although rare, are more likely with higher doses, especially in the immediate-release form. The clinician should carefully monitor patients for these adverse effects, especially those with a history of seizures or mood disorders. Several contraindications limit the use of bupropion. Patients hypersensitive or allergic to bupropion or its constituents should avoid its use. Bupropion, through many trials in clinical practice, has proven to be more effective than single NRT and shows even more efficacy if combined with it. It is safe to take in people with mental illnesses such as depression, anxiety disorders and schizophrenia as it does not worsen the patients' mental health but helps with the management of some of their symptoms.

Conclusion

Understanding the mechanism of action, adverse effects and contraindications of bupropion is crucial for healthcare professionals involved in smoking cessation efforts. With careful monitoring and consideration of individual patient factors, bupropion can be a valuable tool in the comprehensive approach to tobacco addiction treatment. The subsequent exploration of scientific literature further enhances our understanding of the risks and benefits associated with the use of bupropion in smoking cessation. These programs may include a combination of behavioral therapies, pharmacological aids and ongoing support to tailor the approach to individual needs.

Acknowledgement. None.

Disclosure

Funding. No specific funding was received for this study.

Competing interests. None to declare.

References

1. Dai X, Gakidou E, Lopez AD. Evolution of the global smoking epidemic over the past half century: strengthening the evidence base for policy actionTobacco Control 2022;31:129-137

2. World Health Organization (WHO). WHO report on the global tobacco epidemic, 2023: protect people from tobacco smoke.

3. Chaiton M, Diemert L, Cohen JE, Bondy SJ, Selby P, Philipneri A, Schwartz R. Estimating the number of quit attempts it takes to quit smoking successfully in a longitudinal cohort of smokers. BMJ Open. 2016 Jun 9;6(6):e011045. doi: 10.1136/bmjopen-2016-011045. PMID: 27288378; PMCID: PMC4908897.

4. Albuquerque EX, Alkondon M, Pereira EF, Castro NG, Schrattenholz A, Barbosa CT, Bonfante-Cabarcas R, Aracava Y, Eisenberg HM, Maelicke A. Properties of neuronal nicotinic acetylcholine receptors: pharmacological characterization and modulation of synaptic function J Pharmacol Exp Ther, 280 (1997), pp. 1117-1136

5. Prochaska JJ, Benowitz NL. Current advances in research in treatment and recovery: Nicotine addiction. Sci Adv. 2019 Oct 16;5(10):eaay9763. doi: 10.1126/sciadv.aay9763. PMID: 31663029; PMCID: PMC6795520.

6. Niaura R, Sayette M, Shiffman S, et al. Comparative efficacy of rapid-release nicotine gum versus nicotine polacrilex gum in relieving smoking cue-provoked craving. Addiction 2005; 100(11):1720–1730. doi:10.1111/j.1360-0443.2005.01218.x

7. Drug and Therapeutics Bulletin. Republished: nicotine and health. BMJ 2014; 349:2014.7.0264rep. doi:10.1136/bmj.2014.7.0264rep

8. Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev 2012; 11:CD000146. doi:10.1002/14651858.CD000146.pub4

9. Beard E, et al., New Pharmacological Agents to Aid Smoking Cessation and Tobacco Harm Reduction: What Has Been Investigated, and What Is in the Pipeline? CNS Drugs, 2016. 30(10): p. 951-83.

10. A clinical practice guideline for treating tobacco use and dependence: 2008 update. A U.S. Public Health Service report. Am J Prev Med, 2008. 35(2): p. 158-76.

11. Halpern SD, Volpp KG. E-Cigarettes, Incentives, and Drugs for Smoking Cessation. N Engl J Med. 2018 Sep 06;379(10):992

12. Drugs and Lactation Database (LactMed®) [Internet]. National Institute of Child Health and Human Development; Bethesda (MD): Nov 15, 2023. Varenicline

13. Nishino S, Mignot E. "Chapter 44 - Wake-Promoting Medications: Basic Mechanisms and Pharmacology".Principles and Practice of Sleep Medicine (Fifth Edition). W.B. Saunders. 201. Pages 510-526

14. Moser P. "Bupropion".xPharm: The Comprehensive Pharmacology Reference. Elsevier. 2008. Pages 1-4

15. Costa R, Aparecida M et al. Pharmacokinetic and pharmacodynamic of bupropion: integrative overview of relevant clinical and forensic aspects. Drug Metabolism Reviews 51 (2019): 293 - 313.

16. Vardanyan RS, Hruby VJ. "Antidepressants". Synthesis of Essential Drugs. Elsevier. 2006. Pages 103-116

17. Foley KF, DeSanty KP, Kast RE. Bupropion: pharmacology and therapeutic applications. Expert Rev Neurother. 2006 Sep;6(9):1249-65.

18. Benowitz NL, Brunetta PG. "46 - Smoking Hazards and Cessation".Murray and Nadel's Textbook of Respiratory Medicine (Sixth Edition). W.B. Saunders. 2016. Pages 807-821.e3

19. Connarn JN, Zhang X, Babiskin A, Sun D. Metabolism of bupropion by carbonyl reductases in liver and intestine. Drug Metab Dispos. 2015 Jul;43(7):1019-27

20. Khan SR, Berendt RT, Ellison CD, Ciavarella AB, Asafu-Adjaye E, Khan MA, Faustino PJ. "Chapter One - Bupropion Hydrochloride". Profiles of Drug Substances, Excipients and Related Methodology. Academic Press. Volume 41. 2016. Pages 1-30.

21. Hedrich WD, Hassan HE, Wang H. Insights into CYP2B6-mediated drug–drug interactions,Acta Pharmaceutica Sinica B, Volume 6, Issue 5, 2016, Pages 413-425,

22. Sealock T, Sharma S. Smoking Cessation. [Updated 2023 Jan 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482442/

23. Ferry LH. Non-nicotine pharmacotherapy for smoking cessation. Prim Care, 1999. 26(3): p. 653-69.

24. Aubin HJ. Tolerability and safety of sustained-release bupropion in the management of smoking cessation. Drugs. 2002;62 Suppl 2:45-52. doi: 10.2165/00003495-200262002-00005. PMID: 12109935.

25. Elrashidi MY, Ebbert JO. Emerging drugs for the treatment of tobacco dependence: 2014 update. Expert Opin Emerg Drugs, 2014. 19(2): p. 243-60.

26. Hays JT, Hurt RD, Rigotti NA, Niaura R, Gonzales D, Durcan MJ, Sachs DP, Wolter TD, Buist AS, Johnston JA, White JD. Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation. A randomized, controlled trial. Ann. Intern. Med. 135 (2001).

27. Hatsukami DK, et al. Effects of sustained-release bupropion among persons interested in reducing but not quitting smoking. Am J Med, 2004. 116(3): p. 151-7.

28. Rollema H, Coe JW, Chambers LK, Hurst RS, Stahl SM, Williams KE. Rationale, pharmacology and clinical efficacy of partial agonists of $\alpha 4 \beta 2$ nACh receptors for smoking cessation. Trends Pharmacol. Sci. 28 (2007)

29. Hughes JR, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. Antidepressants for smoking cessation. Cochrane Database Syst Rev. 2014 Jan 8;2014(1):CD000031. doi: 10.1002/14651858.CD000031.pub4. Update in: Cochrane Database Syst Rev. 2020 Apr 22;4:CD000031. PMID: 24402784; PMCID: PMC7027688.

30. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev. 2013 May 31;2013(5):CD009329. doi: 10.1002/14651858.CD009329.pub2. PMID: 23728690; PMCID: PMC8406789.

31. Holm KJ, Spencer CM. Bupropion. Drugs 59, 1007–1024 (2000). https://doi.org/10.2165/00003495-200059040-00019

32. Rothmore J. Antidepressant-induced sexual dysfunction. Med J Aust. 2020 Apr;212(7):329-334.

33. Prochaska JJ, Das S, Young-Wolff KC. Smoking, mental illness, and public health. Annu. Rev. Public Health 38, (2017).

34. Baker TB, Piper ME, McCarthy DE, Majeskie MR, Fiore MC. Addiction motivation reformulated: An affective processing model of negative reinforcement. Psychol. Rev. 111, (2004)

35. Lewis A, Miller JH, Lea RA. Monoamine oxidase and tobacco dependence. Neurotoxicology 28, (2007).

36. Tsoh JY, Humfleet GL, Muñoz RF, Reus VI, Hartz DT, Hall SM. Development of major depression after treatment for smoking cessation. Am J Psychiatry. 2000 Mar;157(3):368-74. doi: 10.1176/appi.ajp.157.3.368. Erratum in: Am J Psychiatry 2000 Aug;157(8):1359. PMID: 10698811.

37. Taylor G, McNeill A, Girling A, Farley A, Lindson-Hawley N, Aveyard P. Change in mental health after smoking cessation: systematic review and meta-analysis. BMJ. 2014 Feb 13;348:g1151. doi: 10.1136/bmj.g1151. Erratum in: BMJ. 2014;348:g2216. PMID: 24524926; PMCID: PMC3923980.

38. Lerman C, Niaura R, Collins BN, Wileyto P, Audrain-McGovern J, Pinto A, Hawk L, Epstein LH. Effect of bupropion on depression symptoms in a smoking cessation clinical trial. Psychol Addict Behav. 2004 Dec;18(4):362-6. doi: 10.1037/0893-164X.18.4.362. PMID: 15631608.

39. Hertzberg MA, Moore SD, Feldman ME, Beckham JC. A preliminary study of bupropion sustained-release for smoking cessation in patients with chronic posttraumatic stress disorder. J Clin Psychopharmacol. 2001 Feb;21(1):94-8. doi: 10.1097/00004714-200102000-00017. PMID: 11199956.

40. Gelenberg AJ, de Leon J, Evins AE, Parks JJ, Rigotti NA. Smoking cessation in patients with psychiatric disorders. Prim Care Companion J Clin Psychiatry. 2008;10(1):52-8. doi: 10.4088/pcc.v10n0109. PMID: 18311422; PMCID: PMC2249833.

41. Weiner E, Ball MP, Buchholz AS, Gold JM, Evins AE, McMahon RP, Buchanan RW. Bupropion sustained release added to group support for smoking cessation in schizophrenia: a new randomized trial and a meta-analysis. J Clin Psychiatry. 2012 Jan;73(1):95-102. doi: 10.4088/JCP.10m06143gre. Epub 2011 Apr 5. PMID: 21535998.

42. Banham L, Gilbody S. Smoking cessation in severe mental illness: what works? Addiction. 2010 Jul;105(7):1176-89. doi: 10.1111/j.1360-0443.2010.02946.x. Epub 2010 May 11. PMID: 20491721.

43. Italiano D, Spina E, de Leon J. Pharmacokinetic and pharmacodynamic interactions between antiepileptics and antidepressants. Expert Opin Drug Metab Toxicol. 2014; 10 11: 1457- 89. DOI: 10.1517/17425255.2014.956081.

44. Paslakis G, Gilles M, Deuschle M. Clinically relevant pharmacokinetic interaction between venlafaxine and bupropion: a case series. J Clin Psychopharmacol. 2010; 30 4: 473- 4. DOI: 10.1097/JCP.0b013e3181e5c0e4. PubMed PMID: 20631572.

45. Laugesen S, Enggaard TP, Pedersen RS, Sindrup SH, Brøsen K. Paroxetine, a cytochrome P450 2D6 inhibitor, diminishes the stereoselective O-demethylation and reduces the hypoalgesic effect of tramadol. Clin Pharmacol Ther. 2005; 77 4: 312- 23. PubMed PMID: 15903129.

46. Kummer O, Hammann F, Moser C, Schaller O, Drewe J, Krähenbühl S. Effect of the inhibition of CYP3A4 or CYP2D6 on the pharmacokinetics and pharmacodynamics of oxycodone. Eur J Clin Pharmacol. 2011; 67 1: 63- 71. DOI: 10.1007/s00228-010-0893-3.

47. Ahern TP, Pedersen L, Cronin-Fenton DP, Sorensen HT, Lash TL. No increase in breast cancer recurrence with concurrent use of tamoxifen and some CYP2D6-inhibiting medications. Cancer Epidemiol Biomarkers Prev. 2009; 18 9: 2562- 4. DOI: 10.1158/1055-9965.EPI-09-0516.

48. Spina E, Leon J. Clinically relevant interactions between new antidepressants and second-generation antipsychotics. Expert Opin Drug Metab. 2014; 10 5

49. Mula M. Anticonvulsants - antidepressants pharmacokinetic drug interactions: the role of the CYP450 system in psychopharmacology. Curr Drug Metab. 2008; 9 8: 730- 7. PubMed PMID: 18855610.

50. Huecker MR, Smiley A, Saadabadi A. Bupropion. [Updated 2023 Apr 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470212/

51. Richmond R, Zwar N. Review of bupropion for smoking cessation. Drug Alcohol Rev. 2003 Jun;22(2):203-20

52. GlaxoSmithKline. Approved Product Information for Zyban1 2001.

53. Tonstad S, Farsang C, Klaene G, Lewis K, Manolis A, Perruchoud AP, Silagy C, van Spiegel PI, Astbury C, Hider A, Sweet R. Bupropion SR for smoking cessation in smokers with cardiovascular disease: a multicentre, randomised study. Eur Heart J. 2003 May;24(10):946-55. doi: 10.1016/s0195-668x(03)00003-4. PMID: 12714026.

54. Mills EJ, Thorlund K, Eapen S, Wu P, Prochaska JJ. Cardiovascular events associated with smoking cessation pharmacotherapies: a network meta-analysis. Circulation. 2014 Jan 7;129(1):28-41. doi: 10.1161/CIRCULATIONAHA.113.003961. Epub 2013 Dec 9. PMID: 24323793; PMCID: PMC4258065.

55. Tackett AE, Smith KM. Bupropion-induced angioedema. Am J Health Syst Pharm. 2008 Sep 01;65(17):1627-30.

Author contribution. Acquisition of data: MP, FP, IP, MFB, RR
Administrative, technical or logistic support: MP, FP, IP, MFB, RR
Analysis and interpretation of data: MP, FP, IP, MFB, RR
Conception and design: MP, FP, IP, MFB, RR
Critical revision of the article for important intellectual content: MP, FP, IP, MFB, RR
Drafting of the article: MP, FP, IP, MFB, RR
Final approval of the article: MP, FP, IP, MFB, RR
Guarantor of the study: MP, FP, IP, MFB, RR
Provision of study materials or patients: MP, FP, IP, MFB, RR

Učinkovitost bupropiona u prestanku pušenja cigareta – pregledni rad

Pušenje je i dalje velik neizravan uzrok prerane smrti širom svijeta. Prva linija liječenja s ciljem prestanka pušenja terapija je nadomjeskom nikotina (NRT). Bupropion, lijek prvobitno razvijen kao antidepresiv, u nekim je zemljama prvi lijek licenciran za prestanak pušenja koji nije povezan s nikotinom. Lijek djeluje uglavnom kroz inhibiciju ponovnoga unosa dopamina u neuronskim sinapsama, ali drugi učinci bupropiona također mogu imati ulogu u prestanku pušenja. Provedene su mnoge kliničke studije bupropiona koje su pokazale impresivne rezultate u pomaganju pacijentima s prestankom pušenja. Zbog svoje antidepresivne uloge, koristan je u prestanku pušenja kod pacijenata s depresijom. Kroz godine, bupropion se pokazao kao potencijalno isplativa alternativa NRT-u.