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LETTER

Potential Cardiovascular Risks Associated with Naltrexone-Bupropion Treatment in Overweight Patients [Letter]

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Dear editor

We read with interest the study by Lyu YS et al published[1] in the journal Drug Design, Development and Therapy, which explored the safety and efficacy of naltrexone-bupropion in obese adult patients in South Korea, addressing a research gap concerning its use in Asian populations. We highly commend the authors' work and offer the following suggestions for consideration.

In 2024, a review by Kazi N Islam et al[2] highlighted that bupropion has been shown to enhance neurotransmitter activity by inhibiting the re-uptake of epinephrine and dopamine. The combination of mono-amine oxidase inhibitors, which inhibit mono-amine oxidase activity and slow neurotransmitter metabolism, may lead to a significant elevation in nor-epinephrine and dopamine levels, triggering severe cardiovascular events such as hypertensive crises and central nervous system hyper excitability. Previous studies[3] have revealed a complex bidirectional association between high body mass index (BMI) and depression or anxiety, with mono-amine oxidase inhibitors remaining essential drugs for managing these conditions. In the study population, patients with depression or anxiety were not clearly excluded, potentially underestimating the risk of interactions between naltrexone-bupropion and mono-amine oxidase inhibitors. Therefore, in future studies, it is recommended to conduct a thorough review of participants' medication histories to avoid potential drug interactions.

Nissen SE et al reported in a 2016 study[4] that naltrexone-bupropion use may increase heart rate and blood pressure. Although a 2021 meta-analysis[5] found no significant association between naltrexone-bupropion and the risk of major adverse cardiovascular events (MACE), most studies excluded patients with pre-existing cardiovascular disease. Considering obesity as a significant life-shortening condition, current evidence is insufficient to comprehensively evaluate the safety of this drug in obese individuals at high cardiovascular risk. Any weight loss intervention associated with potential cardiovascular damage warrants particular scrutiny.

Regarding drug efficacy, the study demonstrates that patients across various dose groups achieved significant weight loss, with the 32/360 mg dose group showing the most pronounced effect. However, the unclear dose-response relationship, as evidenced by similar weight loss outcomes in the 16/180 mg and 32/360 mg groups, raises questions about the optimal dosing strategy. In-depth discussions incorporating pharmaceutical or pharmacologic mechanisms are recommended to elucidate the differences in efficacy across doses in future studies. Furthermore, the relatively high dropout rate (due to adverse events or non-compliance) mentioned in the study may have a significant impact on the credibility of the validity analysis. It is recommended that the robustness of the study's conclusions be further verified through sensitivity analysis or imputation methods for missing data.

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Finally, we recommend that the authors incorporate objective cardiovascular risk indicators, such as high-sensitivity C-reactive protein, blood lipid levels, blood pressure, and heart rate, to more comprehensively evaluate the drug's safety and efficacy. Adding a 14-day washout period for mono-amine oxidase inhibitors to the exclusion criteria and exploring the dose-response relationship in greater detail would further validate the drug's safety and effectiveness across diverse populations, providing clinicians with valuable evidence.

Disclosure

The authors report no conflicts of interest in this communication.

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