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Letter to the Editor

The Risk of Falls in Depressed Elderly People Undergoing Bupropion Therapy also Depends on Comorbidities and Co-Medications

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Letter to the Editor

We read with interest the article by Bender *et al*. about a randomized, controlled trial on risk factors for falls in 194 elderly patients with major depression (MDD) [1]. The patients received bupropion in addition to other antidepressants, aripiprazole augmentation, or bupropion monotherapy [1]. The study showed that bupropion increased the fall rate and that the risk of falls was dose-dependent [1]. The study is interesting but raises some questions.

Firstly, no clear inclusion and exclusion criteria were defined [1]. The lack of inclusion and exclusion criteria poses significant disadvantages for the study, particularly regarding validity, reproducibility, and safety [2]. Without strict inclusion and exclusion criteria, studies exhibit high participant heterogeneity, which makes it difficult to establish clear and reliable causal relationships between treatment and outcome [2].

Secondly, the current medications that the included patients regularly took in addition to bupropion or aripiprazole were not recorded and included in the analysis [1]. Since older patients often require medications for comorbidities [3], it is very likely that at least some of the included patients were taking multiple medications concurrently. It is also conceivable that new concomitant medications were added or discontinued during the observation period, or that the dosage of existing concomitant medications was increased or decreased. Since such changes in concomitant medication could have caused adverse effects or interactions, it cannot be ruled out that these newly prescribed medications or the dosage change, and not bupropion, were responsible for the fall.

Third, alternative causes of falls were not adequately considered and excluded in the study cohort [1]. The causes of falls in older people are diverse and must be included in the analysis before concluding that “the risk of falls during bupropion augmentation is a function of the patient’s fall history and the bupropion dosage” [1]. Alternative causes of falls in older people include lower extremity muscle weakness due to sarcopenia, balance disorders, incorrect gait patterns (e.g., shuffling, crossing legs when turning), Parkinson's disease, previous stroke or intracerebral hemorrhage, dementia, hypertension, orthostatic hypotension, diabetes, visual impairment, hearing loss, neuropathy, reduced reflexes, foot pain, inappropriate footwear (e.g., wide, open shoes, high heels), infections, dehydration, constipation, side effects of medications (e.g., sedatives, tranquilizers, antidepressants, hypnotics, antihypertensives, muscle relaxants, antihistamines, polypharmacy), loose carpets, rugs, clutter, electrical cables, dark rooms, stairs, excessive glare, lack of handrails, lack of grab bars in the bathroom, vitamin D deficiency, or slippery floors [4].

The fourth point concerns the fact that no multivariate analysis was performed to identify confounding factors influencing the risk of falls in patients with major depression undergoing bupropion therapy [1]. Since the causes of falls are diverse, the presence or absence of these additional risk factors must be included in the analysis.

The fifth point relates to the discrepancy between the study's objective (assessing fall risk factors) and its methods (measuring the risk of falls due to the addition of bupropion) [1]. This discrepancy should be addressed.

In conclusion, attributing falls in older adults on polypharmacy to bupropion can be misleading unless all fall risk factors are considered and included in the analysis.

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