The Intricate Interplay Between Dementia and Hypnotics

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The connection between the use of hypnotics and dementia has sparked significant interest and controversy in the medical community. This perspective aims to provide a succinct overview of the current understanding of this intricate relationship. Some studies have indicated a potential association between long-term use of specific hypnotics, such as benzodiazepines and Z-drugs, and an increased risk of dementia [1,2]. Consequently, concerns have arisen regarding potential cognitive impairment associated with these medications [3]. However, findings pertaining to the dose-response relationship have been inconsistent, and the precise mechanism by which hypnotics may heighten dementia risk remains unclear. Proposed mechanisms include disruptions in sleep architecture, impaired memory consolidation, heightened susceptibility to falls and resultant brain trauma, and direct neurotoxic effects of certain medications [4]. Nevertheless, several factors warrant contemplation in this context.

Firstly, publication bias should be considered, as researchers may have a propensity to publish positive findings, and the topic of hypnotics-induced dementia may be subject to such biases due to its sensational nature [5]. Secondly, although Taiwanese studies with large sample sizes are frequently cited in relation to hypnotics and dementia, caution is advised as these studies rely on medical insurance data and may have limitations [6]. Thirdly, meta-analyses showing positive results have encompassed heterogeneous subjects [7]. Moreover, while depression has been controlled in most positive studies, more than half of the studies did not control for anxiety [8]. Additionally, most studies have explored the severity of depression and alcohol use as potential confounding factors [1,2]. Fourthly, the emerging hypothesis of the glymphatic system [9], which operates during sleep and removes waste products like beta-amyloid, may provide insights into this discussion. Insomnia, by hindering the proper functioning of the glymphatic system, could potentially contribute to the development of dementia [9]. Conversely, animals under the influence of sleep-inducing medications or anesthetics exhibit normal operation of the glymphatic system, facilitating waste removal [10]. Fifthly, a recently published well-controlled, large cohort study challenges prevailing assumptions. This study found no association between benzodiazepines and Z-drugs and dementia, and intriguingly, even identified potential protective effects against dementia at high doses [8]. The study meticulously controlled for all confounding factors, including alcohol use and depression severity, and boasted an extensive cohort size (n=235,465). Consequently, characterizing benzodiazepines as causative agents of dementia based solely on their cognitive function-dampening effects oversimplifies the matter, and it is challenging to conclude that hypnotics directly induce dementia.

In conclusion, the relationship between hypnotic use and dementia is intricate and necessitates further investigation. Although some studies suggest a potential association, causality has not been firmly established. Clinicians should prioritize alternative treatment strategies and emphasize non-pharmacological interventions. Continued research is imperative to deepen our understanding of the underlying mechanisms and develop safer and more effective approaches to managing sleep disturbances in individuals with dementia.

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REFERENCES