Back to the Future of Psychopharmacology

Archives of Psychiatry Research 2024;60:251-254

DOI:10.20471/sept.2024.60.03.09
Received August 19, 2024
Accepted Sept 09, 2024

Dexmedetomidine

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Postpartum depression (PPD) is among the most frequent psychiatric issue new mothers face, as it affects 10 % to 20 % of women after childbirth. This condition, marked by intense emotional distress, can impact not just mothers but also their families, and the broader community. As a result, developing successful methods to prevent and treat this type of depression has become a key public health priority. Spotting signs and reacting upon them can help reduce symptoms and boost the chances of recovery for women who've given birth. Even so, PPD remains a problem pointing to the need for fresher treatment approaches [1]. Studies have shown how important it is to treat depression during pregnancy, as it often leads to PPD. Checking for depression while women are pregnant allows doctors to spot those at risk and start prevention efforts that might lower the odds of PPD showing up later [2-5].

Recent investigations in the pharmacological field have brought attention to dexmedetomidine, which is a highly selective α2-adrenoreceptor agonist. It is primarily used in a perioperative setting and shows promise for PPD prevention. The concept of using dexmedetomidine as an antidepressant appears to have originated from a 2014 study conducted in India. In this study, dexmedetomidine was administered as an anesthetic to patients undergoing ECT, and it was observed that those who received dexmedetomidine showed reduced agitation and a more significant decrease in depressive symptoms. Preliminary studies indicated that administering dexmedetomidine early in the postpartum period may decrease the occurrence of postpartum depression and that it is generally well-tolerated. It is known for its sedative, anxiolytic, and analgesic properties, and it works by targeting aforementioned α2-adrenoreceptors, which play a role in the development of depression. Studies conducted on individuals who suffered from depression and later commited suicide have shown increased expression of these receptors in various regions of the brain. Similarly, patients suffering from PPD have elevated α2-adrenoreceptors density in their platelets, which decreased upon successful antidepressant treatment. Animal studies support these observations and demonstrate that dexmedetomidine can alleviate depression-like behaviors in sleep-deprived models [6-10].

Certain variations in the α2-adrenoreceptor gene are linked to a higher risk of developing PPD. This kind of genetic predisposition in combination with the neurochemical changes observed in PPD, suggests that dexmedetomidine's modulation of α2-adrenoreceptor activity could be crucial in its therapeutic effects. Additionally, dexmedetomidine has been shown to elevate the production of brain-derived neurotrophic factor (BDNF), which is a molecule involved in neuroplasticity, neuronal survival, and mood regulation [11]. The role of BDNF in depression, including postpartum depression, is well-established, with reduced levels associated with depressive symptoms and a poor outlook. Consequently, increasing BDNF levels may be one of the mechanisms through which dexmedetomidine manifests its antidepressant effects [12-14].

A recent randomized clinical trial was conducted with the aim of evaluation of the dexmedetomidine effec-

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tiveness in preventing PPD among women with prenatal depression. The trial was designed as a double-blind and placebo-controlled to ensure the reliability of the results. Participants who were scheduled for elective cesarean delivery and required postoperative analgesia, were randomly assigned to receive either intravenous infusion of dexmedetomidine or placebo. The primary outcome which was measured was the occurrence of postpartum depression at 7 and 42 days postpartum. Secondary outcomes included the incidence of suicidal thoughts, sleep quality, and pain levels. The study also examined changes in plasma BDNF, with the aim of providing insights into the molecular mechanisms that might underlie dexmedetomidine's potential antidepressant effects. Administration of dexmedetomidine significantly lowered the incidence of positive postpartum depression screenings at both 7 and 42 days postpartum compared to the placebo group. Specifically, at Week 1, 12.6 % of the women in the dexmedetomidine group screened positive for PPD versus 32.1 % of the women in the control group; and at 6 weeks, 11.4 % of the dexmedetomidine group versus 30.3 % of the control group screened positive. A significant increase in plasma BDNF was also observed. This supports the idea that upregulation of BDNF may be a key factor in the drug's antidepressant effects. Furthermore, dexmedetomidine displayed a favorable safety profile, with adverse events similar to those in the control group, apart from a slightly higher rate of hypotension which is a known side effect of the drug [14].

All in all, the results of this clinical trial could mark a significant advancement in the treatment of PPD and show dexmedetomidine's potential as a new treatment in the psychiatric field. By influencing α2-adrenoreceptor activity and increasing BDNF levels, dexmedetomidine offers a novel strategy for preventing and possibly treating PPD, especially in women at high risk due to prenatal depression. Nonetheless, as with any new treatment, further research is needed to fine-tune the dosage, understand long-term effects, and explore its broader applicability, preferentially across different populations. However, these findings show promising new pathways for future research and clinical practice and provide hope for better outcomes for mothers and their families.

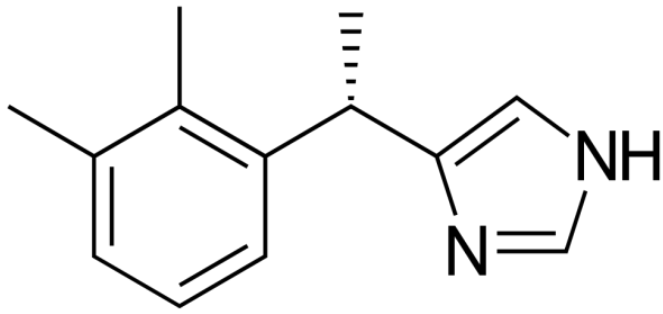

Figure 1. Chemical structure of Dexmedetomidine

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