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SCIENTIFIC ARTICLE

The effects of memantine on recovery, cognitive functions, and pain after propofol anesthesia

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KEYWORDS
Memantine;
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Abstract
Objectives: Postoperative cognitive dysfunction refers to the problems associated with thought and memory that are often experienced after major surgery. The aim of this study is to evaluate the effects of intraperitoneally administered memantine on recovery, cognitive functions, and pain after propofol anesthesia.
Methods: The study was conducted in Gazi University Animal Research Laboratory, Ankara, Turkey in January 2012. Twenty-four adult female Wistar Albino rats weighing 170–270 g were educated for 300 s in the radial arm maze (RAM) over three days. Group P was administered 150 mg kg^{-1} of intraperitoneal (IP) propofol; Group M was given 1 mg kg^{-1} of IP memantine; and Group MP was given 1 mg kg^{-1} of IP memantine before being administered 150 mg kg^{-1} of IP propofol. The control group received only IP saline. RAM and hot plate values were obtained after recovery from the groups that received propofol anesthesia and 30 min after the administration of drugs in other two groups.
Results: The duration of recovery for Group MP was significantly shorter than Group P ($p < 0.001$), and the number of entries and exits in the RAM by Group MP was significantly higher during the first hour when compared to Group P ($p < 0.0001$). Hot plate values, on the other hand, were found to be significantly increased in all groups when compared to the control values, aside from Group C ($p < 0.0001$).
Conclusion: In this study, memantine provided shorter recovery times, better cognitive functions, and reduced postoperative pain. From this study, we find that memantine has beneficial effects on recovery, cognitive functions, and pain after propofol anesthesia.
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PALAVRAS-CHAVE
Memantina;
Anestesia;
Recuperação;
Propofol;
DCPO

Efeitos da memantina sobre a recuperação, funções cognitivas e dor após a anestesia com propofol

Resumo
Objetivos: A disfunção cognitiva no pós-operatório refere-se a problemas associados ao pensamento e à memória que são frequentemente manifestados após uma cirurgia de grande porte. O objetivo deste estudo foi avaliar os efeitos da memantina administrada por via intraperitoneal sobrea recuperação, funções cognitivas e dor após a anestesia com propofol.
Métodos: O estudo foi realizado no Laboratório de Pesquisa com Animais da Universidade de Gazi, Ankara, Turquia, em janeiro de 2012. Vinte e quatro ratos albinos do sexo feminino, adultos, da linhagem Wistar, pesando 170-270 g, foram treinadosdurante 300 segundos no labirinto radial de oito braços (LRB) durante três dias. O Grupo P recebeu 150 mg/kg^{-1} de propofol por via intraperitoneal (IP); o Grupo H recebeu 1 mg/kg^{-1} de memantina IP e o Grupo MP recebeu 1 mg/kg^{-1} de memantina IP antes daadministração de 150 mg/kg^{-1} de propofolPI. O grupo controle recebeu apenas solução salina IP. Os valores doLRB e da placa quente foram obtidos após a recuperação dos grupos que receberam propofol e 30 minutos após a administração dos fármacos nos outros dois grupos.
Resultados: O tempo de recuperação do Grupo MP foi significativamente menor que o do Grupo P ($p < 0,001$), eo número de entradas e saídas do LRBdo Grupo MP foi significativamente maior durante a primeira hora,em comparação com o Grupo P ($p < 0,0001$). Os valores da placa quente, por outro lado, foram significativamente maiores em todos os grupos, em comparação com os valores dogrupo controle, exceto pelo Grupo C ($p < 0,0001$).
Conclusão: No presente estudo, memantina proporcionou tempos mais curtos de recuperação, funções cognitivas melhores e reduziu a dor no pós-operatório. A partir deste estudo, descobrimos que a memantina tem efeitos benéficos sobre a recuperação, funções cognitivas e dor após anestesia com propofol.
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Introduction

Postoperative cognitive dysfunction (POCD) refers to disorders affecting attention, consciousness, orientation, perception, judgment, and insight that develop during the postoperative period. Although the etiology of POCD has yet to be adequately explained, many factors have been found to be responsible. Most recently, disequilibrium in the neurotransmitter systems during the preoperative period, such as acetylcholine, serotonin, glutamate, and aspartate, has been one of the most commonly blamed factors.[1–3]

The effects of the nicotinic system on learning, memory, and cognition have been shown in studies of both humans and animals.[4] This directly influences attention while also affecting learning and memory by facilitating acetylcholine, glutamate, dopamine, noradrenaline, serotonin, and gamma-aminobutyric acid (GABA) releases from the presynaptic nicotinic acetylcholine receptors (nAChRs).[4]

Propofol is a frequently used hypnotic agent that works by potentializing the chloride flow of GABA by connecting to the β-subunit in the GABA receptor. The alpha and gamma (γ_2) subunits also seem to contribute to the modulation of the effect of propofol on the GABA receptor. As a result of this effect on the $GABA_A$ receptors in the hippocampus, propofol inhibits ACh release in the hippocampus and prefrontal cortex. This seems to be significant in the sedative effects of propofol. Propofol diffuses inhibition on N-methyl-D-aspartate (NMDA) which is a subtype of glutamate receptor, by modulating the gate mechanism in the sodium channels and thus contributing to the central nervous system (CNS) effects. Propofol is also effective on the $GABA_A$ and glycine receptors on the dorsal horn of the spinal cord, and modulation of these receptors is known to result in cognitive dysfunction. Propofol is reported to inhibit cognitive functions for up to 6 h.[5,6]

Memantine is a non-competitive receptor antagonist with a low affinity that inhibits the pathological activation of NMDA receptors without changing their physiological functions.[7] Memantine has demonstrated an ability to reverse the changes that develop in the synaptic plasticity of animal models after its use was suggested for various neurological disorders.[8] The use of memantine has yielded positive results on learning, memory, pain, and neuroprotective effects in clinical studies.[9] As a result, it was sent to the Food and Drug Administration (FDA) in 2003 for approval for the treatment of Alzheimer's disease. There have also been studies investigating the use of memantine in the treatment of chronic pain,[10] in which it has been shown to decrease diabetic neuropathy pain in rats.[11]

In the present study, the effects of memantine administration prior to propofol anesthesia on recovery, cognitive functions, and acute pain are evaluated.

Materials and methods

Animals and experimental protocol

This study was conducted in the animal research laboratory of Gazi University in January 2012 with the consent

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