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SCIENTIFIC ARTICLE

Histopathologic comparison of dexmedetomidine's and thiopental's cerebral protective effects on focal cerebral ischemia in rats

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Abstract This study was designed to investigate if dexmedetomidine and thiopental have cerebral protective effects after focal cerebral ischemia in rats. Thirty male Sprague Dawley rats were randomly assigned to three groups: control group (Group C, $n = 10$), dexmedetomidine group (Group D, $n = 10$), thiopental group (Group T, $n = 10$). After all rats were anesthetized, they were intubated, then mechanically ventilated. A catheter was inserted into the right femoral artery for continuous mean arterial pressure, physiological parameters and blood sampling at baseline, 5 min after occlusion and 20 min after reperfusion. A catheter was inserted into the left femoral vein for medication administration. Right common carotid artery of each rat was isolated and clamped for 45 min. At the end of the duration common carotid artery were unclamped and the brain reperfusion was achieved for 90 min. Dexmedetomidine was administered for Group D iv infusion, Group T received thiopental IV. According to histopathologic scores cerebral ischemia was evaluated in all rats in Group C, but no ischemia was evaluated in three rats in Group T and in four rats in Group D. Grade 3 cerebral ischemia was evaluated in three rats in Group C, only in one rat in Group T and D. For histopathologic grades the difference between Group T and Group D was not significant ($p > 0.05$). But the differences between Group C and Group T ($p < 0.05$) and Group C and Group D ($p < 0.01$) were statically significant. In conclusion, we demonstrated that dexmedetomidine and thiopental have histopathologic cerebral protective effects experimental focal cerebral ischemia in rats.

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PALAVRAS-CHAVE
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Rats

Comparação histopatológica dos efeitos protetores cerebrais de dexmedetomidina e tiopental sobre isquemia cerebral focal em ratos

Resumo Este estudo foi projetado para investigar se dexmedetomidina e tiopental possuem efeitos protetores cerebrais após isquemia cerebral focal em ratos. Trinta ratos da linhagem Sprague Dawley foram randomicamente divididos em três grupos: controle (Grupo C, n = 10), dexmedetomidina (Grupo D, n = 10) e tiopental (Grupo T, n = 10). Após a anestesia, todos os ratos foram intubados e ventilados mecanicamente. Um cateter foi inserido na artéria femoral direita para monitoração contínua da pressão arterial média (PAM), dos parâmetros fisiológicos e para coleta de amostras de sangue na fase basal, 5 minutos após a oclusão e 20 minutos após a reperfusão. Um cateter foi inserido na veia femoral esquerda para administração de medicamentos. A artéria carótida comum direita de cada rato foi isolada e pinçada durante 45 minutos. Ao final dos 45 minutos, o pinçamento foi removido e a reperfusão do cérebro foi obtida por 90 minutos. Dexmedetomidina foi administrada por infusão IV no Grupo D e thiopental no Grupo T. De acordo com as pontuações histopatológicas, isquemia cerebral foi avaliada em todos os ratos do Grupo C, mas não foi avaliada em três ratos do Grupo T e em quatro ratos do Grupo D. O grau 3 de isquemia cerebral foi avaliado em três ratos do grupo C e em apenas um rato dos grupos T e D. Para os graus histopatológicos, a diferença entre o Grupo T e o Grupo D não foi significativa ($p > 0,05$). Porém, as diferenças entre o Grupo C e o Grupo T ($p < 0,05$) e entre o Grupo C e o Grupo D ($p < 0,01$) foram estatisticamente significativas. Em conclusão, demonstramos que dexmedetomidina e tiopental possuem efeitos histopatológicos protetores cerebrais sobre isquemia cerebral focal experimental em ratos.

Introduction

It has been demonstrated by prospective epidemiological studies conducted in developed western countries that cerebrovascular diseases (CVDs) are responsible for 10% of all deaths and are ranked third after heart diseases and cancer as a cause of mortality.[1–3] About 75% of CVDs result from thrombotic or embolic cerebral infarcts.[2,4]

The infarct model provided by occlusion of experimental middle cerebral artery (MCA) representing the focal cerebral infarction which is the most common type of CVD in clinical practice has been widely accepted.[2,4,5] Rats bear a very close resemblance to the human brain in terms of cerebrovascular anatomy and physiology and thus, they are widely used in cerebral ischemia studies.[3] The validity of this model of cerebral ischemia highly depends on strict control of physiological parameters which may cause fluctuations and changes in the results such as body temperature, blood pressure, blood gases, and glucose levels.[4]

In clinical use, there is still no ideal medication which bears all the desired characteristics and is effective enough in cerebral ischemia.[6,7] In order to respond to clinical needs, in animal models, a large number of agents from different chemical groups which is thought to have beneficial effects in cerebral ischemia are still being tested and their effects on cerebral ischemia are methodologically examined.[2,4] The novel molecular-level information on the pathophysiology of cerebral ischemia have led to the use of numerous potential therapeutic agents estimated or alleged to be effective on such pathophysiologic mechanisms in experimental studies.[8,9]

The effects of barbiturates as well as the thiopental, an agent mostly used in anesthesia practice in this class, on cerebral blood flow and cerebral metabolism were researched and found to cause a decrease in cerebral blood flow and cerebral metabolic rate depending on the dose. It has been observed that cerebral oxygen metabolism is reduced by 55–60% at a barbiturate dose causing isoelectricity in EEG; however, cerebral metabolism proceeded and the cerebral basal metabolism that is necessary to ensure physiological functions and cell integrity of neurons did not depressed through a further increase of the blood barbiturates dose.[10,11]

There are different views about whether or not barbiturates are neuroprotective. In post-traumatic focal cerebral ischemia; they are found to reduce hyperemia by making a deep depression in the cerebral metabolic rate, improve the harmony of flow & metabolism, increase perfusion in the low-flow region and have brain protective effect by minifying the infarcted area.[12,13] Thiopental and methoheksital were again studied at different doses in the models of focal cerebral ischemia in rats and were histopathologically shown to reduce infarct volume at doses causing burst suppression in EEG.[14]

Dexmedetomidine is a new medication gained popularity in anesthesia practice. A α-2 receptor agonist, this medication provides analgesia without cooperative sedation, anxiolysis and respiratory depression. Alpha 2 adrenoceptors show a broad dissemination in cerebral vascular bed and activation of these receptors causes a specific vasoconstrictive response. Although being very common in the cerebral vasculature, their effects on the control of

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