Gabapentin 抗血小板凝集作用之機轉探討

Mechanism involved in the antiplatelet effect of gabapentin

中文摘要

Gabapentin (Neurontin)是一種新的抗癲癇藥物，但是至今作用機轉仍然不清楚。有研究推測 gabapentin 可以改變血小板對 serotonin 的代謝或攝取（uptake）；然而，血小板在受刺激凝集的過程是否會受到 gabapentin 的影響，至今仍未有一套完整的研究加以證實。本研究在 in vitro 的實驗中發現外加 gabapentin 確實具有抑制血小板凝集之能力。並且在血小板凝集試驗中發現若事先外加 gabapentin，確實有抑制由 collagen、ADP、AA 等血小板活化劑所引起的凝集作用；隨著血小板活化劑使用種類的不同，gabapentin 之 IC50 約爲 120 μM。本研究係探究 gabapentin 在血小板活化過程中對細胞內一些訊息傳遞的影響，亦即抑制血小板凝集之機轉。由研究結果發現 gabapentin 會隨著濃度之增加而有意義的抑制由不同血小板活化劑所引起的人類血小板之凝集現象；gabapentin 會抑制由 collagen 所引起之血小板細胞內 phosphoinositol breakdown；gabapentin 會抑制由 collagen 所引起之血小板細胞內鈣離子的增加；再者 gabapentin 可抑制 TxA2 之形成，對 AA 的代謝路徑有所影響。由研究結果發現 gabapentin 抗血小板活化可能涉及以下路徑：gabapentin 可藉由抑制 phosphoinositol breakdown 的 pathway 及影響 TxA2 之形成的 pathway，進而影響細胞內鈣離子的移動，最後導致細胞內鈣離子的濃度減少而抑制血小板之凝集反應。

關鍵字：Gabapentin，血小板凝集，phosphoinositol breakdown，TxA2，鈣離子

英文摘要

Gabapentin (Neurontin),in clinical use since 1993,is a novel antiepileptic drug. It is used clinically to reduce seizure frequency in patients with epilepsy. But the mechanism of action is not fully understood. Although its exact mechanism of action has yet to be determined, gabapentin is likely to have multiple effects. Nonepileptic use of gabapentin now accounts for roughly 40% of all reports on gabapentin. It has been previously speculated that gabapentin modulates the release of serotonin from blood platelets. But whether there is antiplatelet effect of gabapentin needs to be determined.

In vitro study, gabapentin indeed inhibits the human platelet aggregation induced by various platelet inducers, such as collagen、ADP and arachidonic acid. Gabapentin also inhibits collagen-induced inositol monophosphate formation and inhibits collange-induced thromboxane A2 formation and intracellular Ca2+ mobilization.

On account of these results, we speculate that the mechanism involved in signal transductions of platelet aggregation by gabapentin may be as the following: gabapentin may modulate the phosphoinositol breakdown pathway and thromboxane A2 formation pathway. Then may induce alteration in intracellular Ca^{2+} mobilization and reduce intracellular Ca^{2+} concentration and finally it may inhibit platelet activation.
Key Words: gabapentin, platelet aggregation, PI breakdown
thromboxane A2 , Ca^{2+}.