Ergothioneine對Cisplatin誘導小鼠神經細胞傷害的影響及其作用機制探討

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摘 要

本研究主要目的為探討麥角硫化物(Ergothioneine; EGT)是否有減少化療藥物順箔(cisplatin)對小鼠(CBA品系)腦神經傷害的能力，並且探討EGT保護類神經細胞(PC12)與大鼠初代腦神經細胞的可能機制。動物實驗部分以主動與被動學習躲避電擊試驗，來評估EGT對小鼠腦神經細胞損傷的保護能力。主動躲避學習試驗是成功躲避反應次數越高及躲避時間愈短，表示小鼠學習與記憶能力愈佳；被動學習試驗則是滯留明室的時間愈長，則表示學習與記憶能力愈佳。結果顯示連續餵食2及8 mg/kg的EGT 57天小鼠，在主動及被動躲避實驗中都能顯著使cisplatin誘導傷害的小鼠成功躲避電擊的次數增加，也減少其成功躲避到暗室的延遲時間，由此可知EGT具有減少cisplatin對小鼠學習與記憶損傷的能力。此外，發現EGT能減少cisplatin所誘導小鼠腦組織產生脂質過氧化物，並能降低cisplatin所誘導之腦內乙醯膽鹼酯?′ 〡吨W升，EGT也具有增加因cisplatin而減少的腦內Glutathione (GSH)的含量。在細胞試驗方面，EGT處理具有減少cisplatin對PC12細胞所造成之抑制增生效果，且呈現時間及劑量效應；EGT處理具有減少cisplatin對大鼠初代大腦皮質細胞傷害的能力，顯著隨EGT劑量的增加有減少腦神經細胞的軸突(axon)與樹突(dendrite)的損傷的趨勢。此外，EGT亦可減少由cisplatin所誘導的PC12細胞凋亡，及caspase-3和-9活性的增加。這些結果顯示EGT應具有保護腦神經細胞減少cisplatin傷害的潛力。由本研究可知，供應EGT具有保護神經細胞及減少cisplatin對記憶及學習能力的損傷，而此結果將有助於推展EGT成為未來應用於降低化療藥物-cisplatin副作用的一種輔助療法。

關鍵詞 : 麥角硫化物、順箔、主動與被動學習、神經細胞、細胞凋亡

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