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• 中文摘要

氯胺酮(ketamine)是一種靜脈麻醉劑。在臨床上，以 ketamine 做爲麻醉誘導劑時，常會發生免疫抑制作用。巨噬細胞(macrophages)在宿主的免疫防禦功能上，扮演重要角色。此一研究以巨噬細胞爲實驗模式，探討 ketamine 對巨噬細胞功能可能造成的影響，以及其可能發生的機制(mechanisms)。將巨噬細胞暴露於 10 及 100 μM 的 ketamine(相當於臨床濃度的 0.1 及 1 倍)1、6 及 24 小時，並不會影響細胞的存活率及乳酸脫氫酶(lactate dehydrogenase)的釋放。但，當處理濃度達到 1000 μM 時，ketamine 會增加乳酸脫氫酶的釋放及細胞的死亡。Ketamine 於 10 及 100 μM 濃度下，不會影響巨噬細胞的趨化活性(chemotactic activity)。但，巨噬細胞處理 1000 μM 的 ketamine 會導致細胞移動能力(cell migration)的降低。巨噬細胞處理 ketamine 會降低吞噬能力(phagocytic activities)；Ketamine 亦會抑制巨噬細胞的氧化能力。巨噬細胞處理脂多醣(lipopolysaccharide)會誘導 TNF-α、IL-1β 及 IL-6 mRNA 的產生，單獨處理 ketamine 不會影響 TNF-α、IL-1β 及 IL-6 mRNA 的產量。同時處理 ketamine 及脂多醣會有意義地抑制脂多醣(lipopolysaccharide)所誘導 TNF-α、IL-1β 及 IL-6 mRNA 的量。Ketamine 處理會導致粒線體膜電位(mitochondrial membrane potential)的下降，但不會影響粒線體複合體 I NADH 去氫脢(mitochondrial complex I NADH)的活性。本研究顯示在臨床濃度(100 μM)下，ketamine 會抑制巨噬細胞吞噬與氧化能力，並能抑制發炎細胞激素(inflammatory cytokine)的產生。而其可能的作用機轉，是透過抑制粒線體膜電位(mitochondrial membrane potential)，而非直接造成細胞的毒害作用。

• 英文摘要

Ketamine is an intravenous anesthetic agent. Clinically, induction of anesthesia with ketamine can cause immunosuppression. Macrophages play important roles in host defense. In this study, we attempted to evaluate the effects of ketamine on macrophage functions and its possible mechanism using macrophages as the experimental model. Exposure of macrophages to 10 and 100 ？HgM ketamine, which correspond to 0.1 and 1 times the

clinically relevant concentration, for 1, 6, and 24 h had no effect on cell viability or lactate dehydrogenase release. When the administered concentration reached 1000 ? HgM, ketamine caused a release of lactate dehydrogenase and cell death. Ketamine, at 10 and 100 ? HgM, did not affect the chemotactic activity of macrophages. Administration of 1000 ? HgM ketamine in macrophages resulted in a decrease in cell migration. Treatment of macrophages with ketamine reduced phagocytic activities. The oxidative ability of macrophages was suppressed by ketamine. Treatment with lipopolysaccharide induced TNF- ? H\, IL-1 ? H] and IL-6 mRNA in macrophages. Administration of ketamine alone did not influence TNF- ? H\, IL-1 ? H] or IL-6 mRNA production. Meanwhile, cotreatment with ketamine and lipopolysaccharide significantly inhibited lipopolysaccharide-induced TNF-a, IL-1h, and IL-6 mRNA levels. Exposure to ketamine led to a decrease in the mitochondrial membrane potential. However, the activity of mitochondrial complex I NADH dehydrogenase was not affected by ketamine. This study shows that a clinically relevant concentration of ketamine (100 ? HgM) can suppress macrophage function of phagocytosis, its oxidative ability, and inflammatory cytokine production possibly via reduction of the mitochondrial membrane potential instead of direct cellular toxicity.