砒霜引發惡性胸膜間皮瘤的胸苷酸合成酶下降和細胞凋亡
Dual Action of Arsenic Trioxide on Thymidylate Synthase and Apoptosis in Mesothelioma

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摘要

目的： 惡性胸膜間皮瘤是一個全球性的健康問題。砒霜已被證明能抑制腸癌的胸苷酸合成酶(TYMS)(減慢癌細胞生長)，而且可引發血癌細胞凋亡(死亡)。因此，我們研究砒霜在間皮瘤的效果。

研究方法： 我們利用間皮瘤細胞株測試砒霜對細胞活性，TYMS蛋白表達和活性的影響，以及對凋亡相關蛋白表達的影響。並利用老鼠模型研究砒霜的抗癌效果。

結果： 在細胞模型中應用的砒霜濃度在臨床有效濃度之內。砒霜可抑制TYMS蛋白表達及其活性。同時，通過下調抗凋亡蛋白和上調凋亡蛋白的表達引發細胞凋亡。在老鼠模型中，砒霜治療組的腫瘤體積明顯較小。

結論： 砒霜具有強效的抗癌作用。此研究提供可靠的科學證據支持砒霜治療間皮瘤的臨床應用。

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Abstract

Objective: Malignant pleural mesothelioma is a global health issue. Arsenic trioxide (ATO) has been shown to suppress thymidylate synthase (TYMS) in colorectal cancer (decrease cell growth) and induce apoptosis (cell death) in blood cancer. The effect of ATO in mesothelioma was therefore studied.

Materials and methods: A panel of 5 mesothelioma cell lines was used to study the effect of ATO on cell viability, TYMS protein expression and TYMS activity. Alteration of apoptotic/anti-apoptotic proteins induced by ATO was explored. The effect of ATO was also studied using a mice model.

Results: Application of ATO demonstrated anti-cancer effects in the cell line model with clinically achievable concentrations. Downregulation of TYMS protein and TYMS activity were also observed. The expression of anti-apoptotic factors were decreased while apoptotic factors were increased so as apoptosis was induced. In mice model, the relative tumor volumes were reduced in the ATO treatment group.

Conclusion: ATO has potent antiproliferative and cytotoxic effects in mesothelioma by TYMS downregulation and apoptosis. There is sound scientific evidence to support the clinical application of ATO in treatment of mesothelioma.