Arsenic trioxide suppresses tumour growth in squamous cell lung carcinoma

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LL Leung, SK Lam, JCM Ho
Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Introduction: Squamous cell lung carcinoma (SCC) belongs to the second most common subtype in non–small-cell lung carcinoma. Recently, doublet chemotherapy regimens remain the cornerstone of first-line systemic treatment. Therefore, new therapeutic approach is urgently needed. Arsenic trioxide (ATO) is a traditional Chinese medicine which has multiple anti-cancer mechanisms including apoptosis. ATO has been used clinically in acute promyelocytic leukaemia. ATO has been shown to induce apoptosis in lung adenocarcinoma in vitro and in vivo. The aim of this study was to determine the anti-cancer effect of ATO in SCC.

Methods: Two SCC cell lines were obtained: SK-MES-1 and SW900. Cell cycle arrest, phosphatidylserine externalisation, mitochondrial membrane depolarisation, and reactive oxidative species level were analysed by flow cytometry. Cell viability and protein expression were determined by MTT assay and Western blot, respectively. Effect of ATO was demonstrated by SK-MES-1 xenograft model in vivo.

Results: Upon ATO treatment, G2/M arrest was noted in both cell lines while level of phosphatidylserine externalisation and mitochondrial membrane depolarisation were increased in SK-MES-1 cells only. Hydrogen peroxide was raised in SK-MES-1 cells while decreased in SW900 cells. Superoxide level was decreased in SK-MES-1 cells while unaltered in SW900 cells. Sustained Erk activation was observed in SK-MES-1 cells only. The expression level of p-p38 was increased in SK-MES-1 cells while it was decreased in SW900 cells. Cleaved caspase 3 was elevated in both cell lines. Cleaved PARP was increased in SK-MES-1 cells while Bak was upregulated in SW900 cells. Anti-apoptotic protein XIAP was decreased in both cell lines, while Bcl-2 was downregulated in SK-MES-1 cells only. Transcriptional factor protein, E2F-1, was decreased in both cell lines, while RRM1 and thymidylate synthase were decreased in SK-MES-1 cells only. ATO (7.5 mg/kg) decreased the tumour size in SK-MES-1 xenograft in vivo.

Conclusion: ATO induced apoptotic and anti-proliferative effects in SCC in vitro and in vivo.

Defining criteria for rheumatoid arthritis patient-derived Disease Activity Score (PDAS) that correspond to Disease Activity Score 28 (DAS28) and Clinical Disease Activity Index (CDAI) Based Disease Statuses And Response Criteria

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MH Leung[1], D Farewell[2], E Choy[2], CS Lau[1]
[1] Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong
[2] Section of Rheumatology, Institute of Infection and Immunity, Cardiff University School of Medicine, Cardiff, United Kingdom

Introduction: Patient-derived Disease Activity Score with ESR (PDAS1) and without ESR (PDAS2) in rheumatoid arthritis (RA) are validated patient-reported outcome measures of disease activity and correlate highly with Disease Activity Score 28 (DAS28) and Clinical Disease Activity Index (CDAI). The purpose of this study was to develop and examine their performance of status and responder criteria.

Method: Data from 299 RA patients (originally used to develop PDAS) were analysed using receiver operator characteristic (ROC) curves to determine optimal cut-points for PDAS corresponding to DAS28 and CDAI criteria for remission, low-, medium- and high-disease activities. Data from 56 RA patients started on disease-modifying drugs before and 6 months after treatment were used to determine PDAS thresholds corresponding to the European League Against Rheumatism (EULAR) good or moderate responses. Agreement was assessed with Kappa statistics.

Results: Key cut-points for PDAS1&2 were 3.5, 4.5, 4.8, and 3.8, 4.6, 5.0 respectively. Area under ROC curves ranged from 0.89 to 0.95. Sensitivities ranged from 79% to 99%, and specificities from 61% to 89%. Moderate-to-good agreement with DAS28 categories was observed: respectively, k=0.44 and 0.31 for PDAS1&2. Corresponding agreements with CDAI were k=0.3 and 0.4. Crucially, these agreements were comparable to those of CDAI and DAS28 (k=0.54). The criteria that corresponded to EULAR moderate and good response were 0.4, 0.8 for PDAS1 and 0.3, 1.2 for PDAS2. Area under the ROC curve ranged from 0.88 to 0.93. Sensitivities ranged from 72% to 100% and specificities from 77% to 94%. Agreement of DAS28 response with PDAS1&2 were k=0.46 and 0.38 respectively. Again, these were comparable to the agreement between DAS28 and CDAI in this patient group (k=0.55).

Conclusion: Disease activity and treatment response for PDAS1&2 have comparable agreement to standard criteria DAS28 and CDAI. PDAS has potential use in routine practice and research.