

Simultaneous hyperthermia-chemotherapy effect by arterial injection of Fe (Salen) for femur tumor

Rafikul Islam¹, Masanari Umemura¹, Rina Nakakaji^{1,2}, Kohei Osawa^{1,2}, Ryo Tanaka¹, Yoshihiro Ishikawa¹

¹Cardiovascular Research Institute, Yokohama City University Graduate School of Medicine, ²Department of Oral & Maxillofacial Surgery, Yokohama City University Graduate School of Medicine

Introduction: We previously identified a novel magnetic organic compound, N,N'-bis(salicylidene)ethylenediamine iron [Fe(Salen)], as an anti-cancer agent with intrinsic magnetism. Fe(Salen) can generate heat, i.e. hyperthermia upon exposure to alternating magnetic field (AMF) like an induction cooker. The purpose of the study was to evaluate the antitumor effect of intra-arterial (i.a.) selective injection of Fe(Salen) by catheter with/without the AMF-induced hyperthermia or intra-venous (i.v.) injection. We also investigated the anticancer mechanism of Fe(Salen) and the therapeutic dose through toxicity study. Methods: Rabbit squamous cell carcinoma (VX2) cells were purchased from ATCC. Rabbit tumor model implanted with VX2 cells in the right femur was used. Western blotting, mitochondrial membrane potential and Immunocytochemistry for STAT3 subcellular distribution were performed. Results: Intra-arterial selective injection of Fe(Salen) by catheter showed the greater antitumor effect than that of i.v. injection. The combination of intra-arterial injection of Fe(Salen) and AMF exposure showed the greater effect than either Fe(Salen) or methotrexate (MTX) without AMF. Fe(Salen) showed antitumor effect via MEK/ERK/STAT3 signaling pathways. Conclusion: This is the first report that the effectiveness of Fe(Salen) was evaluated in the point of administration route. These results indicate the effective arterial injection of Fe(Salen) by catheter and the development of new strategy of simultaneous hyperthermia-chemotherapy.