Investigating cobalt toxicity in the context of joint replacement patients – cobalt uptake in primary cardiac fibroblasts and in 3T3 cells.

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Cobalt leaches out from cobalt/chromium metal-on-metal hip implants into patient blood, and its effects are thought to be toxic. There has been a 5% estimated incidence of adverse effects, including toxicity to the heart, in joint implant patients over the last 40 years. This was investigated by examination of the effects of $CoCl_2$ on cell proliferation and viability performed using a range of assays. To assess effects on proliferation, MTT, neutral red and crystal violet assays were all used to compare effects of increasing concentrations of $CoCl_2$ on the Swiss 3T3 fibroblast cell line (3T3s) and primary cardiac fibroblasts (CFs). $CoCl_2$ induced toxicity in both 3T3s and CFs in a time- and dose-dependent manner with IC_{50} values for $CoCl_2$ in the range of ~300 µM in both cells. Over 72h, increasing $CoCl_2$ concentrations (up to 500 µM) resulted in decreased proliferation. Interestingly, in terms of proliferation, the 3T3s were more tolerant of $CoCl_2$ than CFs. Uptake of $CoCl_2$ into the 3T3s and CFs was measured by detecting intracellular metal content using ICP-MS. Cells were cultured and exposed to various concentrations of $CoCl_2$ (0-72 ppm) and different exposure times (24, 48 and 72 h). Analysis of cobalt content of cells revealed that with increasing medium concentration of $CoCl_2$ intracellular Co concentration on both 3T3s and CFs increased, to a range between 0-50 ppb and 0-120 ppb, respectively. Uptake into CFs was greater than into the 3T3s, and this at least partly explains the difference in toxicity between the two cell types.

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