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The Effects of Bupivacaine and Lidocaine on Osteosarcoma Cells

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INTRODUCTION AND OBJECTIVES: Osteosarcoma (OS) is an aggressive malignant tumor of the skeletal system characterized by the direct formation of immature bone by tumor cells. OS typically affects the long tubular bones of children.
Local anesthetics (LAs) have been shown to be toxic to certain malignancies such as breast and prostate carcinoma.
To our knowledge this is the first study investigating the effects of LAs on OS. The purposes of this study were to assess whether bupivacaine or lidocaine could induce apoptosis in an OS cell line and to evaluate the underlying mechanism.

METHODS: A commercially available rat OS cell line (UMR-108) was exposed to various concentrations of preservative free lidocaine and bupivacaine.
A pH buffered saline was used as a control.
Cell viability, cytotoxicity, apoptosis induction, DNA fragmentation and the expression of apoptosis-related markers were examined by MTT assay, colony formation assay, flow cytometry, agarose gel electrophoresis and western blot, respectively.

RESULTS: Bupivacaine and lidocaine induced apoptosis of rat OS cells in a dose- ($p<0.05$) and time-dependent ($p<0.01$) manner.
Apoptosis was confirmed by cell morphology, annexin positivity, and activation of caspase-3 ($p<0.001$).
Molecular data showed that LAs could significantly down-regulate the expression of Bcl-2 ($p<0.001$), survivin ($p<0.001$), pro-caspase-3 ($p< 0.001$), PARP ($p<0.01$), up-regulate expression of Bax ($p<0.05$), and cause cleavage of both caspase-3 and PARP ($p<0.01$).

CONCLUSIONS: These findings demonstrate that LAs are cytotoxic to rat OS cells, decrease colony formation, and cause the cell morphology to resemble that of apoptotic cells. LAs also induce apoptosis in a dose- and time-dependent manner. The caspase-dependent pathway was, at least in part, involved in the bupivacaine and lidocaine mediated apoptosis. These findings are significant in that they have future experimental and clinical implications. Further studies can be performed assessing osteosarcoma cell death in animal models. LAs could potentially be used for local treatment of tumors by methods of direct injection, infusion by catheter with a pain pump and with a Bier block in the extremity.

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