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Amifostine Inhibits the Antiangiogenic Action of X Rays

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Radiation treatment of cancer causes side effects in patients because of the effects of x-rays on normal tissues. These side effects can be reduced either by increasing the sensitivity of tumor tissues or by protecting the normal tissues. Therefore, substances that are either radiosensitizing or radioprotectants are used in clinical trials. Amifostine specifically protects the normal tissues with no (protective) effect on tumor tissues.

After administration, amifostine is metabolized by membrane-bound alkaline phosphatase to a free sulfhydryl compound. This derivative scavenges the free radicals that are produced by radiation, donates hydrogen ions and assists the repair of damaged DNA. The selective protection of normal tissues by amifostine may be explained by the lower levels of membrane-bound alkaline phosphatase and the different pH of the tumor cells.

Radiation inhibits the growth of new blood vessels which are necessary for tumor growth as well as metastasis of tumor cells. Previous studies have shown that x-rays inhibit angiogenesis in the chorioallantoic membrane (CAM) of chicken embryos at the 9th day of development, when the endothelial cells are still proliferating. X-rays have no effect on angiogenesis at the 14th day of embryo development, when there is no cell proliferation and the vascular network is maximum.

The aim of this work was to study if amifostine would influence the antiangiogenic effect of radiation in the in vivo model of the chicken embryo CAM. We radiated CAM at the 9th day of embryo development, when the inhibitory effect of x-rays (10 Gy) was observed. More specifically, 30 min before irradiation we added amifostine at concentrations varying from 0.01 to 10 μg at the area of the CAM that would be irradiated. With an image analysis program we calculated the vascular network 48 hours post-irradiation. It was found that in the CAM of the chicken embryo, amifostine inhibited in a dose-dependent way the antiangiogenic effect of x-rays with no effect on the physiological angiogenesis of the tissue. We plan to investigate the exact mechanisms with which amifostine selectively inhibits the antiangiogenic effect of radiation.