

reduce radiation change in BBB and tried to determine the time of maximal stabilization.

Methods: DDO/Lee mice was sacrificed on the 1, 3, 5, 7 and 9 days after whole brain irradiation (single dose 20 Gy) with or without administration of prednisolone and intraperitoneal injection of trypan blue for gross observation. The radiation change was evaluated microscopically by scoring of histologic damage.

Results: The proportion of vital staining for radiation-prednisolone group (14/25, 56%) was significantly lower than that for radiation alone group (21/25, 84%). Radiation-prednisolone group had significantly lower histologic damage scores for intracellular & interstitial edema ($p = 0.0008$), change of astrocyte ($p = 0.016$) and extravasation of RBC ($p = 0.039$) compared to that of radiation group, respectively. The most prominent differences were noted on 3 days after radiation. The highest histologic damage score was noted on 7 days after radiation. The histologic damage score of radiation-prednisolone group was significantly lower than that of radiation alone group on 3 days ($p = 0.001$) and 5 days ($p = 0.026$) after radiation.

Conclusion: The peak time of acute radiation damage was 7 days after whole brain irradiation and the prednisolone has significant salutary effect on radiation-induced change of the BBB at 3 and 5 days after whole brain irradiation. Additional experiment with variable dose-fractionation scheme using quantitative measurement of the change and electromicroscopic examination are necessary.

1340

POSTER

Can GM-CSF reduce oral mucositis? In vitro studies of GM-CSF effects on cultured human and rat oral mucosa epithelial cells

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Purpose: The use of GM-CSF mouthwash has been claimed to be able to reduce the incidence and severity of oral mucositis caused by radiotherapy (Nicolatou-Galitis et al, data presented at the ESTRO-MITRE meeting Brussels, December 2000). Furthermore studies show that locally applied GM-CSF onto the skin leads to keratinocyte growth, which might support the theory that GM-CSF has a direct stimulatory effect on the growth or regeneration of the oral mucosa (Braunstein et al 1994 and Kaplan et al 1993). The aim of the present study therefore was to assess the effect of GM-CSF on the growth of human and rat oral mucosa epithelial cells cultured in vitro.

Method: Human keratinocytes derived from explants of buccal mucosa were cultured as described in details by Arenholt-Bindslev et al (J Invest Dermatol 1987, 88:314-19). Keratinocytes from primary explant cultures were passages to Micro-Well plates (20.000 cells pr well). From 24 hours after seeding, the cells were exposed to graded dilutions of GM-CSF (final concentration in the growth medium, range 10-11-10-5g/ml; 6 wells per conc.; duplicate experiments). At day 3 of exposure, the MTT-assay was performed according to Langkjer et al (J Exp Clin Cancer Res 1993; 12:225-32). Rat oral mucosa epithelial cells (established in culture according to Arenholt-Bindslev et al (see above) were continuously exposed to GM-CSF (4ug/ml) in the medium during 10 days. Cell proliferation was assessed by trypsinization and cell counting on day 3, 7 and 10. Morphology was evaluated by phase contrast microscopy.

Results: No significant cytomorphological, stimulatory or inhibitory effect of GM-CSF was observed in human and rat oral epithelial cells under the experimental conditions.

Conclusion: Based on the present results we suggest that the previously claimed effect of GM-CSF on mucositis may be due to activation of the local humoral defence in the oral cavity (see i.e. Graham et al 1992) rather than to increased proliferation of oral epithelial cells.

1341

POSTER

Cisplatin-induced apoptosis of mesothelioma cells is affected by potassium ion flux modulator amphotericin B and bumetanide

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Purpose: Chemotherapeutic anti-cancer drugs induce cell death by the process of apoptosis. Efflux of potassium ions (K⁺) is necessary for cell volume reduction during apoptosis and increased inward pumping of K⁺ thus counteracts apoptosis. Potassium flux modulation could therefore interact with apoptosis and affect the efficiency of cancer chemotherapeutics. We explored if the K⁺ efflux stimulator amphotericin B, with or without the

Na⁺, K⁺, 2Cl⁻ -cotransport (K⁺ influx) blocker bumetanide, could affect cisplatin- and carboplatin-induced apoptosis and cytotoxicity in the pulmonary mesothelioma cell line (P31).

Methods: Apoptosis was determined by quantifying free nucleosomes and caspase-3 activity, and cytotoxicity was determined by clone formation and a fluorometric assay. The pan-caspase enzyme inhibitor Boc-D-FMK was used to further determine the role of caspase activity in K⁺-flux-modulated cisplatin-/carboplatin-induced apoptosis and cytotoxicity.

Results: Amphotericin B (3.2 mmol/L) combined with bumetanide (100 mmol/L) potentiated cisplatin-induced free nucleosome and caspase-3 activity. The combination of the K⁺ modulators did, however, not increase cisplatin cytotoxicity. The caspase inhibitor Boc-D-FMK, but unexpectedly also bumetanide, markedly reduced cisplatin cytotoxicity and annihilated the augmented cytotoxicity of cisplatin in presence of amphotericin B. Carboplatin cytotoxicity was reduced by bumetanide, but not affected by amphotericin B. Carboplatin and carboplatin/bumetanide cytotoxicity was further reduced by Boc-D-FMK.

Conclusion: Cisplatin, and to a lesser extent carboplatin, ability to induce apoptosis is indeed influenced by cellular potassium flux modulators. We suggest that K⁺ ionophores such as amphotericin B, and K⁺ influx blockers such as bumetanide, alone or in combination, should be further evaluated for their potential clinical usefulness in influencing tumour cell apoptosis induced by cisplatin and other cancer chemotherapeutics.

1342

POSTER

Skin protection by use of sucralfate cream during external beam radiotherapy for breast cancer: a prospective double blind randomized phase II study

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Introduction: Our aim was to investigate if topic application of sucralfate cream can reduce the incidence of dermatitis, and its overall time to heal when dermatitis appears, in patients treated with radiotherapy for breast cancer. Sucralfate is an anti-ulcer drug that has been used to prevent acute radic enteritis during abdominal and pelvic irradiation. Its mode of action is not well known.

Method and Material: 102 patients were included in the study, and 100 were evaluated. A two steps optimal Simon design (phase II) was performed to detect differences of 20% or more between the cream with or without sucralfate, using $\alpha=0.05$, $\beta=0.2$. They were all diagnosed of breast cancer, treated with conservative or radical surgery, and they could receive hormonal therapy or chemotherapy without antiracines. They had to receive radiotherapy on their breast or toracic wall as part of their treatment, with electrons or 1.2 or 6 MV photons, up to a total dose of 50 to 70 Gy. All of them applied topically on their breast skin a cream, half of them a cream with sucralfate, and the rest the same cream without sucralfate, since the first day of radiotherapy, twice a day, until 2 weeks after the end of radiotherapy or until dermatitis solved. The study was double blind, randomized, so that neither patients nor physicians knew the composition of the cream. Validation of the efficacy of the cream was made by the physician following the criteria for cutaneous toxicity of the EORTC-RTQG score and also by the patient following a scale graded 0 to 4 for pruritus.

Results: All patients completed RT. Toxicities for both groups were maximum in the fifth week of treatment, and differences were not statistically significant. In the non-sucralfate group more grade III dermatitis were reported (21.6 versus 7.8% in overall treatment, and 11.8 vs 2% at the fifth week).

Conclusion: Sucralfate applied topically does not reduce significantly the incidence of dermatitis during breast irradiation, although a slight better tolerance is observed.

1343

POSTER

Scalp cooling in the prevention of anthracycline-induced alopecia

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Introduction: Management of chemotherapy-induced side-effects has improved over the years by better supportive care. Alopecia is therefore increasingly important as a major negative factor in the acceptance of cytotoxic therapy, especially by women. Alopecia is inevitable in anthracycline-based adjuvant chemotherapy for early breast cancer. It is supposed that scalp cooling alleviates hair loss during chemotherapy, but its efficacy is not well proven. A single institution experience with the PenguinR scalp