cused almost exclusively on symptoms that had a dose-limiting effect of chemotherapy.

Conclusion: There is significant variability in the pattern of identifying chemotherapy-related symptoms among oncologists, and when symptoms are identified efficacious actions to manage them are not routinely taken. The routine use of clinical information systems with direct patient input regarding symptom presence and severity should help to ensure symptoms are identified in a timely manner and intervened with appropriately, especially if oncologists receive tailored feedback on the symptom status of their patients and the efficacy of the actions they took to manage the symptoms.

1336 POSTER

Neuroprotective effect of vitamin e supplementation in patients treated with cisplatin-based chemotherapy

A. Savarese[1], A. Pace[2], U. Pacetti[1], V. Maresca[3], G. Del Monte[1], M. Picardo[3], B. Jandolo[2], F. Cognetti[1]. *[1] Regina Elena Cancer Institute, Dept. of Medical Oncology, Rome, Italy; [2] Regina Elena Cancer Institute, Dept. of Neuroscience, Rome, Italy; [3] S.Gallicano Institute, Lab. Cutaneous Physiopathology, Rome, Italy*

Aim: Clinical and neuropathological features observed in cis-platin(DDP)-induced neuropathy are similar to those observed in Vitamin E deficiency neuropathy. The aim of the present study is to evaluate the neuroprotective effect of the antioxidant Vit E supplementation in patients treated with DDP - based chemotherapy (CT).

Patients and Methods: Forty-six untreated patients(pts)were enrolled in the study (age ranged from 20 to 65 yrs). Patients candidate to DDP treatment,given alone or in association with other non neurotoxic drugs, were assigned after informed consent to (group A) oral administration of 300 mg/day of Vit E during DDP treatment,or to(group B) DDP-based CT alone. Neurotoxicity was evaluated by an elettrophysiological examination of sensory median and sural nerves and was performed at basal condition, after 3 and after 6 courses of CT. The neurotoxicity was graded following the Chaudry score. A measurement of Vit E plasma levels was also performed for all patients before treatment and at the end of CT. Statistical analysis was carried out with the paired t-Student test.

Results: Twenty-one pts were excluded due to disease progression(18pts),or discontinuation of Vit E (2pts). Twenty-five completed 6 corses of CT (group A=11, group B=14) and were evaluable for the study. The mean total dose of DDP administered for each pt was 480 mg/m2. No significant difference in response rate was observed in both groups. Median Vit E plasma value measured before treatment was similar in the two groups. Mean neurotoxicity score in pts of group A(Vit E)was 1.6. Only 4/11 pts complained mild signs of peripheral neurotoxicity (36%). Patients of the group B (control) showed clinical signs of neurotoxicity in 11/14 cases, with a mean toxicity score of 4.6 ($p<0.00$). Only 2 pts did not complain signs of peripheral toxicity, while in 12/14 cases(85%,$p<0.00$) neurotoxicity resulted moderate to severe. Vit E plasma levels assessment after 6 couses of CT is still ongoing and will be shown.

Conclusion: Patients undergoing daily assumption of 300 mg of Vit E from the beginning of DDP-based CT to discontinuation of treatment do not complain toxicity,or suffer of mild signs of peripheral neurotoxicity when compared to a control group. These data seem to indicate a neuroprotective effect of Vit E in patients with potential development of neurosensitive damage and encourage to a more extended experiences. Supported by Fondazione per la Ricerca Oncologica (F.O.R.O. ONLUS)

1337 POSTER

The role of serum cystatin c and TC-99M MAG-3 renal scintigraphy for predicting cisplatin induced nephrotoxicity in cancer patients

N. Gunel[1], U. Coskun[1], D. Yamac[1], E. Abamor[2], S. Demirtas[3], T. Atasever[2], L. Karaca[3], G. Celenkoglu[1]. *[1] Gazi University, Medical Oncology, Ankara, Turkey; [2] Gazi University, Nuclear Medicine, Ankara, Turkey; [3] Ankara University, Biochemistry, Ankara, Turkey*

Cisplatin, a nonclassic alkylating agent, is one of the most effective agents available for treating solid tumors. However, its clinical utility is compromised by the onset of severe dose-limiting toxicities, especially nephrotoxicity. In recent years several reports have confirmed that cystatin C demonstrates a better correlation with glomerular filtration rate than serum creatinine. In this study we compared serum cystatin C level with serum creatinine and renal scintigraphy. Serum cys-C, serum creatinine concentrations and 99mTc-MAG-3 scintigraphy were studied in 22 cisplatin-naive cancer patients before and 24 hours after cisplatin-based chemotherapy. Serum cystatin C (0.86±0.34 mg/dl vs 0.96±0.45 mg/dl) and creatinine levels (0.78±0.14 mg/L vs 0.82±0.20 mg/L) increased in cancer patients after chemotherapy, but these differences were not statistically significant ($p>0.05$). Semiquantitative variables of 99mTc-MAG-3 scintigraphy (T **, R 20/max*, Tmax**) significantly elevated after chemotherapy. (T *-min: 10.27±5.00 vs 16.17±9.40, R 20/max: 0.40±0.12 vs 0.67±0.45, Tmax-min: 5.40±4.01 vs 7.59±5.30: *$p<0.001$, **$p<0.01$). Significant correlation was found between pre- and post-therapy values of cystatin C and creatinine ($r=0.61$, $p<0.001$). There was no significant correlation between pre- and post-therapy values of T*, R 20/max and creatinine ($r=0.06$, $r=0.13$, $p>0.05$; respectively). Significant correlation was found between pre- and post-therapy values of T * and cys-C ($r=0.29$, $p<0.05$). No significant correlation was found between pre- and post-therapy values of R20/max and cys-C ($r=0.03$, $p>0.05$). These data suggest that MAG-3 scintigraphy is highly sensitive method to cisplatin-induced nephrotoxicity. The efficacy of cystatin C for early detection of cisplatin-induced nephrotoxicity may be superior compared with creatinine. However, additional long-term, wide scope studies are needed to determine a standard procedure for clinical usefulness of cystatin C.

1338 POSTER

99mTc-MIBI myocardial perfusion scintigraphy in the assessment of early cardiac effects of anthracycline cancer therapy

A. Tzonevska[1], S. Sergieva[1], E. Pipercova[2], K. Timcheva[3], I. Trifonova[4]. *[1] National Oncology Center, Nuclear Medicine, Sofia, Bulgaria; [2] National Oncology Center, Nuclear Medicine, Sofia, Bulgaria*

Detection of early adverse cardiac effects after anthracycline cancer treatment may enable recognition of patients of risk of late cardiotoxicity at retreatment.

We investigated 26 patients/pts (age 32-69, median age 46,6) with breast cancer, before treatment and after 2 courses haemotherapy: Gr.I(n6) with CMF (cyclophosphamide,methotrexate,5 fluorouracil) and Gr.II (n20) with FEC therapy (5 fluorouracil, epirubicine, cyclophosphamide).

Investigation of myocardial perfusion with 99mTc-MIBI and evaluation of systolic function and LVEF (left ventricular ejection fraction) echocardiographicaly were performed. Myocardial perfusion scintigraphy was fulfilled on SPECT gamma camera Siemens,Diacam at rest condition after application of 370 MBq 99mTc-MIBI. Segmental tracer activity was analyzed quantitavely (Siemens Quantitative Heart Application)

Before treatment a total number of patients have normal myocardial perfusion and systolic function.After treat-ment we established 2 groups of patients: Gr.I (CMF)is a control group. A total number of patients (n6) had normal myocardial perfusion after treatment. Gr. II (n20)- FEC therapy: Gr.IIa-12 pts. had normal myocardial perfusion, normal systolic function of LV; Gr.IIb-2 pts. were with myocardial hypoperfusion, decreased LVEF; Gr.IIc- 5 pts.- with myocardial hypoperfusion, normal LVEF; GrIId- 1 pt with normal myocardial perfusion, decreased LVEF. Hypoperfused segments in pts GrIIb were severely hypoperfused- range 37%-43%, mean 40% as well as EF- range 40%-52%, mean 46% also showed decrease. Hypoperfused segments in pts Gr.IIc established mild to moderate hy-poperfusion range 58%-70%, mean 61%. The comparison between the two groups indicated the highest incidence of early cardiac adverse effects after anthracycline therapy.

It is concluded that evaluation of early cardiac effects from anthracycline cancer therapy with 99mTc-MIBI ap-pears to be feasible. In these pts an early identification of myocardial hypoperfusion after low doses anthracyclines may diminish the cardiac risk for cancer retreatment by means of follow up the cardiac status.

1339 POSTER

The effect of prednisolone following whole brain irrdiation on blood-brain barrier of the mouse – In the view of acute change

I.A. Kim[1], K.M. Kim[2], I.B. Choi[1], B.O. Choi[1], Y.N. Kang[1]. *Department of [1] Radiation Oncology; [2] Clinical Pathology, St. Mary's Hospital, Catholic University of Korea, Seoul, South Korea*

Purpose: The radiation induced blood-brain barrier (BBB) breakdown is of interest in the view of pathophysiological mechanism leading to development of acute brain edema. Gluticorticoids are widely used concurrently with radiotherapy for their putative salutary effect on brain edema. But the action mechanism of gluticorticoid on the afflicted brain remains for the most part an enigma. This study was tried to determine the peak time of radiation damage on BBB of mice. We also observed whether prednisolone can

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 tryphan blue for gross observation. The radiation change was evaluated microscopically by scoring of histologic damage.

Results: The proportion of vitial staining for radiation-prednisolone group (14/25, 56%). was significantly lower than that for radiation alone group (21/25, 84%). Radiation-prednisiolone group had significantly lower histiologic 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 irradiaton 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 mesurement 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

S. Langkjer[1], D. Arenholt-Bindslev[2]. [1] *Vejle Hospital, Dept. of Oncology, Vejle;* [2] *Aarhus Univ. Dental College, Aarhus, Denmark*

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

K. Grankvist[1], R. Henriksson[2], L. Marklund[1]. [1] *Umea University, Clinical Chemistry, UMEA, Sweden;* [2] *Umea University, Oncology, UMEA, Sweden*

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

C. Gutierrez[1], S. Villa[1], V. Navarro[1], A. Lucas[1], F. Moreno[1], M. Val[2], J.L. Ponton[2]. [1] *I. Catala Oncologia, Radiation Oncology, Barcelona, Spain;* [2] *I. Catala Oncologia, Pharmacy, Barcelona, Spain*

Introduction: Our aim was to investigate if topic aplication of sucralfate cream can reduce the incidence of dermitis, and its overall time to heal when dermitis 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 antracyclines. 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 dermitis 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-RTOG 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 dermitis were reported (21.6 versus 7.8% in overall treatment, and 11.8 vs 2% at the fifth week).

Conclusion: Sucraltate applied topically does not reduce significatively the indidence of dermitis during breast irradiation, although a slight better tolerance is observed.

1343 POSTER

Scalp cooling in the prevention of anthracycline-induced alopecia

E. Lenaerts, M. Meyen, T. Maes, H. Maes, A. El Mousati, J. Lemmens, L. Dirix, P. Huget. *St.-Augustinus, Oncology Center GvA, Wilrijk, Belgium*

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 PinguinR scalp