Conclusion: Our results confirm a high prevalence of APC resistance in patients with gynecological malignancies or breast cancer receiving chemotherapy compared to the general population. In relation to the short observation period the data indicate, that the factor V gene mutation is an important risk factor for thromboembolic complications during anti-cancer chemotherapy. To improve the safety of cytotoxic treatment in APC resistant cancer patients, a prophylactic anticoagulation therapy (i.e. with low molecular weight heparin) should be considered.

1543 PUBLICATION

Prevention of chemotherapy-induced alopecia using the MSC Cold Cap system

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Alopecia is a common, distressing side effect of chemotherapy. Effective chemotherapeutic agents such as the taxanes (TX), anthracyclines (ANR) and etoposide (ET) have been consistently associated with significant alopecia. We studied the MSC Cold Cap system for the prevention of chemotherapy-induced alopecia.

70 patients entered this study. Thus were devided into 4 groups according to the main alopecia associated agent: Group A – TX based regimes (without ANR), Group B – TX + ANR, Group C – ANR based regimes (without TX), Group D – ET based regimes. The tumour types mainly treated were: lung Ca (21 patients), CUO (11 patients), breast cancer (9 patients). Protection from hair loss was achieved by maintaining scalp temperatures between 5°C and 15°C before, during and after chemotherapy by frequent changing of the caps. Assessment was carried out as follows: Grade 0 – no hair loss, Grade 1 – up to 25needed), Grade 3 – up to 75% and Grade 4 – 75% to total alopecia. Grades 0–2 were considered as satisfactory hair protection, while Grades 3–4 as failures.

57 patients were evaluable for assessment. Eight (11%) pts dropped out after only 1 cycle of chemotherapy due to intolerability of the system and 5 (7%) due to progressive disease. The protection from hair loss (Grades 0, 1, 2) achieved in each group was: A (TX) 88%, B (TX + ANR) 36.5%, C (ANR) 100%, D (ET) 100%.

In conclusion the MSC Cold Cap System is a very effective method for protection from hair loss caused by TX, ANR and ET. Protection was lower with the combination of TX + ANR. Our results are comparable to and in most cases better than those reported in other studies using various alopecia preventive methods.

1544 PUBLICATION

Nail disorders in patients treated with weekly paclitaxel (P)

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Paclitaxel is an important novel drug that has been shown to be active in breast cancer.

In our institution since August 1995 we have conducted a phase II study of weekly paclitaxel 80 mg/m^2 in metastatic breast cancer patients, premedication with dexamethasone, ranitidine and diphenhydramine were given. It was noted that a significant number of patients experienced nail changes, so we started to evaluate the nail changes occurring during these dose dense schedule of treatment (Proc. ASCO 1998, 16: 740).

We report our experience of 10 cases (30%) of nail disorders of 34 patients treated, with a median number of 27 weekly doses. Initially nail changes start as discolouration of the nail with subsequent thickening and separation of the nail plate (onycholysis) and paronychia, that appeared after several weekly doses of treatment (ranging from 18 to 40).

Scrapings were taken for fungal culture, 5 out of 10 were positive for candida albicans.

Most disorders were resolved after 5–6 months stopping chemotherapy. The histopathologic findings of nail bed showed: 1) the presence of fibroedematous lesion with dilated capillaries, 2) local endothelium swelling, 3) hystiomacrophagic cells in the perivascular area (CD 68, and 4) damage of the myelin sheath with vacuolization, like whorls resembling an onion bulb (with antiS 100 and osmium tetroxide).

Patients (pts) were classified according to our toxicity scale:

G0 (no changes) 24 pts.

G1 (asymptomatic changes) 6 pts.

G2 (symptomatic changes without functional impairment) 3 pts.

G3 (symptomatic changes with functional impairment) 1 pts.

We conclude that adverse effects from the use of protracted weekly paclitaxel include nail disorders.

The use of steroid-based premedication probably makes fungal infections prosper.

The histologic findings suggest a neurotoxic effect on nail bed.

Although it is not incapacitating, further analysis are needed to evaluate the impact on patients quality of life.

1545 PUBLICATION

To the question of prevention of long-term hematologic toxicity after radiotherapy

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The base concept of this study was the idea that damage of bone marrow (BM) stroma cells and microcirculation are the main targets for long-term hematopoietic toxicity after irradiation. Therefore, we used BM scintigraphy in order to elucidate relationship between absorbed doses and probability of long-term BM depression.

Methods: BM phagocytic activity, which is very sensitive to blood supply, was estimated by BM scintigraphy with radiocolloids. Grading of scintigraphic images was as follows: 1–2-absence or markedly diminished tracer uptake, 3–4-slightly disturbed or normal BM image. Grades 1–2 corresponded to severe injury associated with BM depression, grades 3–4 – to non significant BM damage with high probability of early (within 4–8 weeks) regeneration.

Results: All except one of 71 regions irradiated within 28–50 Gy showed severe impairment of BM manifested by prominent depression of phagocytic function (scintigraphic images of grade 1 and 2) during the first half a year after the end of radiotherapy. On the contrary, normal scintigraphic images were mentioned as early as 4–6 weeks after the end of radiotherapy in 29 of 36 regions irradiated within 10–23 Gy. In 3 additional cases biopsy proved preservation of haematopoietic function in iliac bones irradiated within 18–21 Gy.

Conclusion: From presented data it can be assumed that reduction of radiotherapy dose to 20 Gy can prevent long-term hematopoietic toxicity in most of the patients.

1546 PUBLICATION

Evaluation of the efficacy of granisétron in patients receiving a high-dose sequential chemotherapy for breast cancer

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Purpose: The objective of this study was to evaluate the efficacy of an antiemetic regimen including Granisétron in a high-dose sequential chemotherapy with hematopoietic growth factor and stem cell support for breast cancer.

Methods: PTS entered in this study had a non-metastatic breast cancer with ≥4 involved axillary lymph nodes. The chemotherapy, administered in a conventional unit, consisted in 4 cycles of high-dose cyclophosphamide (3 or 6 g/m^2) and doxorubicin (75 mg/m^2), every 21 days. The antiemetic prophylaxis regimen associated one vial (3 mg) of Granisétron (Kytril®) and IV dexamethasone 20 mg 30 minutes before chemotherapy then one tablet (1 mg) of Granisétron 12 hours after chemotherapy. Nausea/vomiting were evaluated according to the WHO recommendations and performed after the first cycle of treatment.

Results: From 11/95 to 06/98, 75 pts were evaluated. 19% of them experienced no digestive toxicity, grade 1 nausea occurred in 24% of pts, grade 2 vomiting in 37% and grade 3/4 in 20% of pts. The rate of grade 3 and 4 vomiting was higher for pts receiving 6 g/m^2 of cyclophosphamide (43%) rather 3 g/m^2 (11%); this difference was statistically significant.

Conclusion: In this highly emetic chemotherapy and to improve the tolerability of the treatment, we could add others support treatments and anti-HT3 to this preventive antiemetic regimen.