1538 PUBLICATION

Emesis control in patients receiving adjuvant I.V. CMF or anthracycline chemotherapy for breast cancer

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32 patients (pts) completed a diary card for the first five days of the first cycle of adjuvant chemotherapy. Questions addressed anticipatory nausea and vomiting, vomiting frequency, nausea intensity, appetite, anti-emetic use, sleeep pattern, heartburn and any other symptoms. The standard anti-emetic policy is dexamethasone 10 mg pre chemo, followed by 8 mg daily for three days, granisetron po 1 mg pre chemo, and domperidone po prn up to 80 mg daily for three days. One patient reported anticipatory nausea and vomiting. Emesis control was excellent with only 1 patient vomiting more than once and 4% of patients vomited once only, nausea control again was excellent, 31% of patients had no nausea. Over the five days evaluated as patient days (n = 155), the incidence of no nausea was 70%, mild nausea 21%, moderate nausea 8% and only 1 patient had severe nausea though this only lasted for 1 day. Appetite was not significantly affected. 30% of pts reported an alteration in sleep pattern with insomnia on days 1, 2 and 3 being the main event. 30% of pts reported some heartburn. The other volunteered symptoms were constipation 2 pts and headache in 4 pts. The majority of pts had well controlled nausea and emesis. 30% sleep disturbance and heartburn suggests that, for some, the steroid dose is excessive. The extended audit to 100 pts will give us information on emesis control throughout chemotherapy, anticipatory nausea and vomiting and more detail on the incidence of steroid-related side-effects.

1539 PUBLICATION

Improved feasibility of amifostine (A) by using a new administration schedule

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Purpose: Amifostine (A) has been proved to protect normal tissues from the effect of radiotherapy. The recommended application mode is a 15 min short infusion of A, soluted in 100–250 ml NaCl, 30 min prior to irradiation. A new administration schedule was examined determining influence on side-effects.

Patients: 46 patients (pts) with different tumors were treated with 200 mg/m^2 A, administered in 4 different schedules, followed by radiotherapy given in daily fractions of 2 Gy: Short infusion administration: group I (n = 14 pts) and group II (n = 9 pts): 200 mg/m^2 A in 250 ml NaCl over 15 min or 100 ml NaCl over 5 min, respectively: Bolus administration: group III (n = 12 pts) and group IV (n = 11 pts): 200 mg/m^2 A in 10 ml NaCl over 60 sec. All pts were premedicated with except of group IV.

Results: We observed the following amifostine-related side-effects (hypotension: HT; nausea and emesis; N/E); group I: HT WHO grade 1: 8 pts, N/E WHO grade 1/2: 6 pts; group II: HT WHO grade 1: 3 pts, N/E WHO grade 1/2: 3 pts; group III: HT WHO grade 1: 2 pts, N/E WHO grade 1/2: 0 pts; group IV: HT WHO grade 1: 0 pts. N/E WHO grade 1/2: 3 pts. The incidence of side-effects showed a significant decrease in acute toxicity between the short infusion and bolus injection (p = 0.012). There was no difference concerning the radioprotective effect of A.

Conclusion: These investigations have shown that bolus injection is safe and feasible and can save effort and time in the daily routine.

1540 PUBLICATION

A new technique of scalp cooling in preventing alopecia induced by anticancer chemotherapy

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Purpose: To assess a new scalp cooling technique in the prevention of alopecia

Methods: The "Penguin cold therapy cap system" (MSC™) was used. Main innovations of the system are: even scalp cooling, long lasting scalp cooling and tailoring the number of cold caps to the regimen used. Hair loss assessment was performed by one of us (G.P.), according to WHO criteria. Patients tolerance was assessed by a standardized questionnaire

Results: Among 20 patients included, 2 (10%) requested to discontinue the study, after the 1st cycle, because of intolerance to scalp cooling. Another 3 (10.5%), having developed grade 2 alopecia alter the 2nd cycle, did not wish to continue. Among the 15 (75%) evaluable patients: in 7 (47%), MSC™ scalp cooling allowed the completion of treatment without any hair loss, in 2 (13%) with grade 1 alopecia, and in another 3 (20%) with grade 2 alopecia. In 3 patients (20%), scalp cooling did not prevent grade 3 alopecia. Overall, 12 of 15 (80%) evaluable patients demonstrated a satisfactory response (grade 0–2 alopecia) to scalp cooling. It is interesting that 60% of those who received anthracyclines (>60 mg/m^2) and 50% of those who received taxanes were able to complete their planned treatment with no or only minor hair loss. None of the two patients who received 6 courses of CMF demonstrated hair loss.

Conclusions: the use of Penguin cold cap system achieved satisfactory protection from alopecia in 80% of patients treated with highly depilating chemotherapy. The flexibility of tailoring the number of cold caps to the particular needs of each chemotherapeutic regimen seems essential in preventing alopecia. Despite the fact that some discomfort from the local hypothermia is usual, real intolerance to scalp cooling rarely occurs.

1541 PUBLICATION

Phase II trial of Ceftriaxone (CRO) IV once a day in the outpatient management of short term neutropenic fever induced by chemotherapy

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Aim: To study the safety and efficacy of Ceftriaxone IV once a day for ambulatory care of short term neutropenic fever.

Methods: A pilot, prospective, open non controled clinical trial. Patients (PTS) with solid tumours treated with convencional chemotherapy with fever (axillary temperature over 38°C in two occasions or 38.5°C in a single record), ANC < 500 × mm3 or between 500–1000 expected to fall below 500 in the next 24 hours. Performance status < 2. The antibiotic regimen was CRO 2 gr IV qd for 5 days administrated in the ambulatory chemotherapy room. They have a clinical evaluation dialy by a oncologist, if the fever > 38.5°C at the third day or median blood pressure fall to below 85 mmHg the PTS was admited for treatment inside the hospital. Fever of unknow origen (FUO), clinically documented infection (CDI) and microbilogycal documented infection (MDI) as the same universally criteria. Success: PTS recovery and completed the 5 days of treatment outpatient, Faliure: need other antibiotic or inpatient management.

Results: From July, 1–96 to July, 1–97, 40 PTS were admited. M/F ratio 8/32. Median age 50.4 y (range: 16–74 y) ANC: 187 × mm3 (range: 100–500). Chemotherapy day 10 (range 8–15). Patology: Breast 20, Lymphoma 4, Gastric 4, Sarcoma 6, Ovary 4, Lung 2. Clinical focous: Oral 14, Respiratory 12, Digestive tract 12, Non evidence 2. FUO: 2, CDI: 26, MDI: 12. Bacteremias 12, isolated germenes: E coli 4, Staphylococous epidermidis 8. Success: 30 (75%) PTS and Faliure: 10 (25%) PTS.

Conclusion: we dont have any related dead to the treatment and considered to the CRO as an effective and safety treatment for the ambulatory care of the short term neutropenic fever, it's the first study of this kind in our country and this strategy implies an important cost saving.

1542 PUBLICATION

Resistance to activated protein C due to the factor V Leiden mutation: A risk factor for chemotherapy-associated thrombosis

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Purpose: To evaluate the importance of resistance to activated protein C (APCR) due to the Arg506 → Gln mutation of the factor V gene for the occurrence of thromboembolic complications during chemotherapy, we studied 80 women with gynecological malignancies (n = 20) and breast cancer (n = 60) during six month of adjuvant (n = 29) or palliative (n = 51) chemotherapy.

Methods: Blood samples were obtained prior to chemotherapy and after a six month treatment period. An aPTT based method (APC™ Resistance V, Chromogenix, Sweden) was used for assessing APCR. The results were expressed as APC-ratios (cutt-off APC-ratio < 2). The Arg506 → Gln mutation of the factor V gene was determined using the polymerase chain reaction.

Results: 11 patients (14%) demonstrated resistance to APC. 9/11 patients were heterozygous for the factor V gene mutation. The incidence of thromboembolic complications during the observation period was 4/80 (5%). In 1/4 patients who had suffered from thrombosis the factor V gene mutation was diagnosed.

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.