shown that the survival time of DOX-treated mice receiving CaG was nearly 2.5-fold longer as compared to no CaG. LD_{100} DOX injected with CaG was about LD_{50} as compared to no CaG. The manifistation of DOX intestinal toxicity were lower after the DOX+CaG injection. In chronic experiments CaG caused a two-fold increase in mean survival time of DOX-treated mice and maximum total DOX dose. It was shown also that CaG does not influence on specific therapeutic activity of DOX in tumor-bearing animals. In experiments on the MOPS-406 plasmocytoma-bearing mice we have shown that therapeutic effect of small doses of DOX with CaG was the same as DOX alone. The antitoxic effect of CaG was clearly evident when toxic DOX doses were injected. All DOX-treated mice died earlier than the control tumor-bearing animals. In contrast there were no early deaths in DOX+CaG group and significantly higher DOX efficacy was achieved. Besides, there were cured animals in groups receiving high doses of DOX with CaG· 20 or 40% of mice with 15 or 20 mg/kg DOX+CaG respectively. Comparable results were obtained on hemoblastosis La-bearing mice. We conclude that CaG is perspective modifier which can be used in cancer patients and can increase the efficacy of anticancer DOX therapy by decreasing drug toxicity. Supported: the Russian Foundation for Basic Researches (Grant N 48796).

71 POSTER

Clinical evaluation of azasetron tablets in prevention of cisplatin-induced acute emesis – Multicenter double blind test with ondansetron tablets as control

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Purpose: To evaluate the effectiveness, safety and usefulness of azasetron tablets (Group A) in prevention of cisplatin-induced acute emesis, a double blind test was conducted with ondansetron tablets (Group O) as control.

Materials and Methods: Subjects were inpatients with malignancy receiving cisplatin (≥50 mg/m^2) alone or in combination chemotherapy with cisplatin. Tablets were orally administered before start of cisplatin. Antiemetic efficacy and adverse effects of antiemetic drugs were evaluated. Antiemetic efficacy were evaluated according to the degree of nausea and the number of vomiting episodes.

Results: 245 patients were entered, of whom 232 patients (121 in Group A, 111 in Group O) were accepted for analysis of effectiveness and usefulness, and 245 patients for analysis of safety. The rate of efficacy on acute emesis was 78% (94/121) in Group A and 73% (81/111) in Group O. The equivalence in effectiveness between ondansetron and azasetron tablets was verified. The rate of safety was 94% (120/127) in Group A and 88% (104/118) in Group O (p = 0.074). Adverse reactions were observed in 3 patients in Group A (headache, fever) and in 7 patients in Group O (headache, dull headache, diarrhea, fever and defective colulour vision) with the incidence being 2% and 6%, respectively. The rate of usefulness was 78% (94/121) in Group A and 72% (80/111) in Group O (p = 0.067). Group A was slightly better than Group O about the rate of safety and usefulness, with no significant difference between the two groups.

Conclusion: Group A were as effective as Group O, and slightly better than Group O in safety and usefulness, with no significant differences between two groups. We therefore consider that azasetron tablets is a useful drug in prevention of cisplatin-induce emesis.

72 POSTER

Effect of the perioperative selective bowel decontamination in abdominothoracal resections of the esophagus

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Purpose: The study was designed to evaluate the efficiency of the perioperative selective decontamination of the bowel in patients with abdominothoracal resections of a carcinoma of the cardia or the esophagus.

Method: 73 patients were included in a prospective randomized study. Loss of body weight </> 10% and carcinomas of the esophagus/cardia were stratified. The treatment group (n = 28) orally received 80 mg Gentamycin, 100 mg Polymyxin B and 200 mg Amphotericin B four-times a day starting 4 days prior to surgery. Postoperatively, the drugs were applied by a gastrointestinal tube.

Results are shown in the table.

	Treatment group (n = 28)	Control group (n = 45)
Artificial respiration	3.6 ± 5.0 days*	5.3 ± 9.5 days*
Stay in the ICU	9.1 ± 7.1 days*	11 6 ± 13.7 days*
Hospitalization	33.1 ± 16.1 days*	40.4 ± 27.3 days*
Pneumonia	36%	40%
Sepsis	11%	13%
Mortality	3 6%	8.9%

*[med ± SD]

Conclusion: No statistically significant differences were observed between both groups. The analysis of the postoperative course, however, shows that patients with a delayed postoperative weaning may profit from a perioperative selective bowel decontamination. This therapy should be focussed on this high risk patients.

73 POSTER

Risk factors and reversibility of neurotoxicity induced by high-dose paclitaxel

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Peripheral neuropathy (PN) is the main side effect with repetitive cycles of paclitaxel at standard doses. High-dose paclitaxel (HDP) with peripheral blood stem cell (PBSC) rescue is a novel treatment of patients (pts) with advanced cancer. No systematic evaluation of the neurotoxicity of HDP is available. Neurotoxicity of HDP was evaluated during a Phase I trial of HDP (500–800 mg/m^2 by 24-hour infusion, on day 1) followed by high-dose cyclophosphamide, thiotepa and carboplatin (Antman et al, J Clin Oncol, 1992, 10, 102) + PBSC rescue. Eighteen pts with metastatic cancer were treated with escalating doses of HDP (500 mg/m2, 3 pts; 600 mg/m2, 3 pts; 650 mg/m2, 3 pts; 700 mg/m2, 6 pts; 800 mg/m2, 3 pts) plus CTCb and evaluated before, during and after treatment with neurological examination (Neuropathy Symptom Score (NDS) and NCI common toxicity criteria (NCI-CTC), nerve conduction study (NCS) and evaluation of autonomic function. Four pts had been previously treated with neurotoxic chemotherapy (NC) (cisplatin, 3 pts; vinorelbine, 1 pt; paclitaxel, 1 pt). Pts with prior PN (grade, 2, NCI-CTC) were excluded. All pts had distal paresthesias and 5 had distal motor symptoms. None had vegetative symptoms and 2 had abnormalities on vegetative evaluation. Symptoms started 2.9 ± 0.3 days after HDP, worsened for 9 ± 0.8 days and improved by day 15.2 ± 0.4. Nerve conduction studies showed axonal neuropathy predominantly in the legs. Dose escalation correlated with duration of symptoms and delayed improvement (p = 0.013, Spearman). Previous NC but not dose escalation, was associated with more severe PN (p = 0.005, M-W). PN resolved within 2–4 months. PN induced by HDP is reversible and not dose limiting. Increasing dose is associated with more prolonged PN but not with severity. Neurotoxicity of HDP is moderate except in pts with prior NC.

74 PUBLICATION

Protective action of EHF electromagnetic irradiation on cisplatin-suppressed functional activity of immune system cells

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The question addressed in this study was how low-intensity non-ionizing electromagnetic irradiation (EMI) of extremely high frequency (EHF) range would modulate suppressive action of anticancer drug cisplatin (DDP) on specific activities of immune system cells, in particular, rosette-forming activity of T-lymphocytes (RFA) and phagocytic activity of neutrophils (PCA). G-protein inhibitor pertussis toxin (PT) was used to evaluate the role of cell signaling systems in the effects of DDP and EMI. Mice blood cells were exposed in vitro to DDP, PT and EMI, and assayed for functional responses as described in (A. Luik et al., Exp. Oncol., 1994, v. 16, p. 71–75).

DDP and PT inhibited RFA by 35 and 25%, respectively. Their joint effect was multiplicative (decrease by 55%), suggesting G-protein-independent route of DDP action. EMI did not affect normal or PT-suppressed RFA but completely reversed the effects of DDP, applied either alone or with PT.

Individual effects of DDP, EMI and PT on PCA were similar to their effects on RFA. However, joint effect of DDP and PT on RFA was synergistic rather than multiplicative (decrease by 75%). EMI did not reverse PT effect, activated by 20% PCA suppressed by DDP, and activated by 100% PCA suppressed by DDP+PT.

Therefore, EMI can restore the functional activity of cells of immune system suppressed by cisplatin. This finding may be of potential clinical importance. The observations about DDP interaction with PT point to new possible mechanisms of its cytotoxic effects.

75 PUBLICATION

The effect of adjuvant tamoxifen therapy in postmenopausal women on thyroid function tests

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Purpose: Tamoxifen has been shown to alter serum concentration of many hormones and their binding globulins. In a prospective study we sought to establish these effects.

Methods: We evaluated 45 postmenopausal women who had proven stage I–III carcinoma of breast receiving adjuvant tamoxifen therapy (20 mg/day). Serum tri-iodothyronine (T_3), thyroxine (T_4) and thyroid-stimulating hormone (TSH) concentrations were measured at baseline before tamoxifen treatment, at 3 months and 6 months.

Results: There were increases in the mean values of TSH, T_3 and T_4 from baseline to 3 and 6 months. The elevation of T_4 at 3 months compared to its baseline values was significant ($p = 0.02$). Changes of thyroid function tests in women >60 years old were less than in women <60 years old.

Conclusion: Tamoxifen therapy in postmenopausal women results in increased TSH, T_3 and T_4 concentrations after 3 months. This elevation is less significant after 6 months.

76 PUBLICATION

Premedication one hour before the treatment with taxanes

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Allergic reactions are the most common and serious side effect of treatment with taxanes. The premeditation with histamine H1, H2 antagonists and dexamethasone is established and suggested to start 13 hours before taxane administration. The aim of the present study was to show that one hour premedication is safe.

Material: Two hundred and one patients were reviewed. 169 were treated with Paclitaxel and 32 with Docetaxel. 92 had ovarian cancer, 51 breast, 32 head and neck, 19 lung cancer and 7 sarcomas.

Treatment: One thousand and one hundred ninety eight courses were administered. In 300 courses the premedication with dexamethasone and difenidramine, started 13 hours before the administration of Paclitaxel (or Docetaxel). In 898 courses the premedication was given one hour before Taxanes.

Results Toxicity: No differences in allergic reactions were seen between the two different timing of premedication. Mild allergic reactions of the type of erythema several hours after treatment were seen in few patients. 2 patients had also hypotension without consequences. These reactions were equally distributed in both ways of premedication.

Conclusion: Premedication with anti-allergic drugs one hour before the administration of taxanes has no consequences and can be considered safe.

77 PUBLICATION

Magnetotherapy for treatment of radiodermatitis

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The breast irradiation after conservative surgery shows a 5% of early and late skin complications, causing a worsening of cosmetic results. The aim of this study is to test the ability of Magnetotherapy in the treatment of these complications.

Methods and Patients: from June 95 to June 96, we enrolled 40 patients, treated with conservative surgery and radiotherapy for breast cancer and affected by radiodermatitis grade III. We randomised the patients in two arms of 20 pts each: the experimental arm underwent to 20 minutes daily application of magnetotherapy (intensity: 60 Gauss, frequence: 12 Hz) up to the complete recovery; the control arm was treated with standard medical therapy

Results: all patients were evaluable for toxicity and response. In the experimental arm, every patient showed a complete recovery of radiodermatitis in 12–24 days (mean length 18 days); in the control group, only 17 out of 20 patients had a complete response and in a longer time (30–50 days, mean 42 days).

Conclusions: we believe that Magnetotherapy is a very interesting, innovative and efficient treatment for radiodermatitis and with better cosmethic results. Moreover, avoiding the delay of radiotherapy for acute skin toxicity, it could allow better therapeutic results, too.

78 PUBLICATION

Cardioprotective efficacy of amifostine (WR-2721) in adriamycine-treated rats

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Purpose: The data concerning efficacy of amifostine (WR-2721) in prevention of adriamycine (ADR)-induced cardiotoxicity are scarce. This study was undertaken to evaluate the efficacy of single dose of WR-2721 in prevention of acute ADR-induced cardiotoxicity in male Wistar rats.

Methods: WR-2721 (300 mg/kg ip) was given 30 min before ADR (6 mg/kg iv) The cardiotoxicity of ADR was recorded at 48 hrs after its administration using a model of aconitine-induced ventricular extrasystoles (VES), data on CK, AST, LDH, α-HBDH serum activities and light microscopic examination (haematoxylineosin staining).

Results: VES-inducing dose of aconitine was significantly reduced in ADR-treated rats, while pretreatment by WR-2721 partly reversed arrhythmogenic dose of aconitine to control and prevented the increase of heart rate and appearance of other rhythm disturbances, except VES, during the aconitine infusion. WR-2721 also prevented ADR-induced increase of serum CK, AST, LDH i α-HBDH activity. Our light microscopic examination of the heart has not revealed any changes in ADR-treated rats, opposite to some previous reports concerning this ADR dose. Therefore, protective effects of WR-2721 could not be estimated by this method.

Conclusions: Our results have shown that radio- and chemoprotector WR-2721 has provided successful cardioprotective effects in ADR-treated rats.

79 PUBLICATION

Prophylactic and therapeutic management of acute radiation related morbidity – Results of a German multicenter questionnaire

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Purpose: The management of acute side effects in radiation therapy of the skin and different mucosal sites is often based on individual experiences.

Methods: A questionnaire was sent to all radiotherapeutic departments in Germany. It was to evaluate the prophylactic and therapeutic management of acute side effects according to EORTC/RTOG scales of the skin and the mucosal sites of mouth, esophagus, bowel, rectum and vagina.

Results: From 150 questionnaires submitted in July 1995, eighty nine (59.3 per cent) answers have been received. The recommendations differed very much, especially the oral mucositis was treated in many different ways and combinations. There seems to be a symptom related preference of the chosen therapy, which is indeed caused by individual experiences more than by recommendations from literature.

Conclusions: Systematic prospectively planned clinical investigations are necessary in order to achieve a further reduction in the radiation related acute morbidity. For this purpose, a multicenter collaborative working group has been founded.