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PROTECTION FROM CYTOTOXIC-INDUCED GONADAL INJURY WITH A GONADOTROPIN-RELEASING HORMONE AGONIST (GnRH)

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Introduction: Aggressive chemotherapy (CT) induces gonadal and reproductive dysfunction in both men and women. Continued supraphysiological administration of GnRH agonist inhibits LH and FSH release and consequently suppresses the spermatogenesis and the testosterone (T) production in men. Using this antifertile effect we treated patients with GnRH agonist during CT in order to protect the germinal epithelium from cytotoxic damage.

Patients and Methods: 14 days before CT with cis-platinum, vinblastine and bleomycin Buserelin (Suprefact^{R}) was administered at a daily dose of 3x0,5 mg subcutaneously in 4 patients with testicular cancer. During and 14 days after CT Buserelin was given intranasally at a daily dose of 3x0,4 mg. T, LH and FSH were measured by RIA (Serono) twice a week. Sperm analyses were performed before and in a monthly intervall after CT.

Results: LH, T and FSH serum levels were effectively suppressed during pretreatment with Buserelin and remained low during CT. The hormone levels increased abruptly after discontinuation of agonist treatment and rose above pretreatment levels before falling again to normal values within 4 weeks. All patients were azoospermic 1 month after cessation of CT but showed oligozoospermia 3 months after CT indicating an immediate restitution of spermatogenesis after CT.

Conclusions: 1. T, LH and FSH serum levels were effectively suppressed within 14 days of subcutaneous administration of Buserelin. 2. The antifertile effect of Buserelin was reversible in all patients indicated by normalization of hormone levels and restitution of spermatogenesis. 3. These preliminary data suggest that the germinal epithelium may be successfully protected from drug induced gonadal toxicity by GnRH agonist.

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NCy 32

COMPLETE CONTROL OF PLATIN-INDUCED EMESIS WITH LOW-DOSE COMBINED DEXAMETHASONE (DEX) AND METOCLOPRAMIDE (MCP) THERAPY

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About half of the tumor patients on platin therapy suffer from severe nausea and vomiting, even when MCP (daily doses of 200 to 1000 mg) or DEX (daily doses 40 to 100 mg) are administered in very high doses. We have now established a regimen which controls emesis in platin therapy prophylactically in almost every patient.

DEX 8 mg was pushed iv. followed by slow injection of MCP 10 mg immediately before chemotherapy in the morning and repeated 4 hours later. 14 patients with nonseminomatous germ cell tumors and 8 pts. with platin-based chemotherapy for other malignancies were evaluable.

4 pts. had less than 5 episodes of vomiting during day 1 of their first and second chemotherapy cycles, respectively. The anti-emetic effectiveness of DEX/MCP was complete through days 2 to 5 on 5 days treatment regimens. 17 pts. were without nausea and vomiting for a total of 54 cycles. Appetite and eating behaviour have been normal in all patients. The main side effect was temporary drawsiness in 6 patients. Some pts. developed a transient increase of WBC count within the first days of therapy. All pts. had a sensation of perianal warmth and itching about 30 seconds after iv. push of DEX.

Summary: Low-dose DEX/MCP is more practicable than other antiemetic therapy in the prophylaxis of platin-induced emesis.

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DOSE-RESPONSE CURVES FOR THE ANTIEMETIC POTENCY AND FOR THE SIDE EFFECTS OF METOCLOPRAMIDE (MCL) AGAINST CISPLATIN INDUCED EMESIS.

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The quantal responses (i.e. all or none response) of MCL were studied in patients (age 17 to 71 years) treated with cisplatin in combination with other cytostatic drugs (adriamycin, bleomycin, vincristin, cyclophosphamide). The lowest dose of MCL was 1.75 mg/kg per cycle (n = 25). This was given at 0.125 mg/kg b.w./hr i.v. over two hours as a loading infusion, then 0.0625 mg/kg b.w./hr over 24 hours as a maintenance infusion. At the same schedule three different higher doses were given with total doses 3.5 (n = 44), 7.0 (n = 120), and 14.0 (n = 161) mg/kg per cycle. The mean number of emetic episodes in groups of historical controls without sufficient antiemetic treatment was 4.0, 7.0, 15.0, and 22.0 emetic episodes at the respective doses of cisplatin (25, 60, 90, and 120 mg/m^2).

From the dose-response curves the following doses of cisplatin were obtained which produced < 3 emetic episodes in $\leq 5\%$ of the patients. These were 13, 25, 42, and 80 mg/m^2 respectively. It was found that 95% antiemetic protection against each mg of cisplatin can be obtained by MCL-doses of 0.15 (range 0.13 - 0.18) mg/kg/cycle.

MCL caused dose-dependent diarrhoea (from 20 to 88%) and drowsiness/sedation (up to 55% of the patients). The most prominent extrapyramidal reactions, however, were not dose-dependent: akathisia 22%, 33%, 32%, and 25 % of the treatment cycles, or acute dystonia 4%, 10%, 9%, and 8% respectively.

From the results it follows that the emetogenic activity of cisplatin may be antagonized quantitatively by MCL: 1 mg/kg of MCL antagonizes about 6.5 mg/m^2 of cisplatin.

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NCy 34

EVALUATION OF CHRONIC USE AND COMPLICATIONS ENCOUNTERED IN THE APPLICATION OF INDWELLING CATHETERS IN ONCOLOGY PATIENTS

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This report describes our experience with Hickman catheters on an in- and outpatient basis. We retrospectively evaluated the clinical course of 14 female and 2 male patients (mean age: 33 yrs.) who underwent Hickman catherization between September 1982 and February 1985. Eighteen catheters were utilized for a total duration of 1784 days (range 20-198 days). Three patients had solid tumors; 13 hematologic malignancies. Medication used included a wide range of chemotherapeutic agents (Ara-C, Daunoblastin, Cyclophosphamide, VP-16, Platinum, Methotrexate etc.) used either as injection or infusion.

Reasons for removing catheters were 9/18 for conclusion of treatment and 7/18 for complications (5 infections, 2 for phlebitis with iatrogenic superior vena cava syndrom). Two patients died of cancer with their catheters in place. All of the 5 patients were neutropenic when sepsis developed. Four out of 5 bacteremias cleared with antibiotic administration and catheter removal was not necessary. Staph.albus was the most common pathogen. There were no deaths related to sepsis, embolus, or vascular damage.

Although the patient number is small for comparison, the complication rate in this largely immunsuppressed group of patients was in the same range to that reported by others (J.J.Reilly et al., Cancer 53, 219, 1984).

We feel that a lower complication rate may be attributed to an adequate teaching of the nursing staff and close adherence to catheter care guidlines. This series demonstrates an acceptable incidence of bacteremia and mechanical problems which is outweighed by the convenience and comfort provided by the long term venous access.

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