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EFFICACY OF LAS 30451 IN THE PREVENTION OF CISPLATIN INDUCED EMESIS

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We present the results of a prospective, multicentric, randomized, double-blind study, designed to evaluate the efficacy of LAS 30451 (LAS), a new 5-HT3 antagonist, in the prevention of cisplatin (CDDP) induced emesis.

Material and methods: 127 chemotherapy naive patients, who were scheduled to receive CDDP at dose = or >50 mg/m2, were randomized to receive LAS 0'2 mg/Kg or 0'4 mg/Kg, as single-dose plus placebo (pcb) or two doses, administered 30 minutes before chemotherapy and two hours later. 126 were avaluable. In all patients it was evaluated the number of emetic episodes (EE) registered in the 120 hours after chemotherapy, and the intensity of nausea (N) measured with a visual analogic scale (VAS) of 100 mm of length. We considered complete protection (CP) the absence of EE, major protection (MP) the presence of 1 or 2 EE, minor protection the presence of 3 to 5 EE, and faillure more than 5 EE.

Results: 35% of patients treated with LAS at doses 0'2 mg/kg + pcb, 0'2 mg/Kg x 2 doses or 0'4 mg/Kg + pcb obtained a CP of acute emesis. Those patients treated with 0'1 mg/Kg x 2 doses obtained a 25% of CP. MP was 23%, 23%, 27% and 22% respectively. Best protection against nausea was obtained with 0'2 mg/Kg + pcb (Median VAS 5 mm). Also this schedule obtained the best protection against delayed emesis, with rates of CP+MP of 71%,79%,88% and 88% on days 2, 3, 4 and 5 rspectivcly. The more frequent adverse reactions registered during the treatments were facial flushing in 6 cases, headache in 4 cases, diarrhea in 2, and somnolence in 2 cases.

Conclusions: The eficacy of LAS in the prevention of CDDP induced emesis, at the dose levels studied is low, with rates of CP lower than 40%. The dose of 0'1 mg/Kg x 2 obtains the lowest index of protection (25%), althougt the differences are not statisticaly significants.

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ANTIBIOTIC DOSAGES USING CENTRAL VENOUS CATHETERS (CVC) OR DIRECT POERIPHERAL BLOOD PUNCTURE (DPBP) IN NEUTOPENIC PATIENTS : A COMPARATIVE STUDY

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Aminoglycosides (AG) and glycopeptides (GP) are broadly used for either empiric or curative treatment of bacteriological infectious complications in neutropenic patients, and their monitorings need dosages for cinetic data. To avoid variabilities, samples are usually performed using peripheral puncture. In patients with CVC, we took samples dosages from the catheter, in order to spare their veinous capital and improve their confort. All patients were adults with Acute Myeloblastic Leukemia in neutropenia, treated in the same unit, and had a CVC with 2 lines. All patients received AG and/or GP (amikacin 500mg/8h and vancomycin 500mg/8h respectively). Antibiotics were given by line N°1 of the CVC, and samples taken by line N°2 and by DPBP. Infusion flow was controled by a regulating system. Timing (begining and end of infusion, T0 and T30) was carefully noted. The difference of time average between CVC and DPBP for T30 are 1.56 mn and 1.6 mn for AG and GP respectively. None significant bias related with each technic was found (0.047 and 0.167 at T30, and -0.076 and -0.298 for AG and GP respectively), and student test does not show significant differences with both peak and residual procedures.

We conclude that CVC can be used for dosages of antibiotics
. (1) with a very strict protocol with a well trained team,
. (2) if a control with DPBP in case of suspicious result is realised without delay,
. (3) in patients with double line catheter

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IMPROVING QUALITY OF ANTIEMETIC THERAPY (AT).

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As part of a Quality Assurance (QA) programme in our ward we aimed at improving AT for patients receiving chemotherapy. Still after introducing 5-HT antagonists, nausea and vomiting constitute a major therapeutic problem.Three standardized AT regimens were worked out: a) metoclopramide + dexamethasone, b) ondansetron, c) ondansetron + dexamethasone.The regimens were ranked c > b > a according to their assumed effectiveness and cost. For each course of chemotherapy the patients were selected to one of the regimens by a score of prognostic factors related to age, type of chemotherapy, anxiety and previous emesis problems. A standardized registration form was filled in daily for five days by each patient to register episodes of vomiting and degree of nausea on a four-level scale.The evaluation criteria for successful treatment were "none" or "mild" nausea plus less than two vomiting episodes per day. Initially, in 139 cases of chemotherapy, AT was successful in 73% of all cases on day one,but only in 55% on day two and three.These results were basis for systematic improvement efforts, which seemed to increase the success rates. Our study shows that the success of treatment is not related to costs of drugs. In our experience we find QA to be a useful tool in improving AT on individual and group levels.

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EXPERIENCE WITH PREVENTION OF TOXICITY OF TAXOTERE IN 1 ECTG CENTRE.

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Taxotere is a new antitumor drug, which acts at the cellular level by promotion of the microtubule assembly and shows high anti-tumor activity in phase II studies in solid tumors. Limiting factors in its use are an early acute hypersensitivity reaction (AHSR) and development of peripheral edema after several courses.

Within the phase II studies of the ECTG-EORTC, 50 patients with 9 different types of solid tumors were treated with taxotere in our centre. In 14 patients an AHSR appearing within the first 5 minutes of the start of the infusion occurred : 5 during the first, 8 during the second and 1 during the third course and consisted of acute diffuse rash, dyspnea, hypertension and urticaria, while 3 patients also complained of severe back pain. Interruption of the infusion and treatment with promethazine, cimetidine and dexamethasone intravenously allowed the infusion to be restarted after 10 minutes with the exception of two courses which were restarted later due to practical reasons. No lifethreatening reactions occurred.

Patients who had an AHSR were thereafter pretreated orally 12 and 3 hours before the next cycles of taxotere with 32 mg of methylprednisolone (MP), 10 mg of cetirizine HCl(C) and 1 mg of ketotifeen. In all but 1 patient for a total of 44 courses the AHSR was completely blocked by the above regimen.

Retrospective analysis of the development of peripheral edema in all our patients treated with more than 2 courses of taxotere (N=34), revealed that in patients without an AHSR 8 out of 22 (36.3%) developed peripheral edema. Of patients with an AHSR and treated with the above mentioned regimen only 1 of 12 (8.3%) showed a mild facial edema : 3 patients had 4 courses, 6 patients 6 courses and 3 patients 8 courses.

Pretreatment with this oral regimen limits the AHSR and seems to prevent the development of peripheral edema. Its application is simple in comparison to other described regimens and we have started to further simplify it to only 2 oral drugs (MP and C).

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HICKMAN LINE PRACTICE IN PATIENTS WITH SOLID TUMOURS

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In a 22 month period, 61 Hickman catheters were inserted in 51 patients with non haematological malignancies. The diagnoses were GIT ca (16); head and neck ca (13); breast ca (9); sarcoma (3); lymphoma (3); urogenital tract ca (5); and unknown primary (2). The patients' age range was 21 to 81 years, (median 59).

Indications for line insertion were - administration of infusional chemotherapy (42); poor venous access (5); and needle phobia (4). 45 patients had 50 catheters inserted angiographically, and 6 had 11 catheters inserted surgically. In 2 patients insertion was unsuccessful. Catheters have remained *in situ* for 6390 days. The duration of continuous catheterisation ranged from 2 to 720 days (mean 104.75).

Immediate complications occurred only in angiographically placed catheters, with 9 pneumothoraces (4 patients needed chest drain insertion, 2 cannula aspiration, and 3 conservative treatment) and 1 brief episode of tachydysrhythmia.

The sepsis rate (systemic and superficial) was 2.97 per 1000 catheter days. There were 5 episodes of systemic sepsis in 11 lines surgically placed and 4 in 50 angiographically placed (X^2 $p<0.01$). 10 superficial infections occurred in 8 patients, all successfully treated with antibiotics. Blockage requiring urokinase flush occurred in 3 catheters; 2 developed punctures which were repaired; and 1 snapped during removal. 1 patient developed an AV fistula due to neglected sepsis.

13 lines were removed for complications - systemic sepsis (9); venous thrombosis (2); blockage (1); and extravasation (1). 16 lines were electively removed, and 3 accidentally removed by the patients. 10 patients died with the catheter *in situ* and 16 are alive and continue on treatment. 1 patient is lost to follow up.

Hickman lines can be safely used in patients with solid tumours. Significantly more early but fewer late complications occurred in those angiographically placed.

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ACUTE DISSEMINATED INTRAVASCULAR COAGULATION (DIC) IN CANCER PATIENTS.

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Increased risk of clotting is recognizable in many haematological malignancies and solid tumors. From 1988 to 1992 we observed 8 cases of acute DIC: 4 patients had gastric carcinoma, 3 ductal breast carcinoma and 1 high grade Non Hodgkin's lymphoma (T-Immunoblastic according to Kiel classification). All the patients exhibited major haemorragic syndrome, severe thrombocytopenia low fibrinogen serum levels, prothrombin time prolongation, low antithrombin III activity, increased serum X-oligomers (XDP) levels and positivity of paragoagulation (ethanol and protamine-sulphate tests. In 5 patients (1 gastric carcinoma, 3 breast cancer and 1 high grade NHL) DIC appeared during the course of the disease, while in the remaining 3 patients, all affected by gastric cancer, DIC was the first manifestation of the tumor. All patients has been treated with heparin, fresh frozen plasma and platelets support but, except one patient who showed improvement of clinical conditions, clotting tests and platelet count, however of short duration, all the other patients rapidly died. We wish to emphasize that acute DIC, although rare, can be the first manifestation of gastric carcinoma and the sudden appearance of bleeding accompanied by thrombocytopenia, hypofibrinogenemia and elevated serum fibrinogen degradation products in adult or elderly patients, in absence of infectious disease or bone marrow impairment, must drive to the search of gastric cancer.