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IV GRANISETRON IN CHILDREN: A RANDOMIZED COMPARISON AGAINST CHLORPROMAZINE PLUS DEXAMETHASONE IN PREVENTION OF IFOSFAMIDE-INDUCED EMESIS.

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The anti-emetic efficacy of iv granisetron (gran) 20μg/kg was compared with chlorpromazine (chlor) in combination with dexamethasone (dex) in 88 children (mean age 9.6 yrs, range 2-16 yrs) in a randomised, single-blind, parallel group study. Two thirds of children had received prior chemotherapy and all were scheduled for ifosfamide therapy (≥3g/m²) for 2 or 3 consecutive days. On each day of therapy, they received either iv gran immediately prior to ifosfamide, plus up to 2 more doses within 24h if required, or chlor (0.3-0.5mg/kg iv) every 4 to 6h plus dex (2mg/m² iv) every 8h. Significantly fewer vomits were recorded with gran at 24h (1.5 vs 7.0 median no. of vomits; $p<0.001$) and the percentage of patients having no more than one vomit (50% gran vs 21% chlor/dex; $p<0.01$) and no worse than mild nausea (67% gran vs 38% chlor/dex; $p<0.01$) was also significantly in favour of gran. The time to onset of moderate/severe nausea or vomiting was delayed in the gran group and overall clinical response was rated as 'good' or 'very good' in significantly more children on gran (63% vs 31%; $p=0.019$). Gran was well tolerated and no children were withdrawn from treatment. Two children reported extrapyramidal effects (EPS) with chlor/dex and significantly more children experienced somnolence in this group (19 vs 2; $p<0.001$) resulting in 5 being withdrawn. Gran was shown to possess improved anti-emetic efficacy when compared with chlor/dex in children undergoing chemotherapy with no evidence of sedation or EPS.

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IV GRANISETRON IN CHILDREN RECEIVING HIGHLY EMETOGENIC CHEMOTHERAPY: A DOUBLE-BLIND DOSE-RANGING STUDY.

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The anti-emetic efficacy and tolerability of three prophylactic doses of iv granisetron (10, 20 or 40μg/kg), a potent, selective 5-HT_3 antagonist, were compared in 80 children (mean age 10.3 yrs, range 2-16 yrs) receiving highly emetogenic chemotherapy for malignant disease, in a double-blind randomized study. Patients had received up to 2 previous cycles and were scheduled to receive treatment with either; cisplatin (≥60mg/m²), cyclophosphamide (≥1g/m²), ARA-C (≥3g/m²) or N-Mustard (≥6mg/m²). IV granisetron was infused over 5 mins immediately before chemotherapy, with 2 further open doses (20μg/kg) permitted within 24 h, if required. The median number of vomits at 24 h were 2, 3 and 1 for the 10, 20 and 40μg/kg doses, respectively. The percentage of children reporting ≤1 vomiting episodes were 48%, 42% and 56% for the 10, 20 and 40μg groups respectively. The percentage of children reporting no or only mild nausea were 65%, 46% and 72% in the 10, 20 and 40μg/kg groups respectively. Clinicians' global rating was 'very good' in 48%, 50% and 64% for the 10, 20 and 40μg/kg granisetron groups, respectively. The results showed a small but consistent trend in favour of the 40μg/kg dose although the differences were not statistically significant. There were no dose-related adverse events and no reports of extrapyramidal side effects or sedation. It was concluded that granisetron at a dose of 40μg/kg is well tolerated and an effective anti-emetic in children receiving highly emetogenic chemotherapy.

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PHARMACOKINETICS OF TROPISETRON (TRO) IN CHILDREN

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Tropisetron is a highly selective 5HT3-antagonist that has shown to prevent chemotherapy-induced emesis very efficiently. Experience in adult patients revealed an excellent safety profile with only mild side effects occuring (i.e. headache and obstipation).

Pharmacokinetic and efficacy studies in adults led to the dosage recommendation of 5 mg once daily i.v. or orally for up to 7 days. In order to assess whether the pharmacokinetic profile in children is comparable to those in adults we conducted a pharmacokinetic study in children receiving emetogenic antitumour chemotherapy.

In 3 participating paediatric centers, three dosages were tested in two age groups (A: 3 - 6 years, 2 mg/m², 5 mg/m², 20 mg/m²; B: 7 - 15 years, 2 mg, 5 mg, 20 mg). The study was conducted over 2 chemotherapy courses. In the first course, children received the assigned TRO dose as short i.v. infusion on the day before start of chemotherapy or on day 1 of the cycle. 9 blood samples (2 ml each) were drawn over 24 hours. To assess tolerability and antiemetic efficacy of the oral administration, treatment was continued for up to 6 days with the identical dose once daily orally. In the second study course, children received the same TRO dose p.o for pharmacokinetic testing. Apart from that, the procedure was repeated in an identical manner.

Clinical and pharmacokinetic data will be presented.

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TISSUE-EQUIVALENT DOSIMETRIC PHANTOMS FOR QUALITY ASSURANCE IN RADIOLOGY AND ROENTGENOLOGY.

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The elaborated and produced phantoms are succesfully used to solve the following problems:
-for measuring doses to organs and tissues, including sick organs and surrounding tissues;,
-for precising realization of planned absorbed dosesin radiotherapy;
-for evaluating professional exposure of radiation workers;
-for evaluating efficiency of the protective devices.
Radiosensitiveness of child's tissues is much higher. Besides, as the size of the child's body is small, the vitally important child's organs are affected by the action of radiation more often than those of the adult. Radiation safety of different population categories (especially children) is going to be a serious social problem not only for the country, but also of worldwide importance.

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IMPLICATIONS OF CHEMOTHERAPY IN THE RESULTS OF LOCAL TREATMENT IN EWING'S SARCOMA (EW)

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INTRODUCTION : We operated 72 patients (p.) with EW and precise the value, the possibilities and indications of surgical treatment in EW. MATERIAL & METHODS : From 79 to 91, we treated 72 ES by surgery (other than biopsy), for local relapse following radiotherapy (RT)(21 p),mechanical complication (3 p) failure of induction CT (6 p), or systematic surgery (42 p). Locations were central : 26 (9 iliac, 5 ribs, 7 vertebraes, 4 skulls, 1 cranial), were limbs : 46 (femur 23, tibia 11, humeral 5, fibula 4, radial 2, finger 1). Metastases were detectable in 20 p. Surgery performed debulking (15), complete but contaminated resection (7), en bloc extratumoral resection (50). All p. were treated by CT adapted to the prior treatment and actual protocol. Median FU is 65 m. RESULTS : Survival depends mostly on circumstances of 1st consultation in our center. All p. referred for local relapse after RT died from metastases in a median time of 18 m. (3-50). 4 out of 6 operated for progression died also. In the contrary, 32 out of 42 systematically operated are DFS. Among them 24 out of the 33 included in DD2 and DD21 (out of the 24, 17 out of 19 children) are in EFS. The risk of local relapse is correlated with type of surgery and effectiveness of CT. 6 out of 7 local relapses were seen after RT following intratumoral surgery. No local relapse was observed in p. included in our protocols. RT and CT with or without surgical debulking leads to 30% local relapses followed always by death. CONCLUSIONS : Surgical treatment of EW must be en bloc resection, combinated with pre, peri and postop CT.

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EXCISION OF THE HUMERAL TUMORS IN CHILDREN WITH THE ROTATED CLAVICLE RECONSTRUCTION.

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The application of intensive comprehensive therapy enabled salvage surgery in bone tumors. Reconstruction of the removed part of bone is the great problem, especially in fast growing children. In 2 patients /H.M., 13 yrs 4 mos, osteosarcoma; B.M., 12 yrs 2 mos, Ewing's sarcoma/, the tumor was confined to the proximal half part of humerus, without invasion of shoulder joint. After induction chemotherapy, reduction of tumor size was observed both clinically and radiologically /plain film, scintigraphy and CT/. During operation the broad resection of the tumor together with humerus of 12 cm long fragment, was performed. Afterwards the clavicle was rotated in the place of removed bone, without destruction of brachial ligaments. Humeral stump and clavicle were fixed with the use of metal plate. Adjuvant chemotherapy was used in few days following surgery. After 3 months the connection healed. The movements in shoulder joint are limited, but functions of elbow joint remained normal. Both children are alive and disease free, 1yr and 6 mos respectively.