CPh 12

EVALUATION OF THE ANTIFOLATES 8-DEAZA-METHOTREXATE AND 8-DEAZA-AMINOPTERIN IN COMPARISON TO MTX AND AMINOPTERIN

Michael Kühl

Methotrexate (MTX) and aminopterin are both subject to hydroxylation at the 7-position of the pteridine ring. This is of considerable clinical importance as by 12 h after MTX the levels of 7-OH-MTX can be 10-20 times higher than those of the parent compound. The 7-OH-metabolite is 100-1000 fold less effective, but competes with MTX for transport into the cells. The 8-deaza-analogues of MTX and aminopterin are not hydroxylated at the 7-position. This could be demonstrated by incubating the compounds with partially purified rabbit liver aldehyde oxidase, an enzyme that converted the same amounts of MTX or aminopterin under the same conditions quantitatively to the 7-OH-metabolite. In comparison to their parent compounds, the potential of growth inhibition in cell cultures was found slightly increased (1.5 fold) for both 8-deaza-analogues. Also the in vivo treatment of L1210 and P388 leukemia in BDF1 mice showed a 40-80% increased survival time with 8-deaza-aminopterin as compared to aminopterin. Uptake studies with the respective radioactive compounds showed similar transport characteristics (K_m and V_{max}) for the parent compounds and the 8-deaza-analogues. The data indicate that the 8-deaza-analogues of aminopterin and MTX are not hydroxylated to the less effective 7-OH-forms. The analogues are more effective at a lower dosage than the parent compounds. Pharmacology Dept., St. Jude Children's Res. Hospital, 332 N. Lauderdale, Memphis, TN, 38101, USA.

BTh 01

RADIATION PROTECTION, EQUIPMENT AND QUALITY ASSURANCE IN BRACHYTHERAPY

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Brachytherapy can be classified in terms of the dose-rate into three categories: high-, medium and low dose-rate treatments. Because of the very different dose-rates which vary by a factor of 10 to 100 between the various treatment modalities completely different radiation protection problems arise. Also the demand of the equipment is quite distinct. Common to all of them is the need for a full quality assurance program.

a) High dose-rate brachytherapy

Because of the high dose-rates used the treatment has to be performed in a remote afterloading technique. Radiation protection of the personnel is achieved by a shielded treatment room. The demand for the equipment is highly sophisticated and has to fulfill DIN 6853.

Treatment planning is complicated because of the short duration of the whole procedure and has to be performed in advance. The use of templates for interstitial treatments is indicated.

b) Medium dose-rate brachytherapy

From the radiation protection point of view this kind of therapy gives the biggest problems. Although the dose-rates around the patient is quite moderate the staff has to spend some time close to the patient for care purposes. Manually afterloading permits an exact therapy planning and a reduction of radiation exposure to the operating staff.

c) Low dose-rate brachytherapy

Mainly J-125-seeds are used for this purpose. The dose-rates in 1 m distance of the patient are in the range of 0,5 - 5,0 uSv/h depending on the amount of activity applied and its position within the patient. The very low kV-radiation of J-125 can easily be shielded. In case of discharging or death certain regulations have to be regarded. Using seeds in carriers, resolvable planar gelatine allows to improve the dose distribution in comparison with simple methods.

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BTh 02

PHYSICAL AND RADIOBIOLOGICAL BASIS OF THE COMBINATION OF INTERSTITIAL AND PERCUTANEOUS RADIOTHERAPY

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The combination of the brachy-therapy and teletherapy makes necessary some considerations in relation to localization, volume-factor, time-factor, dose-weighting, and superposition of effective doses.

While the medical localization of the tumour, the physical calculation of the dose distributions, and the spatial fitting of them can be managed fairly exactly, assisted by CT if possible, the biological weighing of the dose after different therapeutic regimes still makes problems.

Our thesis is, that all dose-effect-relations the radiotherapists are using today are proper for dose rates down to 30 rd/h only. In case of the application of lower dose rates - e.g. I-215 or Ir-192 permanent implants - the cell or tumour kinetics have to be taken into account. The treatment over more and more cell cycles enhances the biological effectiveness, which can be shown by an experimental based mathematical system.

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BTh 03

FIRST EXPERIENCES IN BRACHY-CURIETHERAPY OF HEAD AND NECK TUMORS WITH 125 J-SEEDS IN CARRIER AND 192 Ir-AFTERLOADING SYSTEM

W.Schwab and G.Ries

Prognosis of locally advanced head and neck carcinomas is poor despite the use of aggressive surgical resection and/or radiation treatment. Due to local extension and frequent regional spread, recurrences especially concerning tumors of the naso- oro- and hypopharynx as well as the oral cavity (oral tongue, floor of the mouth) are an important cause of treatment failure. The results of retreating local recurrences following surgery and/or external radiation therapy are even poorer than in primary treatment.

Apart from surgery, external radiotherapy or chemotherapy, interstitial radioactive implants may be indicated in case of relapse, even if such patients are irradiated for palliation rather than for curative purposes. This method enables the delivery of a high dose to a limited volume without unacceptable toxicity to neighboring structures. For treatment we used either low-dose-rate 125 J-seeds in carrier (Vicryl) or the high-dose-rate 192 Ir-afterloading system. Regarding radiation protection the afterloading technique is superior for the medical staff. For most of our patients at least a partial regression of the tumormass could be observed combined with improvement of symptoms. However the follow-up was short since most of the patients died within several months of the treatment. Nevertheless interstitial radiotherapy offers good palliation for patients with recurrent head and neck cancer and may also be useful in the definitive management of locally advanced disease as adjunct to external radiation therapy.

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