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Contributors

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1968

'ALKERAN'

for the treatment of
multiple myeloma, malignant
melanoma, and certain other
malignant conditions

'ALKERAN'

brand Melphalan

'Alkeran' (melphalan) (Compound CB 3025), a derivative of nitrogen mustard, was first synthesised in 1953 by Bergel and Stock. It is chemically *p*-di(2-chloroethyl) amino-L-phenylalanine, with the following structural formula:

'Alkeran' is the L-isomer of this phenylalanine mustard.

The compound is active against a number of animal tumours, including Walker 256, I.R. C-741 leukæmia, T–8 Guerin epithelioma, Flexner-Jobling carcinoma, Ehrlich carcinoma and S. 91 melanoma. It proved to be effective also against a suspension culture derived from a human melanoma.

Pharmacology and Toxicity

'Alkeran' has the general pharmacological properties of nitrogen mustard compounds. It is well absorbed by the oral route, both in animals and in man. Administered in arachis oil the LD_{50} in rats by the intraperitoneal route is 11·8 mg. per kg. bodyweight. The main toxic effects in animals are weight loss and depression of the blood-cell forming tissues. Toxic changes also occur in the gastro-intestinal tract; intestinal hyperæmia and hæmorrhages were noted in rats, monkeys and dogs, while diarrhœa was observed in rats and monkeys. Bodyweights and food intakes were decreased. In man, single doses of 25 mg. or more of 'Alkeran' given orally or intravenously occasionally caused mild nausea and vomiting. The effects on the bone marrow are similar to those observed in animals, and the blood count (especially neutrophil and platelet counts) must be watched carefully during treatment.

Indications

The most important indication for the use of 'Alkeran' is in the treatment of multiple myeloma. Very encouraging results appear to have been obtained in the treatment of malignant melanomas and certain other tumours by the isolated perfusion technique. Among tumours which are stated to have shown response to one or other of the nitrogen mustard derivatives are generalised seminoma of the testis, reticulum cell sarcoma, Hodgkin's disease, fibrosarcoma, Kaposi's sarcoma and neurofibrosarcoma.

When cytostatic drugs are used in pregnancy, the possible effect on the foetus should be kept in mind. It is therefore advisable to delay treatment with these drugs as long as possible, and certainly until after the first three months of pregnancy.

Administration and Dosage

Oral

For oral administration, 'Alkeran' may be given in a dosage of 10 mg. daily for seven days (total dose 70 mg.). Do not give another course unless the blood counts, especially the neutrophil and platelet counts, have recovered. If counts are satisfactory, give a further course and

repeat in this way for an indefinite period. Some workers prefer continuous therapy with daily doses between 2 and 4 mg. This method requires even closer attention to the blood count.
In some cases of hypercalcaemia, and in the presence of high blood urea, rapid resolution has followed the use of melphalan, but the toxicity of the drug is enhanced in the presence of uraemia. The use of lower doses and more frequent blood counts is recommended.

Intra-arterial perfusion

Administration of 'Alkeran' by intra-arterial perfusion involves circulating a relatively high dose (i.e., 70-100 mg.) of the drug through the part of the body affected by the tumour. This part should be isolated by operation from the rest of the body and be provided with a separate circulation by means of pumps and oxygenator. Depending on the response of the patient, perfusion may be repeated a second or possibly a third time. 'Alkeran' is regarded by some workers as the drug of choice for perfusion; especially in the treatment of melanomas. Its half-life in blood at 37°C. is about 105-120 minutes, whereas the half-life of nitrogen mustard (HN_2) is about 14 minutes under similar conditions, but can vary considerably. Details of the perfusion technique, including dosages used, will be found in the literature.

Intravenous

For intravenous administration, single doses of 1 mg./kg. have been used. This causes considerable depression of platelet and neutrophil counts. The counts usually return to normal limits in eight weeks after which a further dose may be given.

Presentation

'Alkeran' BRAND **Melphalan**

Tablets: 2 mg. and 5 mg., each in bottles of 25.
Injection: Vials containing the equivalent of 100 mg. sterile anhydrous melphalan, with 1 ml. 'Wellcome' brand Acid-Alcohol Solvent for 'Alkeran' and 9 ml. 'Wellcome' brand Diluent for 'Alkeran'.

'Alkeran'
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