



The Pharmacology of Cytotoxic Agents and its Uses in Cancer

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INTRODUCTION

Cytotoxic agents are the drugs that are toxic to the cells and affect their metabolism and replication, they are mostly used in the treatment of cancer in order to stop or destroy the ability of the cells to replicate and divide invasively. The Cytotoxic agents are classified into many subclasses based on their mechanism of action.

DESCRIPTION

The first one are the Alkylating agents which include nitrogen mustards like Chlorambucil, Cyclophosphate; ethylonimines like thiotepa; Alkyl sulphonates like Busulfan; Triazines like Dacarbazine, Temozolamide; Nitroureas like Carmustine and Lomustine; Hydrazines like Procarbazines. The alkylating agents act by producing a carbonium ion which gets transferred or substituted in the place of alkyl groups which in turn leads to the cross linkage of the DNA and inhibits DNA synthesis and finally leads to the cell death. The adverse reactions of the alkylating agents are bone marrow toxicity, haemorrhagic cystitis, pulmonary fibrosis, alopecia, immuno-suppression. They are mostly used in the treatment of neoplasma.

The next are the Platinum Co-ordination complexing agents. Cisplatin and carboplatin come under this class. They act by binding to the cell and form a co-ordination complex which in turn causes inhibition of DNA synthesis leads to cell death. These drugs are absorbed by oral route, metabolized in the liver and excreted through renal tubular secretion. They are mostly used in the Neoplasmas, acute leukaemia and carcinoma.

The other class is the Anti-metabolites which include Folate antagonist, Purine antagonist, Pyrimidine antagonist. The ex-

ample of folate antagonist is Methotrexate. The drug inhibits the dihydrofolate reductase which inhibits the formation of tetrahydrofolate from the dihydrofolate and inhibits the DNA synthesis. It is orally well absorbed, can be also given as IV And IM, metabolized in the liver by polyglutamates and excreted by kidney. The side effects include nephrotoxicity, allergic pneumonitis, encephalopathy. Salicylates, sulfonamides, and probencid inhibits the renal secretion of the drug. Methotrexate is mostly used in the treatment of carcinoma acute leukaemia, sarcoma, breast cancer, rheumatoid arthritis and psoriasis.

The example of Purine antagonist is 6 Mercaptopurine. It acts by converting into an active metabolite like triphosphate and incorporates into DNA and inhibits the DNA synthesis. The adverse drug reactions include bone marrow depression, anorexia, nausea, vomiting, jaundice and dermatitis. It is used in the treatment of acute leukaemia in children, carcinoma and solid tumour. The Mercaptopurine must not given with Allopurinol. 5 Fluro Uracil is the example of Pyrimidine analogies. These pyrimidine analogues get converted into active metabolites which are later incorporated into the and finally leads to the inhibition of the DNA synthesis which causes cell death.

CONCLUSION

They are majorly used in the treatment of acute leukaemia, acute lymphocytic leukaemia, breast and ovarian cancer and lung cancer. The side effects of the drug include bone marrow depression and flu syndrome. Other than cytotoxic agents there are also different classes of agents like microtubule damaging drugs, topo-isomerase 2 inhibitors, antibiotics, anti-hormonal drugs which are used in the treatment of cancer by the chemotherapy.

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