

Cancer drugs classification pdf

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Home Health & Medicine Medicine Just like scalpels, lasers, and electric currents are used in surgery, the weapons used to fight cancer in chemotherapy are a host of anti-cancer drugs. How differently these drugs kill cancer cells, or prevent them from dividing, depends on their classification. Drugs in the same class kill cancer cells by the same mechanism; they all attack the same target within the cell. Depending on the type of cancer and the kind of drug used, chemotherapy drugs may be administered differently. They can be administered orally (oral chemotherapy), or injected into a muscle (intramuscular injection), injected under the skin (subcutaneous injection), or into a vein (intravenous chemotherapy). In special cases, chemotherapy drugs may be injected into the fluid around the spine (intrathecal chemotherapy). Two or more methods of administration may be used at the same time under certain circumstances. No matter what method is used, chemotherapy drugs are absorbed into the blood and carried around the body. Of all the methods of chemotherapy drug administration mentioned above, intravenous injection is most commonly used. It is the most efficient way to get the medication into the bloodstream. Oral chemotherapy is more convenient and does not require any specialized equipment. In chemotherapy, cancer patients may be given one or several drugs from the available anti-cancer drugs. Since different chemical agents damage cancer cells in different ways and at different phases in the cell cycle, a combination of drugs is often employed to increase the cancerous cell-killing effectiveness. This is called combination chemotherapy. Listed below are several major categories (classes) of chemotherapy agents based on their chemical structures and the way they act on cancer cells: Alkylating agents Alkylating agents were among the first anti-cancer drugs and are the most commonly used agents in chemotherapy today. Alkylating agents act directly on DNA, causing cross-linking of DNA strands, abnormal base pairing, or DNA strand breaks, thus preventing the cell from dividing. Alkylating agents are generally considered to be cell cycle phase nonspecific, meaning that they kill the cell in various and multiple phases of the cell cycle. Although alkylating agents may be used for most types of cancer, they are generally of greatest value in treating slow-growing cancers. Alkylating agents are not as effective on rapidly growing cells. Examples of alkylating agents include chlorambucil, cyclophosphamide, thiotapec, and busulfan. Antimetabolites Antimetabolites replace natural substances as building blocks in DNA molecules, thereby altering the function of enzymes required for cell metabolism and protein synthesis. In other words, they mimic nutrients that the cell needs to grow, tricking the cell into consuming them, so it eventually starves to death. Antimetabolites are cell cycle specific. Antimetabolites are most effective during the S-phase of cell division because they primarily act upon cells undergoing synthesis of new DNA for formation of new cells. The toxicities associated with these drugs are seen in cells that are growing and dividing quickly. Examples of antimetabolites include purine antagonists, pyrimidine antagonists, and folate antagonists. Plant alkaloids Plant alkaloids are antitumor agents derived from plants. These drugs act specifically by blocking the ability of a cancer cell to divide and become two cells. Although they act throughout the cell cycle, some are more effective during the S- and M-phases, making these drugs cell cycle specific. Examples of plant alkaloids used in chemotherapy are actinomycin D, doxorubicin, and mitomycin. Antitumor antibiotic Antitumor antibiotics are cell cycle nonspecific. They act by binding with DNA and preventing RNA (ribonucleic acid) synthesis, a key step in the creation of proteins, which are necessary for cell survival. They are not the same as antibiotics used to treat bacterial infections. Rather, these drugs cause the strands of genetic material that make up DNA to uncoil, thereby preventing the cell from reproducing. Doxorubicin, mitoxantrone, and bleomycin are some examples of antitumor antibiotics. One of the most important decisions for the oncologist is prescribing the right amount of anti-cancer drugs. Although large doses will kill more cells, greater amounts of drugs will produce more severe side effects. However, lowering the dosage to minimize side effects will also reduce the chances of success. The usual practice is to use the maximum safe dose for effectiveness, even at the cost of temporary side effects. The following section will discuss some common side effects caused by anti-cancer drugs and ways to cope with them. • Previous (Chemotherapy)Next (Side Effects) • 1. Anticancer drugs Dr. S. Parasuraman Faculty of Pharmacy, AIMST. 2. Anticancer drugs • The anticancer drug either kill cancer cells or modify their growth. • Discovery of anticancer agents started after 1940's (when nitrogen mustard was used) • Most of the agents were discovered in 1950-1970. • Cancer treatment: - Chemotherapy - Immunotherapy - Radiotherapy - Surgery 3. Cellular Pathways to Malignancy 4. Aim of the cancer therapy - Cure or prolong remission - Palliation - Adjuvant chemotherapy • Cure or prolong remission • Primary treatment modality for Acute leukemias (in children) Choriocarcinoma Wilm's tumour (in children) Hodgkin's disease Ewing's sarcoma (in children) Lymphosarcoma Retinoblastoma (in children) Burkitt's lymphoma Rhabdomyosarcoma (in children) Testicular teratomas, Seminoma 5. Aim of the cancer therapy • Palliation - Life prolong by chemotherapy: Breast cancer, Ovarian carcinoma, myeloma, prostatic carcinoma, chronic lymphatic leukemia, chronic myeloid leukemia, non-Hodgkin lymphomas, head and neck cancer and lung (small cells) cancer - Life prolong by chemotherapy: Colorectal carcinoma, carcinoma pancreas, carcinoma stomach, carcinoma esophagus, renal carcinoma, malignant melanomas, bronchogenic carcinoma (non small cells), hepatoma and sarcoma. 6. Aim of the cancer therapy • Adjuvant chemotherapy: - Drugs used to clear residual malignant cells (micrometastases) after surgery / radiotherapy. Adjuvant chemotherapy may achieve apparent cure (especially in early breast, lung and colon cancer) 7. Therapeutic effect of anticancer agent • Cancer arise form a single malignant cell, the therapeutic goal of cancer chemotherapy may require "total tumour cell kill" • Achievement of a therapeutic effect by combination therapy. • Therapeutic effect achieved by killing actively "growing tumour cells". • Anticancer agents should act only at "specific stages in the cell cycle" (the S phase and M phase). 8. Classification of anticancer agents • Major class of drugs A. Cytotoxic drugs B. Targeted drugs C. Hormonal drugs 9. Classification of anticancer agents Cytotoxic drugs 1. Alkylating agents 2. Platinum coordination: Cisplatin, Carboplatin, Oxaliplatin 3. Antimetabolites 4. Microtubule damaging agents: Vincristine, Vinblastine, Vinorelbine, Paclitaxel, Docetaxel 5. Topoisomerase-2 inhibitor: Etoposide 6. Topoisomerase-1 inhibitor: Topotecan, Irinotecan 7. Antibiotics: Actinomycin D, Doxorubicin, Daunorubicin, Epirubicin, Bleomycin, Mitomycin C 8. Miscellaneous: Hydroxyurea, L-Asparaginase, Tretinoin, Arsenic trioxide 10. Classification of anticancer agents Targeted drugs 1, 2, 3, 4, 5. Tyrosine protein kinase inhibitors: Imatinib, Nilotinib EGF receptor inhibitor: Gefitinib, Erlotinib Angiogenesis inhibitors: Bevacizumab Proteasome inhibitor: Bortezomib Unarmed monoclonal antibody: Rituximab, Trastuzumab 11. Classification of anticancer agents Hormonal drugs 1, 2, 3, 4, 5, 6, 7, 8, 9. Glucocorticoids: Prednisolone Estrogens: Fosfostrol, Ethynodiol Selective estrogen receptor modulators: Tamoxifen Selective estrogen receptor down-regulators: Fulvestrant Aromatase inhibitors: Letrozole, Anastrozole Antiandrogen: Flutamide 5-a-reductase inhibitor: Finasteride GnRH analogues: Nafarelin, Triptorelin Progestins: Hydroxyprogesterone acetate 12. General Principles in chemotherapy of cancer • Single clonogenic malignant cell is capable of producing progeny that kill the host. To effective cure, all malignant cells must be killed. • The proliferation rate of cancer cell is differ from normal cell. The cytotoxic drugs kill cancer cell by first order kinetics. • Combined modality approach can be used for cancer therapy. • Poly pharmacy can be used for achieve "total tumour cell kill". 13. General Principles in chemotherapy of cancer - cell cycle specific kill only actively dividing cells. • G1: Vinblastine • S: Mtx, cytarabine, fludarabine, G-CG, 6-MP, 5-FU, hydroxyurea, mitomycin C, doxorubicin, daunorubicin • G2: Daunorubicin, bleomycin, etoposide, topotecan • M: Vincristine, vinblastine, vinorelbine, paclitaxel, docetaxel 15. 6-Mercaptopurine 6-Thioguanine Methotrexate Summary of MOA and site of action of chemotherapeutic agents Purines and pyrimidines Inhibit purine ring synthesis Ribonucleotides Hydroxyurea Inhibit ribonucleotide reductase Inhibit dTMP synthesis Methotrexate 5-Fluorouracil Deoxyribonucleotides Cytarabine Bleomycin Doxorubicin Dactinomycin DNA Scission of DNA Intercalate DNA Alkylating agents Nitrosoureas Cisplatin L-Asparaginase Vinca alkaloids Paclitaxel Colchicine Inhibit DNA synthesis Cross-link DNA RNA Inhibit protein synthesis Proteins Inhibit microtubule function Protein tyrosine kinase inhibitor microtubules Block activity Enzymes 16. General toxicity of cytotoxic drugs 17. • Cytotoxic drugs have more profound effect on rapidly multiplying cells, because its targeting action in nucleic acid and there precursors. • Bone marrow: Depression of bone marrow results in granulocytopenia, agranulocytosis, thrombocytopenia, aplastic anaemia. • Lymphoreticular tissue: Lymphocytopenia and inhibition of lymphocyte function results in suppression of cell mediated as well as humoral immunity. • Oral cavity: Stomatitis, neutropenia, thrombocytopenia • GIT: Diarrhoea, shedding of mucus, haemorrhages, Nausea and vomiting • Skin: Alopecia (due to damage of cells in hair follicles) • Gonads: Oligozoospermia in males; amenorrhoea in females. 18. • Foetus: Cytotoxic agents causes abortion, foetal death, teratogenesis in pregnant women. • Carcinogenicity: Secondary cancers, especially leukaemias, lymphomas and histiocytic tumours appear with greater frequency many years after the use of cytotoxic drugs. • Hyperuricaemia • Individual drugs may produce specific adverse effects, e.g. neuropathy by vincristine, Cardiomyopathy by doxorubicin, cystitis and alopecia by cyclophosphamide. 19. Thank you

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