

Chemotherapy and its Applications

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Research Article

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ABSTRACT

Chemotherapy is the treatment of cancer with drugs or chemicals that destroys cancer cells. If it is not treated on time you have many complications like Nausea and vomiting which are the most feared side effects of cancer. Based on the occurrence of Chemotherapy can be categorized into three types such as acute, delayed, or anticipatory. If protection during the early stages is not done, you will be a cancer patient. The 5-HT₃-receptor is regarded as the 'gold standard' in antiemetic therapy. The first-line treatment for moderately and highly emetogenic chemotherapy and radiotherapy started in adults and children. The prophylactic use of the most effective antiemetic drugs taken must be adhered in order to prevent nausea and vomiting.

INTRODUCTION

Chemotherapy is the treatment of cancer with drugs or chemicals that destroys cancer cells. These drugs are commonly called as "anticancer" drugs. Chemotherapy includes a variety of drugs and their mode of action is as follows:

1. Intravenous chemotherapy: Drugs that are given into the bloodstream.
2. These drugs can be given over minutes or hours called an infusion.
3. Drugs are also given slowly and continuously over several days using a pump. This is called a continuous infusion.
4. Oral chemotherapy: Drugs that are taken by mouth as pills or liquids.
5. Intra-cavitary chemotherapy: Drugs that are placed directly into a body area.
6. Drugs that are placed on the skin as creams.

Pre-chemotherapy

Chemotherapy during Pregnancy

As we know that some cytotoxic medicines reduce fertility. If you are physically and mentally active pregnancy is possible. Cytotoxic medicines can damage sperm, eggs and an unborn baby so it is not advisable if a woman is pregnant and going for chemotherapy. If you are active and confident then you use reliable contraception to avoid pregnancy. Regular communication with your doctor and check up may be useful [1-10].

Chemotherapy works by inhibiting the rapid cell growth and multiplication. It harms the adjacent healthy cells and cause side effects. Chemotherapy is done along with surgery followed by radiation or biological therapy and can be easily destroyed called neo-adjuvant chemotherapy. It destroys cancer cells which remain after surgery or radiation called adjuvant chemotherapy. Cryotherapy kills cancerous cells within the prostate. It is not widely used because of less information about its long-term effectiveness. It's less invasive than surgery and has a short recovery time. Cryosurgery leads to nerve damage causing impotency in men. There will be a temporary pain and burning sensation in the bladder and bowel.

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Types of chemotherapy agents and regimens

The origin of anthracyclines are anticancer compounds are from Streptomyces and their anti-tumor activities which were established in 1960s. Anthracyclines are red aromatic polyketides which occur in variety of forms due to the structural orientation in the aglycone and the attached sugar residues. These are also called as Anti-tumor antibiotics [11-21].

MAJOR DRUGS IN THE CLASS

Daunorubicin

It was the first anthracycline derivative to be characterized structurally and stereo-chemically. It is also used in treating acute lymphoblastic and myeloblastic leukaemias.

Doxorubicin

Doxorubicin is one of the most commonly used chemotherapeutic agent in combination with other drugs. Doxorubicin is a broad spectrum drug and is an effective drug against solid tumors (e.g., breast, lung and ovarian cancer). Its mode of action is against bladder, stomach, liver, thyroid tumors etc. It is also active against multiple myelomas, leukaemia and cutaneous lymphomas. Only two anthracycline analogs, epirubicin and idarubicin are for clinical use [22-40].

Epirubicin

It is an epimer of doxorubicin. It has less cardiotoxic than doxorubicin. Epirubicin is used for the cancer treatment and soft tissue sarcomas.

Idarubicin

It is similar to daunorubicin and lacks the C-4 methoxy group which increases its lipophilicity.

Valrubicin

Valrubicin is a derivative of doxorubicin and has a rapid entry at the cancer site. It is specifically used for the treatment of early stage bladder cancer.

The other types of chemical drugs are

1. Alkylating agents: DNA damage
2. Antimetabolites: DNA substitution
3. Topoisomerase inhibitors: DNA separation
4. Mitotic inhibitors: inhibit mitosis of the cell cycle
5. Corticosteroids: Anti-inflammatory
6. Alkylating agents mode of action is DNA damage and inhibit phases of cell cycle not allowing the cell from reproducing. They are of 5 types: Nitrogen mustards, Nitrosoureas, Alkyl sulfonates, Triazines, Ethylenimines [41-50].
7. Antimetabolites mode of action is by interfering with the DNA and RNA strands. Some of them are: 5-fluorouracil, 6-mercaptopurine, Capecitabine, Cytarabine, Floxuridine, Fludarabine etc.
8. Topoisomerase inhibitors: The enzymes that inhibit DNS separation are called as Topoisomerase inhibitors. They are useful to treat leukemias, lung and Ovarian cancer. These are of two types Topoisomerase I and Topoisomerase II.
9. Mitotic Inhibitors are of alkaloids and derivatives of natural plant products. Some of the eg are: Taxanes, Epothilones, Vinca alkaloids and Estramustine. The main side effect of this drug is nerve damage leading to impotency.
10. Corticosteroids: Steroids or Steroidal hormones which come under synthesized drugs. These are the chemotherapeutical drugs synthesized in the human body. Some eg are: Prednisone,
11. Methylprednisolone and Dexamethasone. They are useful in treating allergic reactions which are the side effects after chemotherapy.

MODE OF ACTION

The anthracycline mode of action for cancer inhibition is not yet clear. A recent study revealed that the anthracyclines inhibit transcriptional factor HIF-1 by binding to DNA in hypoxic human cells and inhibit tumor growth in human prostate cancer xenografts. Anthracyclines inhibits cell growth through antiangiogenic pathways [51-70].

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Cytotoxic medicines work only on the cancer cells that are rapidly growing. Normally, cells in the body, such as muscle, heart, brain and bone cells do not rapidly divide and multiply. Normal cells are not affected by cytotoxic medicines. Cells in the body which rapidly divide and multiply are called cancerous or tumor cells (for eg: hair and bone marrow). They may be affected by cytotoxic medicines causing side-effects. Generally, normal cells have regeneration capacity than cancerous cells which usually recover after cancer treatment. They enter the cells through diffusion due to cell permeability. Kiyomiya and colleagues proposed the selective transport mechanism of anthracyclines proliferating neoplastic cells. It has been demonstrated with doxorubicin that once it enters the cell, it binds the cytoplasmic proteasomes for high affinity.

DNA INTERCALATION

Anthracyclines cytotoxic nature is due to intercalation of DNA leading to inhibition of synthesis of macro molecules. The characteristic feature of Daunorubicin and Doxorubicin drug is it binds strongly to DNA. It is observed with other anthracyclines that the antitumor activity link with a decrease in DNA affinity. DNA interaction is done by intercalators called Ligands [71-85]. They are polycyclic, aromatic and planar in nature. Low concentrations of doxorubicin have selective displacement of nuclear proteins and chromatin induction. This involves drug intercalation where the DNA is free of nuclear proteins which leads to the structural changes such as unfolding of chromatin aggregation.

ANTHRACYCLINE CYTOTOXIC ACTIVITY

It interacts by regulating the gene expression by inhibiting or promoting the binding of transcription factors. It plays a role in anthracycline cytotoxicity and involvement of SP-1 transcription factor as drug specificity. It involves in inhibiting DNA synthesis by affecting the initiation phase, elongation phase and RNA synthesis by inhibiting the enzyme RNA polymerase. The anthracycline acts as Topoisomerase II poisons. It plays a role in stabilizing the complex between Topoisomerase II and the nicked DNA. The DNA nicks cannot be sealed and this leads to an accumulation of DNA damage that is cytotoxic due to growth arrest in G1, G2 and apoptosis. Doxorubicin and Idarubicin inhibit Topoisomerase I of cytotoxic activity of anthracyclines.

CLINICAL ANALYSIS

Doxorubicin is a genotoxic agent and has been shown to induce the binding of p53 to DNA. As p53 is a major substance in some form of apoptosis, anthracyclines may exert their cytotoxic effect via p53 mediated apoptosis. It has been seen that there are more DNA breaks in p53 cells. It is proposed that p53 exerts this activity by ligating to Topoisomerase II which inhibits its ligase activity. Chemotherapy is a treatment process that uses powerful chemicals to kill fast and rapidly growing cells in your body. Chemotherapy is most often used to treat cancer as cancer cells grow and multiply much more quickly when compared to other cells in the body. Many different chemotherapeutic drugs are available. Chemotherapy drugs can be used alone or in combination to treat a wide variety of cancers. Though chemotherapy is an effective way to treat many types of cancer, it also carries side effects. Some chemotherapy side effects are mild and are treatable, while others can cause serious complications [86-95].

Chemotherapy given orally

Chemotherapeutic medicines or drugs can be taken orally in the form of tablets or liquids which are readily absorbed in the bloodstream.

Free Radical Generation

The semiquinone oxidizes the bond between ring A and daunosamine resulting in deglycosylation. The aglycone formed has higher lipid solubility and can intercalate into biological membranes which affects the sensitive targets. The redox cycle of doxorubicin has been introduced to induce the release of iron from the stores. Doxorubicin forms an iron complex and is capable of releasing hydroxyl ions. Anthracycline activity involves in oxidative damage. The production of reactive oxygen is predominantly observed at supra clinical concentrations which is not the main mechanism of anthracycline activity.

Side effects and its cure

Various strategies are going on to prevent the cardiotoxicity of anthracyclines are also being employed which changes the drugs administration, dosage limitation, liposomal encapsulation, treatment combination, use of

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cardio protectors and production of modified anthracyclines. Mild allergic reactions have been reported for anthracyclines. Symptoms of epirubicin are high fever, hypertension and hypoxia. Prolonging side effects vary depending on the chemotherapy drug and includes: Damage to lung tissue, Heart problems, Infertility, Kidney problems, Nerve damage, Risk of a second cancer [96-100].

Some chemotherapy drugs be a cause of infertility (no children). High chemotherapy drugs doses can be dangerous and cause permanent infertility. It is important to tell the risk of infertility with your doctor before starting treatment. Sometimes it is possible for your doctor to suggest treatment which is less likely to cause infertility. Talk to your partner about this clearly. Men before having starting treatment will prefer sperm banking. Pregnant woman can have fertilised embryos for fertility to lead a happy married life. The fertilisation rate for this treatment is low, as researchers are improving it by developing better techniques. Researchers are freezing the ovarian tissue before preferring chemotherapy and later putting the tissue back. This is still in experiment and not widely done. If interested, talk to your cancer specialist about it. There is more about women fertility in this section.

Life after chemotherapy

Majority 90% feel anxious, afraid and depressed about their lives affect after cancer treatment. These feelings may change your daily routine with the painful treatment its side effects and risk of infertility. Many patients feel this during their treatment process which is a common thing but try to overcome this feeling of being afraid or discouraged.

CONCLUSIONS

Doctors invented many new ways to treat chemotherapy side effects. Consult the doctor or nurse and go for regular check up. Regular communication or consultation with the doctors about the changes help to get rid of the side effects.

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