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HYPERSENSITIVITY REACTIONS: TYPES, FEATURES, DIAGNOSIS AND SPECIAL ATTENTION TOWARDS CHEMOTHERAPEUTIC AGENTS AND MANAGEMENT OF REACTION TYPES ON ELDERLY-A REVIEW

Athira K.B.[1], Neethu J.*, Dilip Krishnan K.[2] and Lal Prasanth M.L.[2]

[1]B. Pharm Student, Doctor Moopen's College of Pharmacy, Wayanad, [2]HOD, Department of Pharmacy Practice, *Associate Professor, Department of Pharmacy Practice, Doctor Moopen's College ofPharmacy, Wayanad.

***Corresponding Author: Neethu J.**

Associate Professor, Department of Pharmacy Practice, Doctor Moopen's College of Pharmacy, Wayanad.

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ABSTRACT

Hypersensitivity is described here as an unanticipated reaction with signs and symptoms that are unpredictably associated with the drug's known toxicity. The majority of adverse responses occur within hours of drug delivery. The majority of responses occur concurrently with or within hours following drug administration. Almost all of them are related to parenteral delivery. Flushing, changes in heart rate and blood pressure, dyspnea/bronchospasm, back discomfort, fever, pruritus, nausea, and various forms of rashes are all symptoms. Chemotherapy and radiation therapy have more frequent and severe adverse effects in the elderly than in the young. Elderly people also recover more slowly from therapy. In most cancers, the elderly will respond just aseffectively as their younger counterparts, assuming that the chemotherapy can be administered properly. Thismay be affected by physiological changes in organ function particularly renal and hepatic function. Some malignancies may behave differently in the elderly when compared to younger individuals when treated differently. Clearly, evaluating these reactions through prospective research is problematic. Some reactions may be triggered by non-immune-mediated histamine or cytokine release, as many patients can withstand reexposure after pretreatment with steroids and antihistamine, as well as gradual readministrationof the drug.

1. INTRODUCTION TO HYPERSENSITIVITY REACTIONS

Hypersensitivity is defined here as an unexpected reaction with signs and symptoms not predictable with known harmfulness of the drug. Most reactions are incidental with or within hours of drug administration. Almost all are related to parenteral administration.

Symptoms include flushing, alterations in heart rate and blood pressure, dyspnea and bronchospasm, back pain, fever, pruritus, nausea and all types of rashes. In most cases hypersensitivity reactions are associated with the specific chemotherapeutic drugs.

Hypersensitivity reactions are overstated or unseemly immunologic responses occurring in response to an antigen or allergen.

Figure 1.1: Medical allergy symptoms.

Mainly four types of hypersensitivity reactions occurs

- Type I: mediated by IgE antibodies
- Type II: mediated by IgG or IgM antibodies
- Type III: mediated by immune complexes
- Type IV: mediated by cellular response

Type I, II and III hypersensitivity reactions are known as immediate hypersensitivity reactions because they happen in something like 24 hours of exposure to the antigen or allergen. Immediate hypersensitivity reactions

are mediated by IgE, IgM, and IgG antibodies. These antibodies show the immediate type hypersensitivity reactions.Types IV reactions that happen more than 12 hours after exposure to the allergen, with a maximal reaction time between 48 and 72 hours these reactions are called delayed hypersensitivity reactions.

Type IV hypersensitivity reaction is a cell-mediated reaction that can happen in response to contact with certain allergens resulting in what is called contact dermatitis.Diagnostic procedures in the tuberculin skin test. Certain allergens should be kept away from to treat this condition.

All hypersensitivity reactions may cause different symptoms in the body.Some times it will cause death mainlyin elderly peoples.

2. HISTORY OF HYPERSENSITIVITY REACTIONS

The reaction was developed in 1882 by Robert Koch, however it was only after the 1940s that Landsteiner and Chase proved that the reaction was mediated by the cellular and not the humoral arm of the immune system.

In type I hypersensitivity reactions, there is a history of atopy or a patient suffering from an allergic condition (e.g., bronchial asthma, allergic rhinitis, or food allergy). It may be associated with recurrent infections caused by viruses and bacteria. For instance, bronchial asthma may link to recurrent bacterial pneumonia. Clinically allergic disorders may be accompanied by airway inflammation, wheezing attacks, bronchial hyper- responsiveness, tachycardia, tachypnea, intense itching of the eyes and nose, sneezing, rhinorrhea, dermatitis, and gastrointestinal symptoms. Anaphylaxis, the most severe type of allergy, is clinically characterized by bronchospasm, angioedema, hypotension, loss of consciousness, generalized skin rash, nausea, vomiting, andabdominal cramps among other symptoms.

In type II hypersensitivity reactions, a patient may report multiple blood transfusions, rhesus incompatibility, and drug history. Clinically, it may manifest as autoimmunity, e.g., autoimmune hemolytic anemia (characterized by jaundice), immune thrombocytopenia (characterized by bleeding disorders), and other blood dyscrasia (autoimmune neutropenia). In this type of hypersensitivity, drugs may attach to red blood cells and stimulate the production of anti-red blood cell antibodies or anti-dsDNA antibodies that cause drug-induced systemic lupus erythematosus (SLE).

Type III hypersensitivity reactions may manifest as immune complex-mediated diseases including glomerulonephritis, vasculitis, serositis, arthritis, and skin manifestations of autoimmunity such as malar rash,which is due to photosensitivity. The prevalence of serum sickness has decreased dramatically as animal anti-serum is rarely used to treat or prevent infectious diseases.

Patients disclose many blood transfusions as well as a drug history. There is a history of atopy or a patient suffering from an allergic condition in type 1 hypersensitivity reaction. It could be linked to recurring infectionscaused by bacteria or viruses.

Many ancient Egyptian stories have been embellished over time. Tutankhamen's curse, for example, was made up. This anaphylactic story is no exception.

Menes was the name given to Egypt's first pharaoh (the first king of the first dynasty). Although semi- legendary, this character was based on a native Egyptian who, according to current chronology, ruled around 3100 BC.

The ebony plate discovered at the entrance to his otherwise empty tomb purports to depict a wasp or hornet and was translated by Waddell in 1930 to suggest that Menes died as a result of a wasp sting. Many notable Egyptologists have contested this, and other readings may be more likely. According to the earliest "contemporary" report from a Greek historian, Menes was murdered by a hippopotamus!

As for the rest of the story, Sargon the Great, ruler of Akkad (in modern Iraq), lived in the 27th century BC. His son and successor was Narim-Sin. They were a warlike family, but there is no evidence that there was anycontact with Egypt at this time, warlike or otherwise, 2600 BC is a period of demonstrable stability and prosperity in Egypt, and there was no evidence of war with anyone during this period. There were no foreign invasions of Egypt until the Syropalestinian Hykos rulers of the 17th century BC. (None of these had names like Menes or Sargon.)

The true fate of Menes may never be known. The consensus would seem to be that, in the absence of more factual data, the tale of Menes dying from a bee sting must be considered a myth, and the remainder of the story as told by Ovary is, at best, inaccurate.

3. CLASSIFICATION OF HYPERSENSITIVITY REACTION

Hypersensitivity reactions are the response of the immune system. Hypersensitivity reaction is the result of antigen antibody interaction. Mainly hypersensitivity reactions are in two categories

1. Immediate type hypersensitivity reaction
2. Delayed type hypersensitivity reaction

IMMEDIATE TYPE HYPERSENSITIVITY REACTION

Hypersensitivity reactions are overstated or inappropriate immunologic responses occurring in response to an antigen or allergen. The name immediate reaction because it occurs within 24 hours of exposure to antigen or allergen. Prevalently reactions are mediated by IgE, IgM and IgG antibodies.

Immediate hypersensitivity reactions are again classified into threeType I hypersensitivity reactions

Type II hypersensitivity reactions Type III hypersensitivity reactions

TYPE I HYPERSENSITIVITY REACTIONS

The anaphylactic responses are mediated by IgE antibodies that are produced by immune system in responses to environmental proteins (allergens)such as pollen grains, dust mites, animal danders. These IgE antibodies binds to mast cells and basophils, which contain histamine granules that are released in the reactions and causeinflammation. Type I hypersensitivity reactions can be seen in bronchial asthma, allergic rhinitis, allergic dermatitis, food allergy, allergic conjunctivitis and anaphylactic shock.

Mechanism of anaphylaxis

- Exposure to the first dose causes sensitization in individuals.Then the IgE antibodies are formed.
- Binding of IgE to Fc receptors on mast cells.
- Exposure of mast cell to antigen with cross- linking of IgE-Fc receptor.
- Releasing mediators. It causes degradation.
- It produces signs and symptoms of inflammation.

TYPE II HYPERSENSITIVITY REACTIONS

IgG and IgM mediate cytotoxic mediated responses against the cell surface and extracellular matrix proteins. The immunoglobulins involved in this type of reaction damages cells by activating the complement system or by phagocytosis.

Mechanism of action 3 mechanisms are involved

1. Complement mediated

When the antigen enters into the body and attacks the cell then the antibodies are formed. Then the antibody attacks the antigen. Then the complement proteins are formed. This leads to phagocytosis.

2. Antibody dependent cell mediated cytotoxicity

Antigen attacks the body then that leads to the formation of antibodies .The antibodies that coated the target cell. These antibodies are recognized by the fc receptor that leads to cell destruction.

3. Anti Receptor antibodies

Anti-receptor antibodies disturb the normal function of receptors. For example In myasthenia gravis, antibodiesto acetylcholine receptors are produced in the body which impair neuromuscular transmission.

TYPE III HYPERSENSITIVITY REACTIONS

Type III hypersensitivity or immune complex hypersensitivity reactions are also mediated by IgM and IgG antibodies that react with soluble antigens and form antigen- antibody complexes.the complement system becomes activated and release hemostatic agents that attract neutrophils and cause inflammation with tissue damage.

DELAYED HYPERSENSITIVITY REACTION

Delayed hypersensitivity reactions are cell mediated reactions. Type IV hypersensitivity reactions are caused by intracellular microbial infections or due to chemicals applied on the skin. It causes a mixed cellular reaction involving lymphocytes and macrophages. This reaction is not induced by circulating antibodies but by sensitized T cells which on repeated contact with the same antigen releases cytokines that produce biological effects on leukocytes, macrophages and tissue cells.

4. ETIOLOGY AND EPIDEMIOLOGY OF HYPERSENSITIVITY REACTIONS

Different causes of hypersensitivity reactions are depend on the type of antigen or allergen that triggers this inappropriate immune reactivity. In type I hypersensitivity reactions, the allergens are proteins with a molecular weight ranging from 10 to 40 kDa. These incorporate cats, dust mites, cockroaches, grass, rats, fungi, plants, and drugs. They enhance the production of immunoglobulins

Hypersensitivity reactions are very common. In 15% of the world population will be impacted by a type of allergic reactions during their lives. In the second half of this century, allergic diseases have increased. The causeof the increase is unknown, but it may reflect lifestyle changes, decreased breastfeeding and air pollution. European data estimate that 0.3% of the population will be troubled by anaphylaxis at some points in their lives worldwide epidemiological information of anaphylaxis are scanty and remain unavailable in many countries.

5. TREATMENT AND MANAGEMENT

The treatment of hypersensitivity reactions includes the management of anaphylaxis with intramuscular adrenaline (epinephrine), oxygen, intravenous (IV) antihistamines, support blood pressure with IV fluids, avoid latex gloves and equipment in patients who are allergic, In case of laryngeal edema surgical procedures are followed such as tracheotomy. Allergic bronchial asthma can be treated with inhaled short- and long-acting bronchodilators (anticholinergics) along with inhaled corticosteroids, leukotriene antagonists, use of disodium cromoglycate, and environmental controls. Experimentally, a low dose of methotrexate or cyclosporine and omalizumab (a monoclonal anti-IgE antibody) has been used. Omalizumab is a monoclonal antibody that interacts with the binding site of the high-affinity IgE receptor on mast cells. It is an engineered, humanized recombinant immunoglobulin. Moderate to serious allergic bronchial asthma can improve with omalizumab.

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HYPERSENSITIVITY REACTIONS OF CHEMOTHERAPEUTIC AGENTS

6. Introduction To Chemotherapeutic Agents

Chemotherapeutic agents, also known as antineoplastic agents, are used to directly or indirectly inhibit the uncontrolled growth and proliferation of cancer cells. There are several types of chemotherapeutic agents. Chemotherapeutic agents are classified based on factors like chemical structure and they work to treat cancer. The cell cycle is the process that cells in the body use to grow and divide.in which the chemotherapeutic agents that will cause to prevent the proliferation of cells. And then prevents the uncontrolled growth of cancercells.

Chemotherapeutic agents work by targeting phases in the cell cycle. Since Cancer cells grow and divide more rapidly than healthy cells, they're a good target for these drugs. The specificity of anticancer drugs perform an important role in reducing the severity of side effects associated with the drugs use. Without a doubt, because cancer cells are similar to normal human cells, anticancer agents are generally toxic to normal cells and can cause numerous side effects, some of which are life-threatening. Such side effects include hair loss, sores in the mouth and on other mucous membranes, cardiac anomalies, bone marrow toxicity, and severe nausea and vomiting. The bone marrow toxicities result in anemia as well as in decreased resistance to infectious agents. Permanent infertility can also result. Those adverse effects may require that the drug dosage be reduced or the drug regimen be changed to make the drug tolerable to the patient.

Table 2.1: Based on Cell Cycle.

Alkylating agents	Topoisomerase inhibitors	Antimetabolites	Molecularly targeted	Tubulinbinders	Miscellaneous
Busulfan	Dactinomycin	Cytarabine	Herceptin	Docetaxel	Bleomycin
Carmustine	Daunomycin	Mercaptopurine	Imatinib	Vincristine	Dexamethasone
Cyclophospha	Doxorubicin	Methotrexate	Sunitinib	Vinblastine	Asparaginase
Alkylating agents	**Topoisomerase inhibitors**	**Antimetabolites**	**Molecularly targeted**	**Tubulinbinders**	**Miscellaneous**
mide					
Mechlorethamine	Etoposide	Thioguanine	Tretinoin	Paclitaxel	Prednisone

Table 2.2: Based on cell cycle chemotherapeutic agents are classified into two1.Cell cycle specific agents.

Antimetabolites	Antitumorantibiotics	Epipodophyllotoxins	Taxanes	Vinca alkaloids
cytarabine	Bleomycin	etoposide	docetaxel	Vincristine
6-mercaptopurine		teniposide	paclitaxel	vinblastine
6-thioguanine				vinorelbine

2. CELL CYCLE NONSPECIFIC AGENTS

Table 2.3: Cell Cycle.

Alkylating agents	Anthracyclines	Antitumorantibiotics	Camptothecins	Platinum analogues
Busulfan	Daunorubicin	Dactinomycin	Irinotecan	Carboplatin
Carmustine	Idarubicin	Mitomycin	Topotecan	Cisplatin
Lomustine	mitoxantrone			Oxaliplatin

Cell cycle refers to the series of events that take place in a cell, resulting in the duplication of DNA and division of cytoplasm and organelles to produce two daughter cells. Most cells do not divide constantly and spend a varying amount of time in a quiescent state outside the cell cycle. This phase is known as the Go phase. With this phase neurons, skeletal muscles and cardiac muscle cells increase in bulk through hypertrophy and spend their life time. After Go phase the growth factor is involved.

The four important stages of cell cycle include:

- Interphase
- Prophase
- Metaphase
- Anaphase
- Telophase
- Cytokinesis

What are the different phases of a cell cycle:

The different phases of a cell cycle include:

- Interphase – This phase includes the G1 phase, S phase and the G2 phase.
- M phase – This is the mitotic phase and is divided into prophase, metaphase, anaphase and telophase.
- Cytokinesis – In this phase the cytoplasm of the cell divides

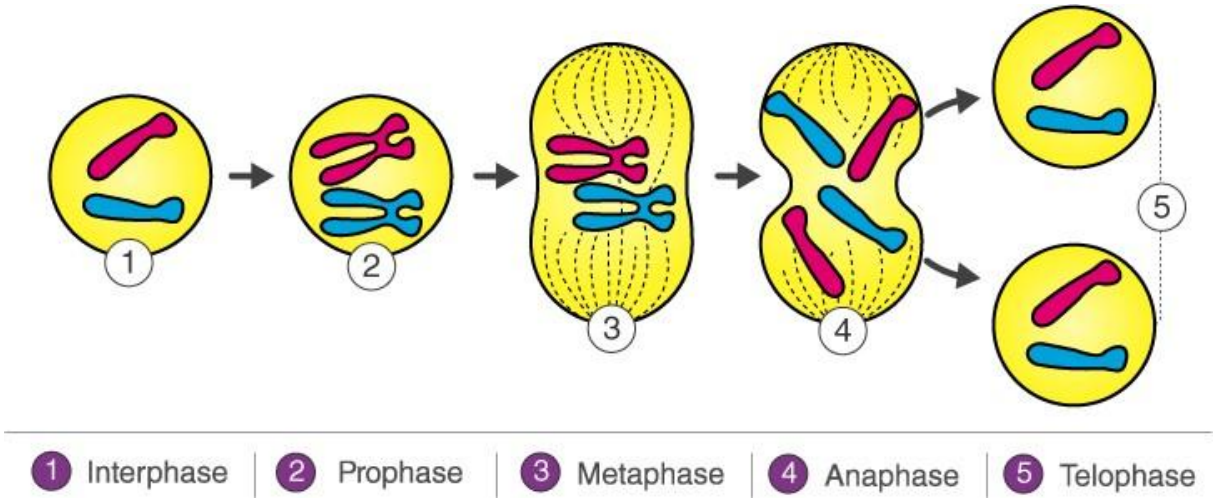

Figure 2.3 Cell division.

1. INTERPHASE

Also known as the resting phase of the cell cycle; interphase is the time during which the cell prepares for division by undergoing both cell growth and DNA replication. It occupies around 95% time of the overall cycle. The interphase is divided into three phases:- During *interphase* the chromosomes are extended long threads that cannot be visibly identified. The DNA of the chromosomes is replicated during this phase, resulting in duplication of the genetic material.

- **G1 phase (Gap 1)** – G1 phase is the phase of the cell between mitosis and initiation of replication of the genetic material of the cell. During this phase, the cell is metabolically active and continues to grow without replicating its DNA.
- **S phase (Synthesis)** – DNA replication takes place during this phase. If the initial quantity of DNA in the cell is denoted as *2N*, then after replication it becomes *4N*. However the number of chromosomes does not vary, viz., if the number of chromosomes during G1 phase was *2n*, it will remain *2n* at the end of S phase. The centriole also divides into two centriole pairs in the cells which contain centriole.
- **G2• phase (Gap 2)** –During this phase, the RNA, proteins, other macromolecules required for multiplication of cell organelles, spindle formation, and cell growth are produced as the cell prepares to go into the mitotic phase.

Some cells like cardiac cells in the adult animals do not exhibit division and some others only divide to replace those cells which have been either damaged or lost due to cell death. Such cells which do not divide further attain an inactive G0 phase also known as quiescent phase after they exit the G1 phase. These cells remain metabolically active but do not divide unless called upon to do so.

2. M-PHASE

This is the mitotic phase or the phase of the equational division as the cell undergoes a complete reorganizationto give birth to a progeny that has the same number of

chromosomes as the parent cell. The other organelles are also divided equally by the process of cytokinesis which is preceded by mitotic nuclear division. The mitoticphase is divided into four overlapping stages:-

1. Prophase,
2. Metaphase,
3. Anaphase, and
4. Telophase

During prophase the chromosomes coil up and contract, becoming short rods. Each chromosome consists of apair of strands, called chromatids, held together at the centromere. At the same time the nuclear envelope disappears, and the centriole divides and the two daughter centrioles move toward opposite poles of the cell.

During metaphase the chromosomes move so that their centromeres are aligned in the equatorial plane of the cell (the metaphase plate), and the mitotic spindle forms. The mitotic spindle is formed of fibers composed of microtubules, which extend from the centrioles to the metaphase plate and to the centromeres of the chromosomes.

During anaphase the chromatids of each chromosome separate, becoming new daughter chromosomes, which are drawn to opposite poles of the cell by the spindle fibers.

During telophase the daughter chromosomes arrive at the poles of the cell, where they are surrounded by two new nuclear envelopes as they begin to uncoil and extend. During this phase, *cytokinesis,* division of the cytoplasm, occurs. A furrow forms around the cell in the equatorial plane and deepens until the two daughter cells are separated.

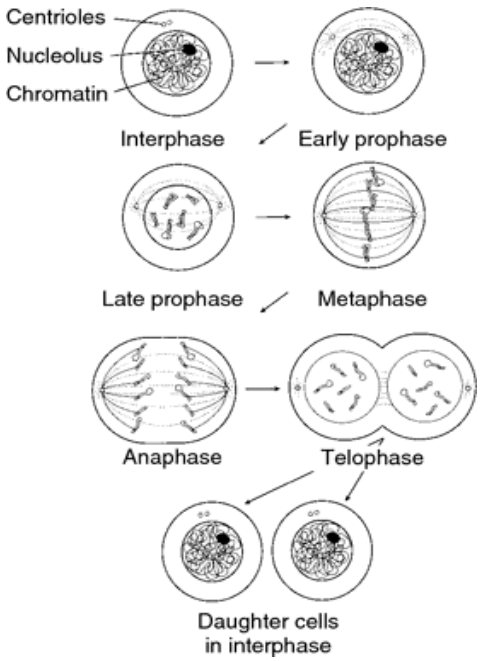

Figure 2.4: Cell cycle.

3. CYTOKINESIS

In this phase, the cytoplasm of the cell divides. It begins as soon as the mitosis ends. Plant cells are much tougher than animal cells, as they have a rigid cell wall and high internal pressure. Thus, cytokinesis occurs in plant and animal cells differently

7. MECHANISM OF ACTION OF CHEMOTHERAPEUTIC AGENTS

7.1. Alkylating Agents

- The first class of chemotherapy agents
- They stop tumor growth by cross-linking guanine nucleobases in DNA double-helix strands directly attacking DNA.
- This makes the strands unable to uncoil and separate.
- As this is necessary in DNA replication,the cell can no longer divide.
- Cell-cycle non specific effect.
- Alkylating agents are also mutagenic and carcinogenic.MECHANISM OF ACTION

Alkylating agents act by cross-linking strands of DNA, and transfer the alkyl groups. Particularly at the N-7 position of guanine. They are nonspecific for cell cycle phase and are thus active during most parts of the cell cycle. Leads to DNA strand breakage leads to cell death.

7.2. ANTIMETABOLITES

All antimetabolites are used in cancer treatment, as they interfere with DNA production and therefore cell division and the growth of tumors.

MECHANISM OF ACTION

Antimetabolites are called a cytotoxic type of drug because they kill cells. They work by mimicking the molecules that a cell needs to grow. Cells are tricked into taking in the drugs and then using the antimetabolites instead of their normal building blocks of genetic material: RNA and DNA.

7.3. 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.

MECHANISM OF ACTION

Plant alkaloids bind to microtubule proteins during metaphase, causing mitotic arrest. The cell cannot divide and dies. This group is mainly cell cycle phase specific for M phase. Major toxicities occur in the haematopoietic, integumentary, neurologic and reproductive systems.

7.4. TOPOISOMERASE

Topoisomerase are enzymes that relax DNA supercoiling during replication and transcription. Topoisomerase I cleaves one strand of the DNA double helix and reseals

the cut strand, whereas topoisomerase II changes DNA topology by breaking and rejoining double-stranded DNA.

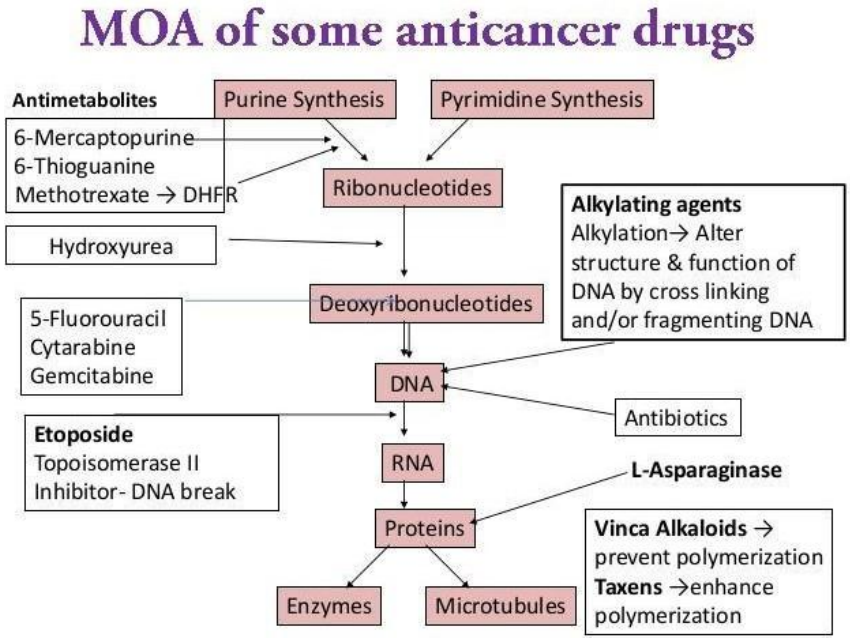

Figure 2.5: Mechanism of action of some anticancer drugs.

8. TYPES OF HYPERSENSITIVITY REACTIONS BY CHEMOTHERAPEUTIC AGENTS

Hypersensitivity reactions to chemotherapy agents are defined as unexpected reactions with signs and symptoms not consistent with known toxicity of these drugs. These reactions range from mild to life-threatening and are difficult to find.

Symptoms include flushing, nausea, difficulty breathing, back pain, hypotension and tachycardia. Hypersensitivity is commonly encountered owing to the increasing use of chemotherapy drugs in clinical practice. Reactions to taxanes usually occur during the first few minutes of the first or second infusion, whereas acute reactions to platinum agents usually occur after multiple cycles of therapy. Basic principles that allow management and possible completion of the regimen should be followed. Certain protocols aim to prevent acute reactions by slowing the infusion rate and by administering steroid and histamine receptor antagonists. Skin testing and desensitization protocols have also been successfully used in case of hypersensitivity to various chemotherapy drugs. Knowledge of all available management options assists physicians in making the most appropriate decision regarding further treatment.

Symptoms include flushing, nausea, difficulty breathing, back pain, hypotension and tachycardia. Hypersensitivity is commonly encountered owing to the increasing use of chemotherapy drugs in clinical practice.

9. DIAGNOSIS AND MANAGEMENT

Hypersensitivity reactions are commonly associated with the use of certain cancer chemotherapy drugs, including platinums, taxanes, asparaginase, procarbazine, and epipodophyllotoxins

1. Platinum agents (cisplatin, carboplatin, oxaliplatin) are associated with IgE-mediated hypersensitivity reactions, and skin testing may be indicated.
2. Taxane (paclitaxel, docetaxel)-related reactions are generally non-IgE mediated, and premedication with corticosteroids and antihistamines is usually effective.
3. Asparaginase has a high rate of hypersensitivity reactions that are likely IgE mediated or related to complement activation. Skin testing has been recommended but has not been validated for asparaginase.

Mainly for the hypersensitivity reaction some testes are as follows.

1. Patch tests
2. Prick tests
3. Intradermal tests

Patch tests, prick tests, and intradermal tests with cisplatin, carboplatin, and oxaliplatin were performed in 21patients.

- Skin tests were positive in 14 of 21 cases.
- Prick tests were positive in 5 cases with the suspected platinum salt.
- Intradermal tests were positive in 12 of 19 cases, always when the hypersensitivity occurred less than 2 hours after infusion.
- Cross-reactions were observed in 4 cases. Delayed readings of skin tests at 24 hours and 48 hours were positive in 3 patients. Patch tests were negative in all the 21 patients tested. Replacement with another

platinum salt was performed in 13 patients using one that gave a negative skin test. A relapse of symptoms occurred in 1 patient.

Intradermal tests are particularly indicated for the diagnosis of immediate hypersensitivity reactions. Their good negative predictive value allows safe retreatment by detecting a potential cross-reaction.

SKIN TEST

Skin testing can be used to evaluate the potential for cross-reactions between two platinum drugs. If indicated, patients with negative skin-test results for a particular platinum agent might be able to continue treatment witha different agent without premedication.

To do a typical skin prick test (also called a scratch test), an allergist (a doctor who diagnoses and treats allergies, asthma, and immune system conditions) or nurse will put a tiny bit of an allergen (such as a pollen or a food) on the skin, then make a small scratch or prick on the skin.

PATCH TEST

Patch testing is generally done to see whether a particular substance is causing allergic skin inflammation(contact dermatitis). Patch tests can detect delayed allergic reactions, which can take several days to develop.Patch tests can detect delayed allergic reactions, which can take several days to develop. Patch tests don't use needles. Instead, allergens are applied to patches, which are then placed on your skin. During a patch test, your skin may be exposed to 20 to 30 extracts of substances that can cause contact dermatitis.

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ELDERLY CONSIDERATION

11. Chemotherapeutic Drug Frequently Associated With HypersensitivityReaction

Hypersensitivity is described as an unanticipated reaction with signs and symptoms that are inconsistent with the drug's recognised toxicity. The majority of responses occur concurrently with or within hours following drug administration. Almost all of them are related to parenteral delivery. Flushing, changes in heart rate and blood pressure, dyspnea/bronchospasm, back discomfort, fever, pruritus, nausea, and various forms of rashes are all symptoms.

Clearly, evaluating these reactions through prospective research is problematic. Some reactions may be triggered by non-immune-mediated histamine or cytokine release, as many patients can withstand reexposure after pretreatment with steroids and antihistamine, as well as gradual readministration of the drug. It works well for taxanes but not so well for platinum compounds. The majority of reactions are influenced by a varietyof factors.

1. Reaction rates
2. Route of administration
3. Rate of administration
4. Previous exposure
5. Dosage of the drug
6. Whether the drug is given as a single agent or in combination
7. Coincident medications that may affect metabolism of the chemotherapeutic drug. 8.concurrent auto-immune disease.

For these reasons, it is difficult to chart comparative hypersensitivity reaction rates for these drugs.

11.1. PLATINUM COMPOUNDS

These medications are often used to treat gynaecological cancers, particularly ovarian and lung adenocarcinoma. Cisplatin was the first to be produced, although carboplatin is currently more commonly used.There has been a high frequency of anaphylactic-like events documented, all occurring within minutes of treatment in patients who had previously been exposed, usually after six courses. Facial edoema, bronchospasm, hypotension, and tachycardia are all symptoms. All of them, including epinephrine, have been reversed with treatment. These symptoms ranged from minor itching and erythema to severe, life-threateninganaphylaxis.

Platinum hypersensitivity symptoms might appear suddenly during infusion or minutes, hours, or days later. A minor rash may be the first sign of hypersensitivity, followed by more severe reactions in 50% of individuals. Skin rash, urticaria, flushing, palmar itching, burning, edoema of the face and hands, gastrointestinal cramping and diarrhoea, back pain, and pruritus are all symptoms of mild hypersensitivity. Antihistamines and steroids usually help them go away quicker. More severe responses occur with

- Bronchospasm,
- Tachycardia,

- Hypotension or hypertension,
- Seizures, and
- Chest pain.

Platinum hypersensitivity symptoms might appear suddenly during infusion or minutes, hours, or days later. The first sign of hypersensitivity may be a small rash, which is followed by increasingly severe reactions. Respiratory issues could be more severe.

11.2. TAXANES

Paclitaxel is used to treat malignancies of the breast, lungs, and gynaecology. Docetaxel is a relatively novel taxane. Because paclitaxel is more likely to cause severe anaphylactic reactions than docetaxel, all patients are given antihistamines and steroids.

Reactions might occur with either the first or second dose. Paclitaxel hypersensitivity is also reduced by pretreatment.

Many paclitaxel patients have mild to severe infusion-related hypersensitivity responses, such as

- Urticaria
- Facial flushing
- Shortness of breath
- Angioedema
- Anaphylaxis.

Most reactions occur during the first or second infusion, 78% within the first 10 to 15 minutes of drug initiation.

11.3. EPIPODOPHYLLOTOXINS

Teniposide is a cancer treatment that is used to treat neurological and hematologic tumours. Etoposide is primarily used to treat testicular cancer and small cell lung cancer.

Etoposide and teniposide have a similar chemical structure and impede cell division in the late G2 phase of thecell cycle.

Except for the brain, these medicines are supplied intravenously and are swiftly and broadly dispersed throughout the body.

Approximately 90-95% of medicines are protein bound, primarily to albumin. As a result, patients with renal failure must alter their dosage.
Etoposide has therapeutic action in germ cell cancer, small cell and non-small cell lung cancer, gastric cancer, and high dose therapy for breast cancer in the transplant context.

Intravenous etoposide is generally well tolerated. A well known but rare toxicity is a type I hypersensitivity reaction, manifested by

- Dyspnoea,
- Chest discomfort,
- Hypotension,
- Bronchospasm
- Skin flushing

12. FACTORS COMPLICATING CHEMOTHERAPEUTIC AGENTS IN THE ELDERLY

Some malignancies may behave differently in the elderly when compared to younger individuals when treated differently.

For example, in breast cancer, the likelihood of local recurrence following lumpectomy decreases with age. In elderly women, this may reduce the requirement for postoperative radiation. Adjuvant chemotherapy was related with a declining survival benefit with increasing age in the Oxford meta-analysis, notably in the over 70 age group. Individual older women who are at high risk of recurrence, on the other hand, may benefit from adjuvant systemic therapy.

Making decisions concerning cancer treatment for the elderly. Consider chemotherapy's response. Theelements that influence chemotherapy are also required. These factors include physiological changes associated with ageing as well as other disorders. Loss of organ function, which influences drug metabolism.

Chemotherapy might be problematic in the elderly due to changes in kidney or liver function or bone marrow reserve. In the case of older people, this can be difficult to assess.

12.1. RENAL FUNCTION

Making cancer treatment decisions for the elderly. Consider the reaction to chemotherapy. Chemotherapy-influencing components are also required. These factors include age-related physiological changes as well as other illnesses. Loss of organ function, which has an impact on medication metabolism. Chemotherapy may be difficult to administer to the elderly due to changes in kidney or liver function or bone marrow reserve. Thiscan be difficult to assess in the case of older adults.

12.2. LIVER FUNCTION

In the elderly, there is a high degree of liver impairment, which makes cytotoxic drug metabolism harder. Certainly, ageing reduces liver blood flow, serum albumin, and cytochrome P450 function. If older patients are given cytotoxics in addition to other medications metabolised by this system, the cytochrome P450 mechanism may become a concern. Cimetidine, for example, is a commonly used medication that inhibits the P450 system.

If the patient's bilirubin level is high, the doses of several anticancer medications must be changed. The greatest examples are anthracyclines and taxanes. Although low albumin causes higher liver extraction of some medications, the increase in body fat with age may reduce the peak dose of a drug. Increase the half-life of medicines that are fat-soluble.

12.3. BONE MARROW

The elderly can have unpredictable myelosuppression, particularly if malnourished. The lack of bone marrow reserve may manifest itself as more prolonged myelosuppression with successive cytotoxic drug doses. The colony stimulating factors such as G-CSF which reverse myelosuppression may be required more often in elderly patients. They can allow adequate doses of chemotherapy to be given without as great a risk of life-threatening febrile neutropenia.

Figure 12.3: Bone marrow.

In most cancers, the elderly will respond just as effectively as their younger counterparts, assuming that the chemotherapy can be administered properly. This could be due to changes in organ function, particularly renal and hepatic function. Deteriorating organ function increases the likelihood of unfavourable outcomes and, as a result, a negative impact on quality of life.

Elderly patients should be given the option of chemotherapy for responsive advanced cancers. As with younger patients they make their decision balancing any predicted positive outcome against the treatment's adverse effects that, even if temporary, will impact upon their quality of life.

13. CANCER CARE DECISIONS FOR OLDER ADULTS

Previously, doctors would make choices without consulting with patients. Today, things are different. Your health care team wants to know about your health problems, answers, and questions. Patients, according to the health care staff, have the right to make their own decisions. Working with a health care team to develop a treatment plan might give you a sense of control.

TO CONSIDER

Before making any treatment decisions, talk with health care team about:

- The type of cancer, if it has spread, and how far
- All your treatment options, and the risks and benefits of each one
- Any other medical conditions that might cause problems with treatment or increase your hypersensitivity reactions.
- How cancer treatment can affect your physical health, emotional health, and lifestyle

Thinking about your personal situation is also very important. You might want to consider:

- Possible emotional and social challenges. Who can help with your care and provide emotional support? If you live alone, will you feel lonely or cut off from other people? How can you get support during treatment?
- Financial challenges. Older adults are more likely to have a limited budget, live on a fixed income, or both. But costs of treatment vary based on several factors. And there are resources to help people with the costs of care. Ask the health care team about ways to get financial help with cancer treatment.

Also consider what your life will be like physically, emotionally, and socially. These factors put together are called quality of life. Think about each of the areas listed below:

- Physical comfort
- Relationships
- Nutrition
- Ability to keep taking care of yourself, do usual activities, or live independently
- Financial security
- Having a meaningful life
- Your ideas about a dignified or peaceful death

It is important to talk honestly with your health care team about what quality of life means to you. Sometimes, managing side effects from treatment can make an important difference in your quality of life.

CONCLUSION

Chemotherapy and radiation therapy cause side effects more often and in greater severity to the elderly than to the young. Elderly patients also recover from treatments more slowly. In most cancers the elderly will respond as well as their younger counterparts provided the chemotherapy can be given safely. This may depend on physiological changes in organ function particularly renal and hepatic function.

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