Antiviral drugs

College of dentist medicine- 3rd year - pharmacology

- As obligate intracellular parasites the replication of viruses depend on synthetic processese of the host cell.
- Antiviral drugs can exert their actions at several stages of viral replication including
- Viral entery, nucleic acid synthesis , late protein synthesis and processing and in the final stage of viral packaging and virion release.

Drugs for herpes virus. HSV

- Most drugs active against herpes viruses are antimetabolites bio activated via viral or host cell kinases to form compounds that inhibit viral DNA polymerase.

Acyclovir

- Mechanism:-
- It is a guanosine analog active against HSV and varicella zoster virus VZV.
- It is activated to form acyclovir triphosphate and acts as a competitive substrate for DNA of
- Resistance to acyclovir involves changes in viral DNA polymerase.
- Resistant strains of HSV lack thymidine kinase, the enzyme involved in the initial viral specific phosphorylation of acyclovir.
- Pharmacokinetic: - the drug administered topically, orally and IV.
- Clinical use:- oral acyclovir is commonly used for the treatment mucocutaneous and genital herpes lesions.

Other drugs for HSV

- Several newer agents have characteristic similar to acyclovir .
- **Valacyclovir**:- prodrug converted to acyclovir by hepatic metabolism after oral administration and reaches plasma levels 3-5 times greater than those achieved by acyclovir.
- Has longer duration of action.

- **Penciclovir**:- undergo activation by viral thymidine kinase and the triphosphate form inhibits DNA polymerase .
- **Famciclovir**:- prodrug converted to penciclovir by first-pass metabolism in the liver.
- Used orally in genital herpes and for herpes zoster.
- The drug is weel tolerated and similar to acyclovir in its kinetic.
- **Docosanol**:- inhibits fusion between the HSV envelop and plasma membrane.
- It prevents viral entery and subsequent replication.
- Used topically.

Ganciclovir:-

- Is a guanine derivative, is triphosphorylated to form a nucleotide theat inhibit DNA polymerase of cytomegalovirus and HSV.
- The drug given IV and peneterate well into tissues including the eye and the CNS.
- Clinical use:- for prophylaxis and treatment of CMV retinitis.

Cidofovir:-

- Is activated exclusively by host cell kinase and the active diphosphate which inhibits DNA polymerase of HSV and CMV.
- Because phosphorylation does not require viral kinase, cidofovir is active against many acyclovir resistant strains.
- Resistance is due to mutations in the DNA polymerase gene.
- Clinical use:- effective in CMV retinitis , in mucocutaneous HSV infections, including those resistant to acyclovir.

Foscarnet:-

- It is a phosphonoformate deriviative that does not require phosphorylation for antiviral activity.
- Inhibit viral RNA polymerase, DNA polymerase, and HIV reverse transcriptase.
- Resistance involves mutation in the DNA polymerase gene.
- Used to treat herpes infection in acyclovir resistant strains.

Vidarabine

- It is an adenine analog and has activity against HSV (herpes keratitis).

Idoxuridine and trifluridine

- These pyrimidine analog are used topically in herpes keratitis ,they are too toxic for systemic use.

Anti-influenza agents:-

Amantadine and rimantadine>

- Inhibit an early step in replication of the influenza A virus.
- They prevent (uncoating) by binding to a protein M2.
- This protein functions as a proton ion channel required at the onset of infection to permit acidification of the virus core,
- Which in turn activates viral RNA transcriptase.
- These drugs are prophylactic against influenza A virus infection and can reduce the duration of symptoms if given within 48 h after contact.A