Antiviral drugs

This article has been translated from WikiSkripta; ready for the **editor's review**.

Antivirals or *virostatics* are substances that are used to treat viral diseases. Common viral diseases (colds, colds, flu) are treated symptomatically - analgesics, antipyretics. Some are vaccinated (influenza, hepatitis, childhood infections). Viral infections are treated less often, especially in patients with weakened immunity, antiviral drugs are always administered. Antibiotics are only given if a bacterial infection supersedes a viral infection.

Mechanism of action

- Blockade of virus absorption by the cell membrane – enfuvirtif, maraviroc (HIV), docosanol (HSV), palivizumab (RSV).
- Blocking virus penetration into the nucleus - interferon alfa (HBV, HCV).
- Prevents the release of viral nucleic acids in the host cell - amantadine, rimantadine (influenza).
- They block the assembly and release of the virus from the host cell - neuraminidase inhibitors (influenza)
- They block the synthesis of nucleic acids by inhibiting nucleoside and non-nucleoside reverse transcriptases (HIV).
- They block the synthesis of viral proteins - protease inhibitors (HIV).
- False substrates - e.g. acyclovir (HSV, VZV)

Disadvantages of therapy

- It is impossible not to affect the host cell at the same time.
- With retroviruses, we cannot cure the cell because the viral nucleic acid is part of the nucleus.
- Often, the infection becomes symptomatic only after irreversible cell damage, when it is already too late for treatment.

Substances against herpes infections

Acyclovir

It is a derivative of **guanine**, it contains an aliphatic residue instead of deoxyribose. It is taken up by infected cells, where it is converted by the virus-specific thymidine kinase into a monophosphate, which is then converted into an effective triphosphate by cellular enzymes (this enzyme normally has a very low affinity for acyclovirus, but a greater affinity after a virus attack). It inhibits the viral DNA polymerase and, when incorporated into the viral DNA, acts as a chain terminator. It has a far greater affinity for the viral kinase than for the human one (which is why it is effective and safe). We mainly indicate it against herpes simplex (local or p.o. administration) and herpes zoster (p.o. administration) infections.

Brivudine (herpes zoster treatment in immunocompetent patients), famciclovir, valaciclovir (prodrug of aciclovir, which makes it more bioavailable) have similar effects as aciclovir, or 'adenosine-arabinoside**, which works in the same way, the indication is identical.**

⚠**Adverse effects**: rare, decreased kidney function, neurological problems (tremor, confusion), herpes viruses resistant to acyclovir have been found in immunocompromised patients.

Agents against cytomegalovirus infections

They are **more toxic** than acyclovir, their use is indicated in immunodeficient patients.

- **Ganciclovir** - is a guanosine analog, which inhibits DNA polymerase (acyclovir derivative). Compared to acyclovir, it has higher toxicity, which is why it is only used in severe cytomegalovirus infections and in immunodeficiency conditions (AIDS, conditions after cytostatics). ⚠Undesirable effects are blood formation disorders, neutropenia, liver and kidney function disorders.
- **Foskarnet** - blocks the binding site for pyrophosphate on viral polymerase and reverse transcriptase, pyrophosphate must be cleaved from triphosphorylated nucleosides during DNA polymerization. It is indicated i.v. in severe CMV retinitis in AIDS patients (in 80% stabilizes the image of the fundus) and diseases resistant to acyclovir (HSV). ⚠It is nephrotoxic.
- **Cidofovir'** - i.v. application, a cytosine analog. It is mainly indicated for CMV infection, but also HSV, EBV, VZV. It has significant adverse effects, mainly high nephrotoxicity → therefore rather a "backup" antiviral in the case of CMV retinitis, resistance to acyclovir.

Substances against influenza viruses

Amantadine

It is a stable tricyclic amine also used to treat Parkinson's disease. It inhibits the replication of influenza A viruses by preventing the release of the nucleic acid of the virus (uncoating) by blocking the ion channel of the virus (M2-protein). It is rarely used for the prophylaxis of influenza type A2. It is contraindicated in patients suffering from reduced kidney function. ⚠Side effects: GIT disorders, thinking disorders, nervousness.

Rimantadine

It inhibits the M2 protein of the viral membrane, which functions as a hydrogen channel, thereby preventing the acidification of the internal environment of the virus. Without this mechanism, it will not peel off. It acts on the influenza A virus, when it can be used both as a prophylaxis and as a treatment for the flu.

Neuraminidase inhibitors

They are used for the treatment and prophylaxis of *influenza types A and B*, which also include the so-called bird flu, H5N1 and the so-called swine flu viruses. It acts on the surface enzyme of the influenza virus ('*neuraminidase'* ***- it splits the mucus and allows the virus access to the cells of the respiratory tract, and also allows the viruses to be flushed out of the host cells.Neuraminidase inhibitors thereby*** *prevent the release of newly emerging viruses from infected cells.*) Representatives are **oseltamivir'** (Tamiflu, p.o.) and **zanamivir'** (Relenza, inhalation). Side effects are mild, mainly in the form of vomiting and nausea.

Retroviral Antivirals

Their use does not lead to the eradication of the infection, but to the **suppression of viral replication'*, thereby positively affecting immune functions and thus also the course of HIV infection. Slowing down the course of the infection results in a*** **prolongation and higher quality of the patient's life*, an improvement in the general condition, a reduction in the risk of opportunistic infections and tumors, and a decrease in mortality. With properly administered treatment, an increase in CD4+ lymphocytes and a*** *decrease in the viral load to almost zero values* are achieved in most patients, when the patient de facto ceases to be infectious to the environment. **They are used in combination.**

HIV protease inhibitors

A group of peptides that inhibit the active center of the HIV protease and thereby suppress the maturation of HIV viruses, **disrupt their completion and maturation*, and therefore act at the end of the formation of a new virus. The disadvantage is cross-resistance and*** *frequent drug interactions''* (cytochrome P450). Adverse effects include nausea, vomiting, diarrhea, disruption of lipid metabolism. Usually, due to the poor tolerance of higher doses, a combination with other HIV protease inhibitors is used, which simultaneously reduces resistance and optimizes their pharmacokinetics (longer duration of action).

Examples: **ritonavir**, **indinavir**, fosamprenavir (strong effect, but usually in combination with ritonavir), lopinavir and others.

Reverse Transcriptase Inhibitors - Nucleosides

They disrupt the cycle of the HIV virus by **incorporating a phosphorylated nucleoside** into the viral DNA chain. Common adverse effects are mitochondrial toxicity, lactic acidosis, lipodystrophy, disorders of fat metabolism, osteonecrosis and the so-called immune reactivation syndrome.

- **Zidovudine** - thymidine analog, false substrate (phosphorylation by kinases to triphosphate, competitive inhibition of reverse transcriptase, blocks the transcription of HIV genetic information from RNA to DNA). In addition to the side effects mentioned above, the risk of hematopoietic disorders is described (CAVE myelosuppressive drugs together with zidovudine – dapsone, cotrimoxazole, amphotericin).
- **Lamivudine** - cytosine analog, best tolerated. In addition to HIV, it is also used for **HBV** infections.
- **Tenofovir'** - Viread (Prof. Holý), possible use also in hepatitis B.

Non-nucleoside reverse transcriptase inhibitors

They act by **direct competitive inhibition of HIV-1 reverse transcriptases** without the need for activation. They also act through incorporation into the viral DNA chain. They are **substrates for CYP3A4**, they can be inducers (nevirapine), inhibitors (delavirdine), or both inducers and inhibitors (efavirenz, etravirine). Rashes are a common side effect.

Examples: **efavirenz**, nevirapine, delavirdine, etavirine.

Others

- Maravirok – antagonist of *CCR5* (chemotactic receptor), prevents HIV from entering the cell.
- Enfuvirtide – **fusion inhibitor** (by binding to the viral glycoprotein gp-41, it blocks the fusion between the membrane of the virus and the host cell).
- Raltegravir, elvitegravir, dolutegravir – **integrase inhibitors'** (the enzyme needed to incorporate the virus genome into the host cell genome).

Other antivirals

- **Ribavirin** - a nucleoside antiviral showing in vitro activity against a number of DNA and RNA viruses, ideal for the treatment of infections caused by the RS virus. However, it works on a wide range of viruses (including togaviruses). It used to be indicated in combination with interferon a2B: therapy of chronic hepatitis C. Adverse effects are hemolysis, anemia, neutropenia, potential teratogenicity and carcinogenicity. **In the treatment of hepatitis C, other treatment regimens are currently used without the use of ribavirin and interferons (for more details, see the article on hepatitis C).**
- **Palivizumab** - monoclonal antibody, against influenza in newborns and children.
- **Interferons** - interferon α, β and γ therapy for hepatitis B and C, cause flu-like symptoms, administration in non-oncology patients should be considered.
- **Immunoglobulins** - produced from donor plasma, immediate protection (it takes time for the body to create its own antibodies), non-specific in immunodeficiency, specific - against a specific antigen (HBV, CMV, etc.). Adverse effects are rare (chills, fever, nausea, vomiting, hypotension, tachycardia, allergic reaction).

Links

Related Articles

- Herpesviruses
- Cytomegalovirus
- AIDS

References

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