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Influenza: Do antiviral drugs like Tamiflu work and what are their adverse effects?

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IQWiG

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Influenza or 'the flu' is an upper respiratory tract infection (a disease of the breathing system or airways). Almost everybody recovers from influenza within a week, although they may have a cough and feel ill for a week or two afterwards. However, children, older people and people with serious illnesses are at greater risk of getting very sick and having complications like pneumonia (a lung infection). Because the disease is particularly common in these high-risk groups, thousands of people die from complications of influenza every year. People who are otherwise healthy are very unlikely to die from common forms of influenza.

Influenza can cause a wide range of symptoms, including fever, chills, muscle ache, fatigue, headache, sore throat, a cough and a blocked nose. You can read more about differences between cold and flu symptoms here (URL: http://www.informedhealthonline.org/fact-sheet-the-common-cold.2010.1753.html).

How antiviral drugs work and how they are used

Influenza is caused by viruses. Many other infectious diseases are caused by bacteria, and can be effectively treated with antibiotics. But antibiotics do not help fight the viruses that cause influenza. Drugs that aim to stop viruses multiplying in your body are called antivirals. Four different antivirals have been developed for influenza. Three of these have been approved for use in Germany. They have to be prescribed by a doctor.

The two older drugs, called amantadine (trade name Symmetrel) and rimantadine (not approved for use in Germany), only target viruses in the group called "Type A" influenza. Two newer drugs act against both "Type A" and "Type B" influenza. They are called oseltamivir (trade name Tamiflu) and zanamivir (trade name Relenza). These newer drugs belong to the group of neuraminidase inhibitors, which means they inhibit a protein called neuraminidase. The virus needs neuraminidase in order to multiply in the body. Oseltamivir (Tamiflu) is a pill, and zanamivir (Relenza) is a powder used with an oral inhaler (inhaled through the mouth, not the nose).

To have any chance of making a difference, antiviral drugs need to be used within 48 hours of symptoms starting. The illness is over in a week, so if a person has already had symptoms for days, it is probably too late to take this medication. But family members can also take antivirals to protect themselves from infection when someone else is ill with influenza. When it is used in this way, it is called post-exposure prophylaxis (or preventive treatment).

One of the problems with using antiviral influenza drugs is that they only work against influenza viruses, and not against many other viruses which can cause flu-like symptoms, like cold viruses. But to find out whether someone who has flu symptoms actually has an influenza virus, lab tests need to be done. These tests involve quite a lot of effort and are not routinely carried out. If antiviral drugs are not used properly, viruses might become resistant (unresponsive) to them.

Research on the efficacy of antiviral influenza drugs

Researchers from Italy, Australia and the USA looked for clinical trials that tested antiviral influenza drugs. They found 53 trials. 20 of them looked at one of the newer drugs (oseltamivir and zanamivir) and 33 trials studied amantadine, rimantadine or both of these drugs. Some tested prophylactic use, some tested treatment and some tested a combination of prophylactic use and treatment. The people in these trials were between 16 and 65 years old and, other than having influenza, they were healthy. There were more than 12,000 people in the trials of Tamiflu or Relenza, and about 27,000 in the trials of amantadine and rimantadine.

The results of research on amantadine and rimantadine

If used within the first 48 hours of symptoms starting, amantadine and rimantadine can shorten the length of fever by up to one day in people who have Type A influenza. But the researchers do not recommend the routine use of these drugs. One reason for this is because influenza viruses can become resistant to (get used to) these drugs quite quickly. And they also have a lot of adverse effects. For example, amantadine causes nausea, insomnia and hallucinations. There is not as much research on rimantadine, and there is also not enough research on whether amantadine or rimantadine can prevent complications associated with influenza.

The results of research on Tamiflu and Relenza

Oseltamivir (Tamiflu) and zanamivir (Relenza) can also

shorten the length of the flu by about one day. Both of these drugs have been shown to reduce the risk of people getting influenza if they take them after they have been in close contact with someone who has influenza and before they have symptoms of the illness. The protection might be as high as 60 to 90% if they have been in contact with someone who has influenza. But they hardly provide any protection for people who have not had direct contact with someone who is infected.

It is not clear whether oseltamivir can prevent complications of influenza. Although there have been several studies on this, the company that makes oseltamivir has not published all of them. This means that it is not possible to answer this question at the moment. There is not enough research to say whether zanamivir lowers the risk of complications.

The adverse effects of these drugs are very similar to flu symptoms. Oseltamivir often causes adverse effects, especially nausea. At least 1 out of 20 trial participants (5%) who took oseltamivir to try to prevent influenza experienced nausea, depending on the dose. The trials of zanamivir did not provide detailed data about the frequency of adverse effects.

There have been some reports of oseltamivir (Tamiflu) and zanamivir (Relenza) having psychological effects in young people, allegedly leading to suicide in some cases. These events were rare and it is not yet known if they were definitely caused by the drugs. The US drug agency, the FDA, issued a recommendation advising people to look out for untypical behavioural changes when taking them and to seek medical help if necessary.

Using antiviral drugs for new types of flu like bird and swine flu

Both oseltamivir and zanamivir have been used in people who were infected with the bird (avian) flu virus. But there is not enough research to say how effective these drugs are in the treatment of new influenza viruses. For the treatment of swine flu, the World Health Organisation (WHO) recommends using oseltamivir or zanamivir in people with severe symptoms and people at high risk of complications. Complications are more likely in people who, for example, have certain chronic illnesses or a weak immune system.

None of the drugs have been shown to have a big impact on the amount of virus ("viral load") in the noses of people with influenza. This is important, because influenza is usually spread by infected droplets from the nose. So people taking these antiviral drugs are probably just as contagious, and therefore just as likely to spread the virus, as people who are not taking the drugs. The most important advice when there is a flu outbreak is still: try to stop the infection spreading. You can read more about that here (URL: http://www.informedhealthonline.org/fact-sheet-protecting-yourse .

Author: German Institute for Quality and Efficiency in Health Care (IQWiG)

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Glossary

antibiotics

Antibiotics are medicines that can be used for bacterial and some fungal infections. Antibiotics do not work against viruses. Well-known antibiotics include penicillin, tetracycline and chloramphenicole.

bacteria

Bacteria are micro-organisms that, unlike viruses, can exist on their own. Viruses, on the other hand, can only exist inside a living cell. Most bacteria are not harmful to people, and some are actually beneficial. Bowel bacteria support bowel health. However if they get into the urinary system, they can cause an infection there. Doctors prescribe antibiotics for illnesses where bacteria need to be stopped or killed off. Immunisation is also possible against some bacterial infections, such as diphtheria, tetanus or whooping cough.

infection

In medicine, we speak of an infection when a person has caught a germ (an infectious agent). This germ can be a bacterium, a virus, a fungus or a worm. The germ multiplies and then either spreads throughout the body or only attacks one particular organ. As long as there are no signs of a disease, this is called an asymptomatic infection. When the body shows a reaction to the germ in the form of symptoms, this is called a symptomatic infection (an infectious disease). The period between the moment the germs enter the body and the moment the first symptoms of the disease appear, is called the incubation period. It may last a few hours or days, or even many years. An infection does not necessarily have to lead to the onset of a disease.

immune system

The immune system is the body's defense system and its task is to protect the body against germs or degenerated cells (like cancer cells). The immune system is very complex and has not been understood in every detail yet. There are two components: the cellular immune defense (for example "scavenger cells" and "killer cells") and the complement system ("antibodies", for example).

virus

Viruses are germs that enter living cells (plant, animal or human cells) to multiply. Viruses cause illnesses and diseases such as smallpox, influenza, colds, hepatitis, herpes and AIDS.

pneumonia

Pneumonia ("pneu" is of Greek origin and means "breeze") is the medical term for an inflammation of the lung. It can be caused by viruses, bacteria or fungi that pass through the upper airways to get into the lung. It is a disease that more commonly affects old and very young people and other persons with a weak immune system. The symptoms include coughing up sputum, breathlessness, chest pain and fever. Breathing is rapid and can be accompanied by crackling or rattling noises.

fatigue

Fatigue is a term used to describe paralyzing mental and physical exhaustion that may also be accompanied by heightened emotional sensitivity. In contrast to usual tiredness, fatigue only responds to rest or sleep to a very limited extent.

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The German Institute for Quality and Efficiency in Health Care (IQWiG)

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Evidence basis of our health information

Our information is based primarily on systematic reviews of the effects of health care. Systematic reviews are necessary to gain an objective picture of health care. In order to do this, a clear question is formulated. Researchers then find all the relevant studies that could answer this question. They then evaluate those studies.

You can find a list of the evidence and other scientific literature on which this information is based at **www.informedhealthonline.org**

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