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Cardiovascular diseases: How do ASA and clopidogrel compare?



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People who have survived a heart attack or stroke have a higher risk of further cardiovascular disease. But there is a lot that they can do to prevent new problems developing. For many years now it has been known that the drug acetylsalicylic acid (ASA, called ASS in Germany; the drug in medications like Aspirin) lowers the risk of complications. People who have symptoms in their legs due to poor circulation can also benefit from ASA. Doctors might recommend taking this medication regularly over a long period of time. The commonly used term “blood thinners” is not, strictly speaking, the correct name for these drugs because they actually slow down the blood-clotting process rather than making the blood thinner. So the correct name is anti-clotting medication.

Medications containing another, newer drug called clopidogrel have also been approved for use in Germany since 1998. They are also taken regularly over long periods of time to try to lower the risk of further cardiovascular disease. The German Institute for Quality and Efficiency in Health Care (IQWiG) did research to find out how this newer drug compares to ASA.

Arteriosclerosis is the most common cause of cardiovascular diseases

Cardiovascular (heart and circulation) diseases are usually caused by “hardening of the arteries”. Over time, fats and other substances in the blood attach to the inner wall of the blood vessels and build up. As a result, the arteries gradually become narrower and harder. The medical term for this is “arteriosclerosis”. Arteriosclerosis does not cause any symptoms at first. But if the deposits get bigger, greatly reducing the amount of blood that can get through the blood vessels, it can lead to various illnesses.

If the coronary arteries become narrow, the heart no longer gets enough oxygen. This is called coronary heart disease (CHD), or coronary artery disease (CAD). Should a coronary artery suddenly become so narrow that part of the heart muscle can no longer be supplied with oxygen, the person has a heart attack. If this is not treated in time, part of the muscle tissue dies. This can be life-threatening. The likelihood of surviving a heart attack has greatly increased over the years: in Germany, about 3 out of 4 people survive a heart attack nowadays.

The signs of a heart attack include chest pains which, for example, spread to the left arm, upper abdomen or lower jaw, as well as breathing difficulties and nausea. The signs may be less typical though, like sudden pain in the upper abdomen. You can find more information about how to recognise the signs of a heart attack here (URL: <http://www.informedhealthonline.org/index.230.en.html>)

Stroke is another possible consequence of arteriosclerosis. This is where a blood vessel in the brain suddenly becomes blocked. Here, too, it is important to get treatment quickly, in order to prevent any permanent damage to the brain. Strokes can cause various symptoms. These include paralysis on one side of the body, problems speaking or swallowing, dizziness or blurred vision. Some people become unconscious. You can find out more about the signs of a stroke here (URL: <http://www.informedhealthonline.org/index.612.en.html>) .

Arteriosclerosis can also affect blood vessels in the legs, causing blood circulation problems. The medical name for this is peripheral arterial disease (PAD). At later stages of the disease people usually have pain in their legs when they walk longer distances, and this pain then goes away again when they rest. PAD is also sometimes called “window shopper’s disease” in German, because people keep stopping to rest while walking. This disease is associated with a higher risk of heart attack and stroke. Measuring someone’s ankle and arm blood pressure can give doctors an indication of whether or not they have PAD, even if they do not have any symptoms yet.

Medication to prevent cardiovascular diseases

People who have had a heart attack or stroke, and people who have symptoms caused by blood circulation problems in their legs, usually take anti-clotting medication to lower the risk of complications. Anti-clotting medications can be divided into two groups. So-called anticoagulants prevent clotting factors from being made or working properly, and antiplatelets act on the blood platelets (thrombocytes).

The best studied antiplatelet is acetylsalicylic acid (ASA). A new antiplatelet called clopidogrel has also been available for a number of years now. Like ASA, it prevents blood platelets from sticking together.

Anti-clotting medication can have adverse effects too. The most common adverse effect is bleeding. Light bleeding,

as with nose bleeds, is usually not a problem. But heavy gastrointestinal bleeding (bleeding in the stomach and bowel) is also possible, and urgent medical treatment is needed if that happens.

Comparing ASA and clopidogrel

The German Institute for Quality and Efficiency in Health Care (IQWiG) – the publisher of this website – wanted to find out how ASA and clopidogrel compare. Together with researchers from Bremen and Bielefeld in Germany, researchers from IQWiG looked for trials that compared the two drugs. They found five trials involving almost 20,000 people. In four of these trials there were only a few hundred participants. The other trial – the so-called CAPRIE trial – was by far the largest, and was very important for the researchers when evaluating these drugs.

More than 19,000 people took part in the CAPRIE trial. They had all either had a heart attack or stroke in the recent past, or currently had advanced PAD, so clopidogrel or ASA were possible treatment options. The aim of the trial was to find out whether one of the two drugs was more effective than the other at lowering the risk of further cardiovascular disease. The participants were 63 years old on average. About 70% of them were men.

The people in the trial were divided into three groups depending on their medical reason for needing treatment (heart attack, stroke or advanced PAD). Each of these groups was then randomly assigned to one of two treatment groups. One of the treatment groups took ASA, and the other took clopidogrel. Neither the doctors nor the patients knew which of the two drugs the patients were taking (in other words, they were “blinded”). Click here (URL: <http://www.informedhealthonline.org/index.61.en.html>) to read about why it is important to do trials using random allocation and blinding in order to get reliable research results. The drug doses used in the trial were 325 mg of ASA and 75 mg of clopidogrel per day. The trial lasted almost 2 years.

Clopidogrel has advantages over ASA for people with advanced PAD

Overall, the CAPRIE trial found clopidogrel to be more effective than ASA. However, one clear advantage only affected people who had advanced PAD. In this group of patients, clopidogrel had a greater benefit than ASA: only about 4 out of 100 people in the clopidogrel group went on to have a heart attack or stroke, or die of a cardiovascular

problem (4%), compared to about 5 out of 100 people in the ASA group (5%). This means that, compared to ASA, clopidogrel protected one extra person out of 100 people with advanced PAD (1%).

Proton pump inhibitors can lower the risk of gastrointestinal complications

Clopidogrel is believed to cause less bleeding than ASA. But there is not enough research to say whether switching from ASA to clopidogrel can lower the risk of this adverse effect. Although adverse effect data were collected in the CAPRIE trial, the participants took a much higher dose of ASA than is typically used in Germany: the dose used in the CAPRIE trial was 325 mg per day, but most people in Germany who have cardiovascular problems only take 100 mg of ASA per day or less. Other research has shown that the risk of adverse effects from ASA is a lot lower if it is taken in smaller doses – but it is just as effective.

People who are taking ASA and have had gastrointestinal bleeding in the past can lower their risk of further bleeding by taking a proton pump inhibitor as well. Proton pump inhibitors are drugs that reduce the production of stomach acid.

Anti-clotting medication can only have a positive effect if it is taken regularly. Many people find it hard to take medication over a long period of time – particularly if they are feeling quite healthy and do not notice an immediate difference. There are a number of things that can help people take long-term medication properly. You can find out more about that here (URL: <http://www.informedhealthonline.org/medication-use.511.56.en.html>).

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

Note

This health information is a summary of a scientific report published by IQWiG. It is not an assessment of the right to have health care services reimbursed by statutory health insurance funds in Germany. By law, decisions about the reimbursement of diagnostic and therapeutic procedures can only be made by the German Federal Joint Committee (G-BA). The Federal Joint Committee takes IQWiG reports into consideration in its decision-making process. You can find information about

the decisions of the German Federal Joint Committee on its English-language website, www.english.g-ba.de (URL: <http://www.english.g-ba.de/>).

Glossary

stroke

A stroke (also sometimes called brain attack, or apoplexy, which is Greek for “struck down”) is an acute condition where the brain does not get enough oxygen. It is most commonly caused by a blood clot that has travelled through the bloodstream and is blocking blood vessels in the brain. In rarer cases bleeding in the brain may also result in a stroke. Depending on which part of the brain is affected, there may be paralysis of either all or certain parts of one half of the body, facial nerve impairment, vision problems, trouble balancing and severe problems speaking. A stroke is a medical emergency: the parts of the brain that are affected need to be supplied with oxygen as quickly as possible, to avoid the death of more brain tissue. The risk of having a stroke is greater for older people and people who have hypertension or chronic arteriosclerosis.

Sources

German Institute for Quality and Efficiency in Health Care (IQWiG). *Clpidogrel versus acetylsalicylic acid in the secondary prevention of vascular diseases. Final report A04-01A. Version 1.0.* Cologne: IQWiG. June 2006. [Full text (URL: http://www.iqwig.de/download/A04-01A_Final_report_Clopidogrel_versus_ASA_for_secondary_prevention_of_vascular_diseases..htm)]

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

The German Institute for Quality and Efficiency in Health Care (IQWiG) was established by legislation to provide evaluations of the effectiveness, quality and efficiency of healthcare services. This includes the assessment of medicines as well as the publication of health information for consumers and patients.

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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