

Dementia in Alzheimer's disease: How well do cholinesterase inhibitors work?



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Dementia is a chronic and progressive disease affecting the brain, in which the nerve cells gradually change or become damaged over time. The most common form of dementia is Alzheimer's disease. This disease causes the person's mental abilities, memory and emotional control to deteriorate. It becomes increasingly difficult to master everyday activities which used to be easy, such as going shopping, doing household chores, eating and drinking. Accompanying symptoms, including depression, anxiety and sleeping problems, can seriously reduce quality of life too. As the disease progresses, carers have to support and look after their loved ones more and more, and they have to find a way to cope with the mental changes that happen.

In the near future we will publish a special feature on dementia, including information about medication, non-drug treatment and support options. We will let you know when that goes online here.

Treatment options

There is no cure for Alzheimer's disease, but there are various medications and other strategies which aim to relieve the symptoms and slow down the progression of the disease. Non-drug strategies include memory training or the encouragement of social activities. The available medications include cholinesterase inhibitors, memantine, and the herbal drug Ginkgo biloba. You can read more about the treatment options at different stages of the disease here (URL: <http://www.gesundheitsinformation.de/dementia.603.56.en.html>)

Certain nerve cells in the brain (so-called cholinergic neurons) play an important role in the regulation of many bodily functions. Researchers have discovered that these nerve cells are a lot less active in people who have advanced Alzheimer's disease. This means that it takes longer for brain signals to be sent. Cholinesterase inhibitors aim to increase communication between the nerve cells to try to reduce the symptoms of the illness. These drugs have been approved for use in mild to moderate Alzheimer's disease. Three different cholinesterase inhibitors are currently available in Germany: donepezil, galantamine

and rivastigmine. They are taken in the form of tablets. Rivastigmine is now also available in the form of a patch. Here the drug is absorbed into the body through the skin.

How cholinesterase inhibitors were evaluated

Together with researchers at the universities of Freiburg and Ulm, a group of researchers at the German Institute for Quality and Efficiency in Health Care (IQWiG) analysed randomised controlled trials which looked at the effects of cholinesterase inhibitors in people with Alzheimer's disease. In these trials, either one group of participants took one of the three cholinesterase inhibitors and a control group took a dummy treatment (a placebo), or the drugs were compared directly with each other. You can read about why it is important to carry out good quality studies in this way here (URL: <http://www.gesundheitsinformation.de/evidence-based-medicine>). In their first analysis, which they did in 2007, the researchers found 27 trials that lasted at least 16 weeks. There were over 9,800 people in these trials.

The researchers wanted to see whether the medication improved people's cognitive (mental) abilities, reduced psychological problems or made it easier for them to perform daily activities. The varying quality of the studies meant that it was not possible to find answers to all of these important questions.

What they found

The analysis showed that the cholinesterase inhibitors donepezil, galantamine and rivastigmine can slightly delay the loss of brain function in people who have mild to moderate Alzheimer's disease. More specifically: patients who took one of these medications for at least four months were able to, for example, remember things more easily than people who took a dummy medication.

There was also some evidence to suggest that people who took one of these medications were able to carry on living independently for somewhat longer than people who took a dummy medication. More research is needed to be sure though. The researchers could not draw any conclusions about the drugs' effects on accompanying psychological problems like depression and anxiety because there was not enough good-quality data. Although there is some evidence to suggest that galantamine helps, it is very weak evidence. Galantamine could also possibly reduce the need for support and improve caregivers' quality of life. However, the effect that the researchers saw was very

small here too.

It was not possible to evaluate the influence of the drugs on death rate, disease-related quality of life, or the need for nursing home care, because there was not enough good quality data on these factors, or even no data at all. They were also unable to draw conclusions about whether age, gender or accompanying illnesses influence the effects of the drugs.

The IQWiG researchers concluded that, according to what is known at the moment, none of the three drugs is considered to be better than the other two. All three cholinesterase inhibitors were found to have a stronger effect when taken in moderate to high doses than when taken in very low doses. However, donepezil already has a beneficial effect in smaller doses, whereas small doses of galantamine and rivastigmine had no effect, or at least no clear effect. All three medications can cause adverse effects like nausea, vomiting and diarrhoea. The higher the dose, the greater the likelihood of adverse effects. These are probably most common in people who are taking rivastigmine. The trials did not include information about rare adverse effects or those that only occur after taking the drugs for longer periods of time.

It is also still not clear how effective cholinesterase inhibitors are in the long term and how well they work compared to other types of (drug and non-drug) treatment. IQWiG is evaluating other treatments for Alzheimer's disease, including ginkgo-based products, the drug memantine and non-drug therapies. The results of these reports are published here (URL: <http://www.gesundheitsinformation.de/dementia.603.56.en.html>)

In September 2009 IQWiG did a search to see if there were any new trials of the use of cholinesterase inhibitors in people who have mild or moderate dementia. The researchers found 9 new trials in total. They came to the conclusion that, compared to earlier trials, these trials did not lead to any important new findings about donepezil and rivastigmine tablets.

The results of several new trials of the cholinesterase inhibitor galantamine had not been published at the time of their search. This means that the researchers could not say whether the outcomes affected the conclusions of previous research on galantamine.

There were also four trials of rivastigmine patches. Here

too, only two of these trials had been published. Without access to the unpublished trials, it was not possible for the IQWiG researchers to assess the advantages and disadvantages of rivastigmine patches.

Researchers at IQWiG are currently carrying out a detailed analysis of the new trials of galantamine and rivastigmine. The Institute will ask the manufacturers of these drugs to provide information about the unpublished trials, so that they can do a comprehensive analysis. We will report on the results of IQWiG's analysis here as soon as it is published.

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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

evidence

Evidence is what we call scientific proof from well-conducted, good-quality scientific trials that have been carefully designed to answer specific questions. Depending on the types of questions, different scientific research methods (types of study) are most appropriate to find reliable answers to these questions. Randomized controlled trials (RCTs), for example, are the best way to get reliable evidence on the effectiveness of medical treatments (interventions). This type of study, however, is not the best form of evidence for all possible questions, and does not provide the best answers to all kinds of questions, either. Epidemiological studies, for example, are very suitable for establishing well-founded proof for the spreading of a disease in the population.

depression

Depression is one of the most common mental illnesses, and it can be mild, moderate or serious. There are several different types of depression that can be recognised by different signs. Which symptoms of depression occur and how strong and frequent they are vary from person to person. People in any social or age group can be affected, both women and men. If someone has had at least two of the following symptoms for longer than two weeks, it might mean that they are depressed: deep sadness; listlessness; loss of interest in the things they usually care about.

Sources

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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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