Promethazine for rapid tranquillisation

Information for the public
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About this information

This information explains the evidence summary about the off-label use of promethazine for rapid tranquillisation. The evidence summary is an overview of the available information about this medicine. It aims to help prescribers and patients when they are considering whether or not to use an unlicensed or off-label treatment. The summary does not contain recommendations from NICE on whether the medicine should be used.

Licensing medicines

In the UK, medicines need to have a licence before they can be marketed. To get a licence, the manufacturer of the medicine has to provide evidence that shows that the medicine works well enough and is safe enough to be used for a specific condition and for a specific group of patients, and that they can manufacture the medicine to the required quality. Medicines can be prescribed without a licence (an 'unlicensed medicine') if there is no suitable licensed alternative and it is likely to benefit the patient.

A medicine can also be prescribed 'off-label'. This means the prescriber wants to use it in a different way than is set out in the terms of its licence. This could mean using the medicine for a different condition or a different group of patients, or it could mean a change in the dose or that the medicine is taken in a different way. There is more information about licensing medicines on NHS Choices.
What is rapid tranquillisation?

Psychiatric units, wards and emergency departments need to be places where people can feel safe and comfortable and have privacy and dignity. It is important that the risk of violence or harm to any person is kept as low as possible in these places. Rapid tranquillisation is when medicines are given to a person who is very agitated or displaying aggressive behaviour to help quickly calm them. This is to reduce any risk to themselves or others, and allow them to receive the medical care that they need.

Before giving rapid tranquillisation, nurses and doctors will usually try and calm the person without using medicines, for example by talking to them and trying to find out what would help to make the person feel better. If this does not work, rapid tranquillisation is usually given as a last resort because the risk to the person or others is too large unless they are given help to calm down. During and after rapid tranquillisation the person will be kept safe, treated with dignity and respect, and a member of staff will tell the person what is happening.

More information on rapid tranquillisation is available in the violence information for the public that NICE has produced, which is based on the NICE clinical guideline on violence.

About promethazine

There are various different medicines that can be used for rapid tranquillisation. The types of medicines that are most commonly used to try and calm agitation or aggression are a group of drugs called benzodiazepines and a group of drugs called antipsychotics. Usually they are given by mouth (orally) but injections may be used if a person refuses to take a medicine by mouth, or if the staff have good reason to think that oral medicines won't calm the person down quickly.

Sometimes the usual treatments aren't suitable for an individual. In very exceptional circumstances, haloperidol plus a drug called promethazine may be injected into a muscle. Promethazine is a medicine that is licensed to relieve the symptoms of some allergies (called an antihistamine). It also has some calming (sedative) effects and can help to induce sleep. Promethazine is not licensed for use in rapid tranquillisation and so this would be an off-label use of promethazine.
Summary of possible benefits and harms

How well do promethazine and haloperidol work?

A group of 4 studies (including more than 1000 people) carried out in Brazil and India have looked at how well promethazine and haloperidol, when taken together, work for rapid tranquillisation compared with other medicines that are used to treat agitation and aggression.

Of the 4 studies, 2 compared promethazine and haloperidol with another type of medicine called benzodiazepines. The studies had mixed findings. One found that people were more likely to be calm or asleep after 30 minutes if they were given promethazine and haloperidol than if they were given the benzodiazepine called lorazepam. Whereas the other study found that people were less likely to be calm or asleep after 30 minutes if they were given promethazine and haloperidol than if they were given the benzodiazepine called midazolam.

The difference between the results of these 2 studies does not appear to be only due to the different types of benzodiazepines used. For some reason, only two-thirds of people (67%) taking haloperidol and promethazine in the first study were calm or asleep by 30 minutes compared with almost all of the people (95%) in the second study (comparing the combination treatment with midazolam). It is not known why this is.

The other 2 studies compared promethazine and haloperidol with antipsychotics. One of these studies found that people were more likely to be calm or asleep if they were given promethazine and haloperidol than if they were given haloperidol by itself (haloperidol is an antipsychotic). The other study found that people were equally likely to be calm or asleep whether they were given promethazine and haloperidol or an antipsychotic called olanzapine.

Overall, the 4 studies provide some evidence that the combination of haloperidol and promethazine works for rapid tranquillisation. However, it is unclear how the combination compares with other treatments because the results of some of the studies are inconsistent. The benefits of the different treatments needed to be weighed up against their possible harms.

What are the possible harms or side effects?

When promethazine is used with haloperidol for rapid tranquillisation, the main risk is that the medicines will not just calm the person or make them go to sleep, but that they will deeply sedate the person or cause them to lose consciousness. If this happens, there is a risk that the person may
not be able to breathe so well, or it could affect their heart rate or blood pressure. For this reason, a person needs to be carefully monitored after they have been given promethazine and haloperidol.

Aside from tiredness, other known side effects of promethazine include feeling dizzy, restless or disorientated, and having headaches, blurred vision or a dry mouth.

Some of the other side effects that can happen are effects of haloperidol, rather than promethazine. Haloperidol can cause restlessness (the medical name is akathisia), rigid muscles (dystonia) and unwanted uncontrolled movements (dyskinesia). The study that compared promethazine and haloperidol with haloperidol taken on its own found that these side effects were less common in people given the combination than they were in people given haloperidol alone. However, other trials did not find any clear evidence that these side effects were less common when a person was given promethazine as well as haloperidol.

Please note that the results of the research studies only indicate the benefits and harms for the population in the study. It is not possible to predict what the benefits and harms will be for an individual patient being treated with promethazine.

Prescribing promethazine

If a prescriber wants to use an unlicensed or off-label medicine, they must follow their professional guide, for example for doctors the General Medical Council’s good practice guidelines. These include giving information about the treatment and discussing the possible benefits and harms so that the patient has enough information to decide whether or not to have the treatment. This is called giving informed consent.

But in an emergency, healthcare professionals may need to give treatment straightaway, without getting informed consent, when it is in someone's best interests. This is likely to be the case in many situations where promethazine would be used with haloperidol for rapid tranquillisation.

A full version of the summary aimed at healthcare professionals is available on the NICE website. The summary for healthcare professionals does not contain recommendations from NICE on whether the medicine should be used.

More information

The evidence summary and this information for the public were produced for NICE by Bazian Ltd.
NICE has published information about how evidence summaries for unlicensed and off-label medicines are developed.

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