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Paracetamol overdose

Paracetamol overdose is common and may occur accidentally or in the context of self-harm. Significant overdose can result in liver failure if not promptly treated with the antidote.

What happens when you overdose on paracetamol?

Paracetamol is usually taken by mouth and is available in various ways, such as in tablet, caplet, soluble and liquid forms. They will pass to the stomach and intestine into the body and lead to pain relief and lowering of a high temperature (fever).

After this, paracetamol is inactivated before being removed from the body. About 20% of the medicine is processed in the intestinal wall and the remainder in the liver. As a result a small amount of a toxic compound (n-acetyl-p-benzoquinone imine, or NAPQI) is formed in the liver but is quickly detoxified by a substance called glutathione.

However in overdose the stores of glutathione can be depleted so that there isn't enough to remove the increased amounts of NAPQI. The NAPQI can then build up and damage the liver.

Paracetamol is the most common medicine taken in overdose. It can lead to liver failure in a number of days, despite using medication to protect the liver. Liver failure can be fatal.

In 2021, there were 227 deaths recorded in England and Wales due to paracetamol overdose.

Why would someone take an overdose?

There are many reasons for someone to take an overdose. This could be to end one's life or to cause serious self-harm. An overdose can also be taken accidentally - for example, toddlers may like the taste of liquid paracetamol and people with poor eyesight may take the wrong tablet by mistake.

In some, the act of taking an overdose is a spur-of-the-moment thing, whilst in others it can be pre-planned. Those who have pre-planned may have stockpiled medication, sorted out their affairs (such as writing a will) and also written a suicide note.

Some people take higher-than-recommended doses of paracetamol for pain over several days. They may not intend to kill themselves, and occasionally may not even realise they are harming themselves until they begin to feel unwell. This might also occur if they are taking two different preparations which both contain paracetamol.

Some people are at increased risk of liver damage from paracetamol. This includes:

- Those on certain medications, such as rifampicin, phenobarbital, phenytoin, carbamazepine and alcohol.
- Those who are malnourished for example, through chronic illness or eating disorders.
- Those with alcohol-related liver disease.

Why paracetamol?

Paracetamol is widely available from shops and is present in most homes. The government has made rules to limit how much can be bought in one go, which may help reduce the number of overdoses. It is reasonably easy to take and so the government had also ruled that it should only be available in blister packs which can mean the tablets are trickier to get out.

What are the symptoms of paracetamol overdose?

There may be no symptoms for the first day. A feeling of sickness (nausea) and being sick (vomiting) may occur a few hours after taking the overdose. After 24 hours there may be pain under the ribs on the right side (where the liver is) and there may be yellowing of the whites of the eyes and the skin (jaundice). Other features include:

- The brain can also be affected with confusion and disorientation (called encephalopathy).
- The kidneys can also be affected with a reduction in urine, and kidney failure can occur.
- Low blood sugar (hypoglycaemia) may occur.
- There may be a build-up of acid in the blood, which can cause the patient to breathe faster.
- There may also be features of depression but not always.

Sometimes it is carers who will discover that someone has taken an overdose. They may find empty packets or a suicide note. It is important to bring the empty packets and notes with you to the hospital.

How is paracetamol overdose assessed in hospital?

The healthcare professional will make a full assessment and will also ask about:

- The number of tablets taken.
- What time the overdose was taken.
- Whether the medicine was in tablet, caplet, liquid or soluble form.
- Whether any other tablets were taken at the same time.
- Whether any alcohol was taken at the same time.
- Any suicide risk, such as whether a note was written.

They will also undertake a full examination which early on may not find anything. Once liver damage sets in there may be jaundice, a tender liver and presence of brain involvement (called encephalopathy). Unfortunately, it is often too late to do anything by this point, other than a liver transplant.

What investigations are needed?

This mainly consists of blood tests and includes:

Paracetamol levels

- If the tablets were all taken in one go: the paracetamol level needs to be checked four hours after the time of the overdose. If the time is unknown or more than four hours have passed then a sample will be taken immediately.
- If the tablets have been taken over several hours or days: this is called a 'staggered overdose' and a paracetamol level will be taken immediately and treatment started before the level is back. The level here only tells us that paracetamol has been taken.

Liver function tests

These are a group of blood tests that reveal how the liver is functioning. Early on, they may be normal. When they go high this tells us that liver cells have died and liver failure is possible. A blood clotting test (called prothrombin time) is an earlier and better indicator of liver damage.

Prothrombin time

As part of the blood clotting tests that will be requested, this gives an idea of how 'thin' the blood is. The liver makes important factors for blood clotting. When the liver becomes damaged, the prothrombin time rises. The higher the level, the more severe the liver involvement. It will be checked several times.

Renal function tests

These are blood tests looking at the function of the kidney. They will show if there is any kidney damage or kidney failure.

Blood sugar levels

Low levels (called hypoglycaemia) can occur when the liver is failing. A fingertip test will need to be done hourly.

Arterial blood gas

This involves an arterial blood sample being taken (usually at the wrist where the pulse is taken) and reveals levels of acid in the blood. Acid levels are very tightly controlled by the body and in paracetamol overdose acid levels can rise early. These patients are probably going to be sicker and some will develop liver failure.

Other tests that are requested will depend on each individual case and the patient's course. For example, if other medications were taken then their levels may need to be checked.

How can paracetamol overdose be treated?

Immediate management will require resuscitation and stabilisation. If the patient is unstable - such as having low blood pressure - or there is overwhelming liver failure, they will need to be treated on an intensive care unit.

The paracetamol levels will be sent off and once the result is back this is compared with a standard graph - patients who are above a certain line will need treatment. Those below the line may not require treatment.

Treatment is with intravenous N-acetylcysteine (NAC) and is given to all who have high paracetamol levels. If there is any doubt about the time of the overdose or there has been a 'staggered overdose', intravenous NAC is started without delay.

All patients will need to be seen by the psychiatric team before discharge. If there is concern about the risk of ongoing severe harm to the patient then they may be admitted to hospital, either with their agreement, or without their agreement under the Mental Health Act (colloquially known as 'being sectioned').

N-acetylcysteine (NAC) treatment

NAC protects the liver and this may be the result of it restoring the glutathione levels. It may also help the liver to combat toxicity. A full treatment course consists of three consecutive bags of the medicine, mixed with intravenous fluid and given over approximately 24 hours.

During that period several blood tests may be taken to monitor the liver and kidneys. It is most effective when given within eight hours of taking the paracetamol overdose.

If, however, there is ongoing damage from the paracetamol overdose then the NAC treatment may need to be prolonged. NAC is used in children and also in pregnant women. In pregnant women the paracetamol overdose can affect the liver of the fetus as well and NAC can help prevent this.

The main complication following a paracetamol overdose is liver failure.

The patient may need to be referred to the specialist liver unit if the bloods confirm liver failure.

Other features which will help the healthcare professionals to decide if the patient needs to go to a specialist unit include:

- Involvement of the brain.
- Abnormal clotting.
- Kidney impairment.
- Low blood pressure (hypotension).
- Low blood sugar (hypoglycaemia) and high blood acid levels.

Urgent liver transplantation is the only treatment when overwhelming, irreversible liver failure occurs.

Further reading

- Ferner RE, Dear JW, Bateman DN; Management of paracetamol poisoning. BMJ. 2011 Apr 19;342:d2218. doi: 10.1136/bmj.d2218.
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- Number of deaths from drug poisoning by paracetamol in England and Wales from 1993 to 2021; Statista, 2022

• Koppen A, van Riel A, de Vries I, et al; Recommendations for the paracetamol treatment nomogram and side effects of N-acetylcysteine. Neth J Med. 2014 Jun;72(5):251-7.

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