

New two-drug approach to treat type of respiratory disease

August 11 2011



Chest X-ray image before treatment

(Medical Xpress) -- A therapy combining two existing drugs could provide an effective new approach for treating patients with pleural infections, a serious condition where infected fluid builds up in the space between the ribs and lungs.

A randomised clinical trial conducted by researchers from Oxford and Bristol Universities and published in the [New England Journal of Medicine](#) has shown that two drugs for breaking up the thick [pleural fluid](#), when used together, improve drainage of the fluid from the chest.

The combination of [tissue plasminogen activator](#) (t-PA) and DNase also appears to significantly reduce the need for surgery, shorten the time

patients spend in hospital and reduce [fever](#).

‘This is an exciting result because this combination of two drugs has not been tested before for this condition. While neither [drug](#) appears to work on its own, the combination therapy very significantly improves the drainage of the infected fluid,’ says Dr Najib Rahman of the Oxford Respiratory Trials Unit at Oxford University, and first author on the study.



Chest X-ray image after treatment

Taking the UK and US together, around 65,000 people a year get pleural infections, which usually develop from [lung](#) infections such as pneumonia. The condition can cause breathlessness as the infected fluid underneath the rib cage pushes down on the lungs, and can lead to serious consequences for the patient.

‘This tends to be a disease of the very young and the very old, and the number of cases seems to be rising,’ explains Dr Nick Maskell of the University of Bristol's School of Clinical Sciences, who was also involved in the study.

Standard treatment involves giving patients antibiotics to treat the infection and a tube inserted into the chest to drain the fluid. But in around a third of cases this treatment fails.

Where treatment fails, options then normally involve surgery to drain the infected fluid, but this is invasive and may not always be suitable for older and more unwell patients where there may be other complications. As well as surgery, it can mean long hospital stays and in some cases, a slow and uncomfortable decline with a mortality rate of more than 20 per cent.

‘Reducing the 30 per cent failure rate for treatment is vital,’ says Dr Maskell.

The researchers at Oxford University led by the late Professor Robert Davies, along with colleagues at the MRC [Clinical Trials](#) Unit in London, set out to investigate whether two agents to break down components in the infected pleural fluid would help drainage and improve outcomes for patients.

They conducted a trial in which 210 adult patients at 11 UK centres were randomised to receive one of four study treatments for three days: placebo; t-PA alone; DNase alone; or both t-PA and DNase.

The two drugs when used together showed significantly improved drainage of the fluid from the chest, the primary outcome measure for the trial.

Over the course of a week, patients receiving both drugs saw a 30 per cent reduction in fluid volume seen in their chest X-rays, compared to 17 per cent for the placebo group. There was no effect above placebo for either drug on its own.

The number of patients referred for surgery over the next three months was also significantly lower for those receiving both drugs, and the mean hospital stay was between six and seven days less compared to the placebo group. However, these are secondary measures in the trial and larger studies involving more patients are needed to confirm the findings.

Any adverse events did not differ in frequency between study groups, suggesting the treatment is safe for these patients.

‘We’ve shown that the therapy clearly improves drainage of fluid in patients with pleural infection,’ says Dr Rahman of Oxford University. ‘But we still need to be cautious - it is not yet certain whether clearance of the chest X-ray translates in to important outcomes for patients, like reduced surgery rates, fewer fevers, and shorter stays in hospital. Although our results strongly suggest this is the case, larger studies are now needed to confirm this.’

Dr Rahman adds: ‘Our view is that it is not clear yet whether this combination of t-PA and DNase should be used for every patient as a first-line treatment, as it’s not proven that it would be best for everyone.

‘But in cases where perhaps patients have a large amount of fluid and are very breathless, or where treatments have failed and patients aren’t fit for surgery, then this drug combination is now a possible new treatment option.’

The two drugs are well known but treatment would cost around £1,000 per patient. However, the researchers believe the savings from shorter hospital stays suggested by their study may balance this out, even before considering any reduction in surgery cases – this will need to be looked at in further studies.

More information: 'Intrapleural use of tissue plasminogen activator and DNase in pleural infection' by Najib Rahman and colleagues is published in the *New England Journal of Medicine*.

Provided by University of Bristol

Citation: New two-drug approach to treat type of respiratory disease (2011, August 11) retrieved 20 April 2024 from

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