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Does tumour necrosis factor-alpha (TNFα) inhibitor therapy help reduce depression and anxiety in people with chronic physical illness?

Tumour necrosis factor–alpha (TNFα) is an important messenger protein in the body. It helps regulate our immune response to infection and plays a central role in promoting inflammation.

What did we find?

- Treatment that targets TNFα in people with rheumatoid arthritis, psoriasis and ankylosing spondylitis is associated with reductions in depression.
- Treatment that targets TNFα in people with rheumatoid arthritis and ankylosing spondylitis is also associated with reductions in anxiety.
- None of the studies found were able to determine whether the changes in depression and anxiety occurred independent of, or prior to, any changes in the physical illness itself.

Why did we do this review?

Depression is two to three times more common in people with chronic physical illnesses than in the general population. Chronic physical illnesses are health problems that can be managed but not cured, such as diabetes and arthritis. The causes of depression in the physically ill are complex. There is however growing interest in the role of inflammation in contributing to the development of depression in people with physical illness. For example, in some illnesses, treatments that induce inflammation have also been associated with the onset of depression.

New drug treatments for many chronic physical illnesses, such as arthritis and psoriasis, act by targeting tumour necrosis factor-alpha (TNFα). One of the roles of TNFα is to promote inflammation. If inflammation causes depression, then targeting TNFα may result in reductions in depression.

This review sought to determine whether treatment targeting TNFα in people with chronic physical illness is associated with reduced symptoms of depression, and if so whether these changes occur prior to any changes in the illness itself. Finding out whether reductions in inflammation reduce depression is important for future treatment of depression in chronic illness.

How did we do this review?

The research was a systematic review. This brings together all existing research on a particular question. To find studies that might help us to answer the question we searched the relevant academic literature. In particular, for this review, we looked for randomised controlled trials.

Six multi-site trials were found: one in the UK, one in South America, two across the United States and Canada, and one across Europe and Asia. The trials involved individuals with rheumatoid arthritis, psoriasis and ankylosing spondylitis, with the mean age of participants ranging from

Treatment targeting TNFα was found to reduce depression across the variety of clinical populations, irrespective of the depression assessment tool used. Although not measured in all studies, targeting TNFα treatment was also found to reduce anxiety.

None of the studies were able to determine whether the changes in depression and anxiety occurred independent of, or prior to, any changes in the physical illness itself.

Quality of the research and cautionary notes

While the evidence came from randomised controlled trials, reducing depression and anxiety were not the primary aim of the trials.

What next?

Understanding the causes of depression is of central importance in the management of individuals with chronic physical illnesses as it offers the opportunity to: i) identify those at greatest risk of additional illness burden due to depression, ii) identify those at risk of worse medical outcomes and iii) potentially reduce the risks of adverse medical outcomes, either by treating depression or increasing the intensity of medical management. To identify whether inflammation plays a causal role, future research studies in this area would benefit from more careful consideration given to the timing of measures of inflammation, physical illness and depression.

Contact details and further information about the published paper:

The PenCLAHRC EST is part of Evidence Synthesis and Modelling for Health Improvement (ESMI), at the University of Exeter Medical School. Further information about this research is available on the University of Exeter Medical School website: **http://medicine.exeter.ac.uk/esmi/workstreams/**

The full version of the systematic review of these findings are published in the Journal of Psychosomatic Research. You can access the paper here: **http://www.sciencedirect.com/science/article/pii/S0022399915002445**

If you would like copies, please email the evidence synthesis team on: **evidsynthteam@exeter.ac.uk**

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