

Diabetes drug reduces complications of long-term steroid therapy

February 25 2020



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A drug used to treat type 2 diabetes could offer a simple and cheap solution to reduce dangerous side effects of steroid treatment, new research from Queen Mary University of London suggests.

The phase 2 clinical trial, funded by Barts Charity, looked at the effects

of the diabetes drug metformin on patients currently receiving high doses of glucocorticoids, a type of steroids used to treat [chronic inflammatory diseases](#).

The researchers analysed results from over 50 non-diabetic patients on [glucocorticoid](#) treatment from Barts Health NHS Trust and found that patients treated with metformin showed improved clinical outcomes. This included a 30 percent reduction in the rate of infections and lower hospital admissions, in comparison to the placebo group.

They also observed that treatment with metformin strengthened the intended anti-inflammatory effects of glucocorticoids and had beneficial results on several cardiovascular, metabolic and bone markers over the 12-week trial period.

The study is published today in the journal *The Lancet Diabetes & Endocrinology*, funded as part of a wider £25m commitment by Barts Charity to support innovative medical research at Barts and the London School of Medicine and Dentistry at Queen Mary.

Since the discovery of their therapeutic effects in the 1950s glucocorticoids, such as prednisolone, have revolutionized treatment of patients with chronic inflammatory disease. Now glucocorticoids are used to treat a range of conditions where the immune system is overactive, including rheumatoid arthritis, asthma, inflammatory diseases, and in [cancer therapy](#).

However, prolonged use of these medicines at high doses can lead to serious metabolic side effects such as weight gain, high sugar levels, loss of bone and muscle mass, and increased risk of infection and thrombosis.

Long-term, these features can lead to Cushing's syndrome, a potentially

fatal disorder which also exists in patients where the body makes too much of the stress hormone cortisol.

Several biological medicines have been developed as alternatives to steroids but these drugs are expensive and can present their own adverse effects.

Previous research from Professor Márta Korbonits and colleagues found that steroids are able to influence a key metabolic protein, called AMP-kinase or AMPK. Other experimental studies have suggested that metformin acts, at least partly, via the AMPK protein and in the opposite way to steroids. Based on this evidence, the researchers reasoned that the diabetes drug held the potential to reverse the unwanted side effects of steroids.

Professor Márta Korbonits, Professor of Endocrinology at Barts and the London School of Medicine and Dentistry at Queen Mary, said: "Our findings are strikingly positive and suggest that a simple and immediately available intervention, treatment with the diabetes drug metformin, can improve the clinical status of patients on glucocorticoid treatment, even if they do not have diabetes. The results could have a huge impact on the large number of patients on long-term glucocorticoids, improving treatment-related complications and their cardiovascular prognosis.

"Whilst developed countries may be increasing the use of biologics or other steroid-sparing agents, in many other parts of the world there's still a heavy reliance on glucocorticoids. Therefore, doctors and patients have been waiting for a safe, cheap and effective treatment that can prevent the major metabolic complications of these medicines, but does not affect, or could even improve, their anti-inflammatory properties. Our results suggest metformin has the potential to help these patients."

Fiona Miller Smith, Chief Executive of Barts Charity, said: "At Barts Charity we are funding research to pioneer improvements in healthcare that not only enhance the lives of patients in our hospitals and local community but can also have an impact worldwide.

"Steroids are used to treat a vast range of conditions, from cancer to [rheumatoid arthritis](#), and a large number of over 60s need to take these drugs to manage chronic conditions that could otherwise become extremely debilitating. The promising findings of this study show how funding innovative research can help us rethink long-standing problems facing patients and healthcare professionals, and in this case, even deliver new, simple and cost-effective treatment options for the NHS."

It is estimated that around three percent of the general adult population and up to 11 percent of over 80s are currently prescribed long-term steroid treatment for chronic inflammatory disease.

More information: *The Lancet Diabetes & Endocrinology* (2020).
[DOI: 10.1016/S2213-8587\(20\)30021-8](https://doi.org/10.1016/S2213-8587(20)30021-8) ,
[www.thelancet.com/journals/lan ... \(20\)30021-8/fulltext](https://www.thelancet.com/journals/lan.../fulltext)

Provided by Queen Mary, University of London

Citation: Diabetes drug reduces complications of long-term steroid therapy (2020, February 25) retrieved 10 April 2024 from
<https://medicalxpress.com/news/2020-02-diabetes-drug-complications-long-term-steroid.html>

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