

Methotrexate use in men who wish to conceive a child



Treatment with methotrexate is not associated with testicular toxicity.

INTRODUCTION

Immune-mediated inflammatory diseases (often shortened to IMID) include rheumatoid arthritis, psoriatic arthritis, and psoriasis. These chronic inflammatory diseases can affect people of all ages, which can impact people's decisions to start a family – and their treatment choices.

There are many treatments available for IMIDs, including traditional drugs such as methotrexate, as well as newer biologic and targeted synthetic therapies. Methotrexate is one of the most frequently prescribed immunosuppressive drugs for the treatment of several IMIDs. However, despite how common it is, there is not much evidence about whether methotrexate affects the quality of a man's sperm. This has resulted in conflicting recommendations about the safety of methotrexate in men who wish to have children.

It is known that an enzyme called FPGS (short for folylpolyglutamat-synthase) has to modify the methotrexate structure before it can have an effect in the body, but it is not known if this happens in sperm or semen.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to find out if methotrexate is safe for men who want to start a family.

WHO WAS STUDIED?

The study looked at 20 men diagnosed with an IMID, and 25 men without an IMID (the control group). Everyone was aged 18 or older.

HOW WAS THE STUDY CONDUCTED?

This was a prospective observational study. This means that the people taking part were not randomised to receive any particular drug, but instead were simply observed in normal clinical practice and their data recorded.

The men diagnosed with an IMID taking part were all already going to start methotrexate. They agreed to give two semen samples: one before starting methotrexate, and one after 12 weeks. The authors measured several markers of testicular function, male fertility, and toxicity. The results were compared both before and after methotrexate treatment, and against the control group who did not have an IMID.

The authors also looked to see whether methotrexate can be activated or 'switched on' in semen by the FPGS enzyme.

WHAT WERE THE MAIN FINDINGS OF THE STUDY?

The main finding was that there were no differences in sperm quality. This included between samples from before and after methotrexate treatment, and between the men with IMID and controls.

The activated form of methotrexate was detected in the sperm and semen fluid, but importantly the enzyme responsible for turning on the drug's activity was not very active in the sperm.

ARE THESE FINDINGS NEW?

Yes. To the best of the authors' knowledge this is the first study designed specifically to evaluate the effect of methotrexate on several markers of male fertility. In addition, this is also the first study to demonstrate the activity of FPGS in sperm.

WHAT ARE THE LIMITATIONS OF THE STUDY?

One limitation is the study used only a small group of men, and did not take samples from people who had taken methotrexate for a long time. Also, the researchers took only one semen sample per study visit, but ideally this should have been two samples, with an average value reported. It is known that sperm concentrations vary widely between samples, so this could have influenced the results.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

The authors are recruiting more chronic users to see if long-term exposure to methotrexate can be also considered as safe in terms of testicular toxicity. However, they say that the findings from this study that show that the enzyme responsible for activating methotrexate is poorly active in sperm are reassuring. As such, they do not expect chronic methotrexate use to result in testicular toxicity.

WHAT DOES THIS MEAN FOR ME?

If you are a man taking methotrexate for an IMID – and want a baby – these findings suggest that it is safe to carry on taking your treatment while you are trying to father a child. There is no evidence that methotrexate is associated with testicular toxicity in men diagnosed with an IMID.

If you have any concerns about your disease or its treatment, you should talk to your doctor or a healthcare professional involved in your care.

Disclaimer: This is a summary of a scientific article written by a medical professional (“the Original Article”). The Summary is written to assist non medically trained readers to understand general points of the Original Article. It is supplied “as is” without any warranty. You should note that the Original Article (and Summary) may not be fully relevant nor accurate as medical science is constantly changing and errors can occur. It is there for every important that readers not rely on the content in the Summary and consult their medical professionals for all aspects of their health care and only rely on the Summary if directed to do so by their medical professional. Please view our full Website Terms and Conditions. <http://www.bmj.com/company/legal-information/>

Date prepared: June 2023

Summary based on research article published on: 1 June 2023

From: Perez-Garcia LF, et al. Is methotrexate safe for men with an immune-mediated inflammatory disease and an active desire to become a father? Results of a prospective cohort study (iFAME-MTX). *Ann Rheum Dis* 2023;82(8):1068–75. doi:10.1136/ard-2023-224032

Copyright © 2024 BMJ Publishing Group Ltd & European League Against Rheumatism. Medical professionals may print copies for their and their patients and students non commercial use. Other individuals may print a single copy for their personal, non commercial use. For other uses please contact our [Rights and Licensing Team](#).