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Treatment with methotrexate and risk of lung disease in patients with rheumatoid arthritis

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Patients with rheumatoid arthritis (RA) often suffer from what is referred to as interstitial lung disease (ILD). For years, standard medication with Methotrexate (MTX) has been suspected of either increasing the risk of, or worsening, this aspect of rheumatoid arthritis. This suspicion is now refuted by two current studies. The results have been presented at the annual conference of the European League Against Rheumatism (EULAR 2020).

Interstitial lung diseases (ILDs) are a common and serious consequence of rheumatoid arthritis (RA). The prevalence varies depending on population and diagnostic method, but at least 5 to 10% of all RA patients suffer from this condition, which leads to inflammatory changes in lung tissue and pulmonary alveoli. It is accompanied by a dry cough and breathing difficulties. A severe course may lead to scarring of lung tissue, which is referred to as lung fibrosis. This may lead to a life-long dependency on oxygen supply or even a lung transplant. "In approximately 10 to 20% of all RA patients, lung disease is the cause of premature death," explains EULAR President Professor Dr. med. Iain B. McInnes from The University of Glasgow, Scotland, Great Britain. "Particularly in these times when we are concerned about respiratory infections, the reduction of additional risk factors for lung damage of rheumatoid arthritis patients must be evaluated."

For this reason, rheumatologists welcome the results of two new studies

indicating that the immunosuppressant Methotrexate, which can provoke an acute lung condition (acute pneumonitis), does not appear to be an additional risk factor for chronic interstitial lung diseases in RA patients. In previous years, it was suspected that this immunosuppressant may increase the risk for RA-associated chronic ILD.

"RA patients have a higher risk of suffering from interstitial lung disease than the general population. However, based on our large dataset, there is no evidential correlation to the treatment with Methotrexate," explains Professor Dr. Lene Dreyer from Aalborg University in Denmark, summarising the results of her current cohort study. Dr. Dreyer's research refers to patient data from the Danish National patient registry as well as the DANBIO registry for rheumatic conditions. In cooperation with the team of researcher Else Helene Ibfelt from the Steno Diabetes Center Copenhagen, Denmark, she examined a total of 30,512 RA patients registered there between 1997 and 2015 for ILD and breathing conditions, taking into account their respective medication.

A current case control study also examining the connection between treatment with MTX and lung diseases in France came to the same conclusion. "In a total of 1,223 RA patients, we were not only able to show that MTX has no impact on the development of interstitial lung diseases but, in fact, may contribute to delaying this development," summarises the author Dr. Pierre-Antoine Juge from Bichat-Claude Bernard Hospital in Paris, France. The number of RA patients affected by ILD therapy was reduced by more than half in comparison with RA patients not receiving any MTX treatment."

"Of course, further examinations are required to support the results and assure patients and physicians that treatment with MTX does not have any negative impact on the pulmonary health of patients suffering from rheumatoid arthritis," explains Professor Dr. John Isaacs, EULAR Scientific Chair, The University of Newcastle, Great Britain. Currently

there are very few effective treatments for interstitial lung disease, increasing the importance of these results, which may even suggest methotrexate as a potential therapy. But, notwithstanding these data in relation to RA-associated ILD, it remains important to remember that MTX can cause an acute pneumonitis.

Due to the still existing general risk for ILD, experts recommend examining RA patients regularly for any pulmonary changes to enable timely treatment–particularly in times of the COVID-19 pandemic. In case of any suspicion of ILD, the degree of reduction in pulmonary function can be determined by means of functional examinations of the lung. ILD can also be diagnosed by means of medical imaging such as computer tomography or bronchoscopy.

More information: Giulia Cassone et al. Treatment of Rheumatoid Arthritis-Associated Interstitial Lung Disease: Lights and Shadows, *Journal of Clinical Medicine* (2020). DOI: 10.3390/jcm9041082

Treatment with methotrexate and risk of lung disease in patients with rheumatoid arthritis: a nationwide population-based cohort study from Denmark. DOI: 10.1136/annrheumdis-2020-eular.1609

Methotrexate and rheumatoid arthritis associated interstitial lung disease. DOI: 10.1136/annrheumdis-2020-eular.1678

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