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Treatment of rheumatoid arthritis may reduce cardiovascular risk

Reducing rheumatoid arthritis activity itself may be more important in cardiovascular risk than worrying about the cardiovascular hazard of drugs commonly used to treat patients with rheumatoid arthritis.

Dr Christopher Edwards (Consultant Rheumatologist, Southampton University Hospitals NHS Trust) reported that the use of conventional disease-modifying anti-rheumatic drugs (DMARDs) may be less important as predictors of cardiovascular events such as myocardial infarction than the traditional culprits, such as age, sex and diabetes.

Dr Edwards and colleagues trawled a UK database of more than 34 000 adults with rheumatoid arthritis to estimate the incidence of myocardial infarction and assess whether DMARD and corticosteroid therapy played a role.

The investigation documented 6.49 heart attacks per 1000 people per year among patients with rheumatoid arthritis compared to only 2.96 per 1000 people each year in a control group.

The myocardial infarction incident rate ratio (IRR) was increased by a diagnosis of rheumatoid arthritis (2.23, $P<0.001$). Of 966 cases of myocardial infarction occurring in rheumatoid arthritis patients, 705 (73%) received a DMARD or prednisolone during the study (before the myocardial infarction) with 538 (56%) receiving a DMARD or prednisolone in the 2 months immediately before the myocardial infarction.

The chance of having an myocardial infarction among patients with rheumatoid arthritis who had been prescribed a DMARD or prednisolone was reduced compared to the chance of myocardial infarction in patients who had not been prescribed either.

When analysing DMARDs separately, hydroxychloroquine (IRR *vs* no drug 0.42, $P=0.03$), methotrexate (IRR *vs* no drug 0.67, $P=0.03$) and sulphasalazine (IRR *vs* no drug 0.69, $P=0.004$) were each protective against myocardial infarction among rheumatoid arthritis cases, whereas prednisolone increased the risk (IRR *vs* no drug 1.49, $P<0.001$).

In a second study, Dr Edwards and colleagues found that treatment with lipid-lowering drugs was associated with a significant 25% reduction in the incidence of myocardial infarction (IRR 0.75, $P=0.003$). Treatment with anti-hypertensive drugs had no significant effect (IRR 0.92, $P=0.062$).

However, when they looked at the effect that traditional risk factors have on myocardial infarction, they found that although these factors were important, the effect of having rheumatoid arthritis itself was greater.

Dr Edwards concluded: 'Individuals with rheumatoid arthritis have an increased risk of myocardial infarction that remains after adjusting for traditional risk factors. Lipid-lowering medications produce a significant reduction in this risk.

'However, rheumatoid arthritis itself appears to be the key – and treating rheumatoid arthritis with the right DMARDs or biologic therapies may help to reduce cardiovascular risk over time. Other traditional risk factors cannot be ignored and have to be addressed.'

Stephen Pinn

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B-cell depletion to treat lupus

Nearly 90% of patients using B-cell depletion therapy with rituximab to treat systemic lupus erythematosus achieved partial or complete remission.

Professor David Isenberg (Professor of Rheumatology, University College Hospital, London) reported new data on long-term therapy with rituximab in 50 patients who had failed conventional immunotherapy (96% female, mean age 32.8 years, mean disease duration 10.4 years).

Patients received a combination of rituximab (1 g), cyclophosphamide (750 mg) and methylprednisolone (125–250 mg) administered twice 2 weeks apart to achieve B-cell depletion (an absolute CD19 count $<0.005 \times 10^9$/litre after treatment).

The mean duration of follow-up after B-cell depletion was 39.6 months, with 35 of 45 patients (78%) followed-up for at least 12 months. After B-cell depletion, the clinical outcome at 6 months in 45 patients was full remission in 19 (42%), partial remission in 21 (47%) and no improvement in five (11%).

Stephen Pinn

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Combining methotrexate with tocilizumab improves outcomes

International investigators reported 'remarkable' findings after combining methotrexate with tocilizumab.

Professor Paul Emery (Professor of Rheumatology and Head of Musculo-Skeletal Medicine, University of Leeds) outlined data from RADIATE (Research on Actemra Determining effIcacy after Anti-TNF failures), which investigated the efficacy and safety of tocilizumab + methotrexate in 499 rheumatoid arthritis patients who had responded inadequately to treatment with at least one anti-tumour necrosis factor agent (etanercept, infliximab or adalimumab). The combination of methotrexate and tocilizumab overcame earlier treatment failures.

With the larger of two tocilizumab doses (8 mg/kg) studied, 30% of anti-tumour necrosis factor failures achieved remission after 24 weeks.

Stephen Pinn

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