Biologic therapies for rheumatoid arthritis may protect against rapid bone loss

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A new review by the International Osteoporosis Foundation (IOF) Chronic Inflammation and Bone Structure (CIBS) Working Group concludes that early and aggressive treatment of Rheumatoid Arthritis (RA) with biologic drugs, specifically biological disease-modifying anti-rheumatic drugs (DMARDs), may be most effective in halting progressive bone loss in patients with RA.

Co-Author Dr. Cristiano Zerbini MD, Director of the Centro Paulista de Investigação Clinica (CEPIC) in Sao Paolo, Brazil, stated:

"Bone loss is one of the most harmful effects induced by chronic inflammation as well as by medications taken to treat rheumatoid arthritis, such as glucocorticoids. It is therefore important that we gain a better understanding of which medications used to treat patients with chronic inflammation are less likely to impact negatively on bone health ."

The progressive bone loss in RA has a number of causes. The development of chronic inflammation impacts on the immune system and this leads to signs and symptoms that may enhance bone loss. Anorexia, malnutrition, muscle wasting, cachexia and depression are directly or indirectly related to chronic inflammation. Decreased functional capacity and lack of exercise associated with joint pain and deformities further contribute to progressive bone loss. Most importantly, the use of corticosteroids during RA treatment, even a small dose of prednisone of 5mg/day or equivalent for more than 3 months, is

associated with rapid and persistent loss of bone. One study has shown that continuous treatment with prednisone at 10 mg/day during 90 days or more increased the risk of vertebral fractures 17-fold and hip fractures 7-fold.

The review 'Biologic therapies and bone loss in rheumatoid arthritis' presents the best evidence available regarding bone loss in RA patients. It takes an in-depth look at the mechanisms of bone destruction in RA, including: RA serum markers and bone loss; anti-citrullinated protein antibodies (ACPAs) and bone; effects of biologic DMARDs on bone such as TNF-? inhibitors and their effects on bone mineral density (BMD)and on biochemical markers of bone turnover; and Interleukin-6 blockade. It also reviews the latest information on biologic therapies that target the lymphocyte, specifically the blockade of the B-lymphocyte; co-stimulation blockade; biologic anti-osteoclast treatment.

The Working Group concluded that:

- Early and "aggressive" treatments were more effective in rapidly achieving a low level of inflammation and halting the progressive loss of bone.
- Therapies targeting specific cytokines and its signaling pathways with biologic DMARDs may protect the skeleton and should be introduced as soon as possible. However, it should be noted that outcomes in these clinical studies were based mostly on changes in biological markers and only a few reported modifications on BMD or localized osteoporosis. Only three retrospective studies reported reduction in fracture risk after anti-TNF therapy.
- The TNF blockade studies showed that, even in RA patients not responsive to treatment, a protective effect on bone was observed suggesting the possibility that anti-TNF therapy may restore coupling of the bone remodeling independently of its anti-inflammatory action.

- Lack of efficacy of TNF blockade on hand bone loss was found, despite its preservation of BMD in lumbar spine and hip. Better results regarding localized bone loss were observed with anti-IL6 treatment.
- Very few studies reported inhibition of bone loss after rituximab and abatacept treatment.
- Anti-RANKL therapy showed beneficial effects in the preservation of bone mass in RA, especially in juxta-articular osteoporosis, although this treatment cannot alter the inflammatory process.
- New non-biologic therapies but potent inhibitors of the cytokine network may offer future options for skeleton preservation in RA.

Professor Patricia Clark, MD, Co-author, Head of Clinical Epidemiology, Hospital Infantil de Mexico, Mexico City, stated:

"Although several studies reported favourable actions of biologic therapies on bone protection, it is clear that there are still unmet needs for research into their actions on the risk of bone fractures in RA patients. In the meantime, we recommend that all physicians treating RA remain vigilant of the high risk of bone loss and fractures in their patients. For many such high risk patients, it is important that osteoporosis treatment be considered to reduce fracture risk."

More information: C. A. F. Zerbini et al, Biologic therapies and bone loss in rheumatoid arthritis, *Osteoporosis International* (2016). DOI: 10.1007/s00198-016-3769-2

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