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Paroxetine and rivastigmine mitigates adjuvant-induced rheumatoid arthritis in rats: Impact on oxidative stress, apoptosis and RANKL/OPG signals.

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Abstract

Rheumatoid arthritis (RA) is considered a form of inflammatory autoimmune disease with unknown etiology, but environmental and genetic causes are sharing. T-cells, B-cells, synovial cells, osteoclast, and chondrocytes are the main cell types in RA pathophysiology. The present study aimed to investigate the anti-rheumatic effects of paroxetine, a selective serotonin reuptake inhibitor (SSRI), and rivastigmine, acetyl choline esterase inhibitor (AChEI), in complete Freund's adjuvant (CFA)-induced RA. Adult female rats were categorized into five groups of eight rats each: normal control received vehicles only, RA control received CFA (0.4 ml, s.c) dexamethasone group (1 mg/kg/day, p.o), paroxetine group (10 mg/kg/day, i.p) and rivastigmine group (1 mg/kg/day, i.p). All treatments were administered for 13 consecutive days. Specific rheumatoid marker rheumatoid factor (RF), cartilage oligomeric protein (COMP) and matrix metalloproteinase-3 (MMP-3) were determined. Serum MDA and reduced GSH levels were investigated as oxidative stress biomarkers. IL-6, TNF-α, and monocyte chemotactic protein-1 (MCP-1) were also determined as inflammatory biomarkers. Tissue Receptor activator of nuclear factor kappa-B ligand/osteoprotegerin (RANKL/OPG) expression levels were detected using qRT-PCR. Paroxetine and rivastigmine significantly reduced RF, COMP, MMP-3, IL-6, TNF-α, and MCP-1 serum levels. Tested drugs also significantly reduced serum MDA and increased GSH levels. In addition, paroxetine and rivastigmine attenuated histopathological variations by reducing pannus formation and return synovial fluid near to normal. Administration of paroxetine or rivastigmine normalized caspase-3 and RANKL/OPG in CFA-induced RA. In conclusion, paroxetine and rivastigmine possess antirheumatoid effects in CFA-induced RA which is mediated through antioxidant, anti-inflammatory, antiapoptotic and modulation of RANKL/OPG expression levels.

KEYWORDS:

Apoptosis; Paroxetine; RANKL/OPG; Rheumatoid arthritis; Rivastigmine

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