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Title:	A COMPARISON OF CLINICAL EFFICACY OF LEFLUNOMIDE VS OTHER THERAPEUTIC OPTIONS IN THE TREATMENT OF RHEUMATOID ARTHRITIS
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OBJECTIVES:The objective of this study was to compare efficacy and safety of leflunomide with biological antirheumatic drugs (adalimumab, etanercept, infliximab, rituximab, anakinra) in active rheumatoid arthritis.

METHODS: Comparison was based on systematic review, carried out according to guidelines published by the Cochrane Collaboration and Agency for Technology Assessment in Poland. The most important medical databases (EMBASE, MEDLINE, CENTRAL) were searched. Two reviewers independently selected trials, assessed trial quality and extracted data. No head to head trials were identified so indirect comparison using Bucher's method was performed.

RESULTS:The results of 33 randomized controlled trials were included in indirect comparison. Leflunomide was shown to have better ACR20 response than anakinra (RR=1.44 [1.14; 1.81]) but no significant differences in ACR response were found in comparisons with other drugs. Comparisons of HAQ disability scores indicate that leflunomide reduces disability better than adalimumab (WMD=-0.15; [-0.29; -0.01]), infliximab (WMD=-0.35 [-0.50; -0.20]), anakinra (WMD=-0.47 [-0.69; -0.25]), rituximab (WMD=-0.38 [-0.59; -0.17]), but not etanercept (WMD=-0.18 [-0.37; 0.01]). Radiographic improvement was better in comparison with anakinra (WMD=-2.99 [-5.82; -0.16]) and rituximab (WMD=-4.05 [-6.67; -1.43]) whereas worse in comparison with adalimumab (WMD=2.67 [0.87; 4.47]), etanercept (WMD=1.75 [0.01; 3.49]) and infliximab (WMD=2.06 [0.42; 3.70]). Leflunomid significantly increases the risk of treatment discontinuation due to the adverse events in comparison with etanercept (RR=3.50 [1.55; 7.88]). No significant differences in safety outcomes were noted between leflunomid and other drugs.

CONCLUSION: Indirect comparisons indicate similar efficacy of leflunomid, adalimumab, etanercept, infliximab or rituximab. Leflunomide seems to be more effective than anakinra. Safety profile of leflunomide is worse in comparison with etanercept, whereas in comparison with other analyzed drugs no differences were found.