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**Comparison of intra-articular injection of Naproxen and glutathione
in treatment of knee rheumatoid arthritis in a male rabbit model**

Abstract

Rheumatoid arthritis (RA) is a chronic progressive inflammatory joint disorder. Targeting drug delivery spares adverse effects and optimizes therapy. This study sought to compare the hematological and immunological impacts of intra-articular Naproxen sodium and glutathione (GSH) in an arthritis rabbit model. Twelve adult male rabbits (2.5–3.5 kg weight), were placed in separate cages under standard conditions and divided into 4 groups (3 each). The positive control group (PCG) was given intra-articular (IA) bovine serum albumin (BSA), the negative control group (NCG) was given IA normal saline, the GSH group was given IA BSA with GSH for three days, and the Naproxen group was given IA BSA with Naproxen for three days. Blood samples were collected from the lateral saphenous vein and marginal ear vein at day seven post treatment with BSA into plain tubes to separate serum for the rheumatoid factor (RF) test. The second collection of blood fraction was used for blood indices, including RBCs (red blood cells), Hb (hemoglobin), HCT (hematocrit), MCV (mean corpuscular volume), MCH (mean corpuscular hemoglobin), MCHC (mean corpuscular hemoglobin concentration), RDWCV (red cell distribution width – coefficient of variation). The Naproxen group showed the highest RBCs (6.4 ± 0.2), Hb (14.2 ± 0.4), and MCHC (33.6 ± 0.5), while also demonstrating elevated MCH (22.3 ± 0.6) and maintaining HCT levels (42.1 ± 1.0). The GSH group demonstrated the lowest levels of these parameters. Regarding WBCs, the GSH group showed the highest value in WBCs (10.5 ± 1.64), compared to the positive control ($P = 0.003$), negative control ($P = 0.021$), and Naproxen groups ($P < 0.001$). The Naproxen group demonstrated the lowest total WBC count (5.7 ± 1.0) and markedly reduced lymphocyte percentage (55.9 ± 6.1) compared to all other treatment groups. The PLT count revealed marked variations in the four treatment groups, with the positive control group demonstrating significantly lower PLT versus all other groups. The positive control group reported significantly elevated RF (24.0 ± 13.5) levels compared to other treatment groups ($P < 0.001$ for negative control and glutathione, $P = 0.002$ for Naproxen). The results confirmed significant improvement in WBC count in the glutathione group compared to the Naproxen group. This study concluded that an intra-articular glutathione injection may alleviate arthritis. Yet, further investigation is required to better understand the role of glutathione role in the healing course of arthritis.