
**Differential impact of biologics and glucocorticoids on TNF secretion and %CD14$^+$CD16$^+$ monocytes derived from synovial fluids of PsA patients in vitro**

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**Background**: The potential beneficial role of intra-articular injection of tumor necrosis factor (TNF) inhibitors (i) compared to glucocorticoids (GCs) in reducing synovitis has not been well studied. The inflamed synovial fluid is rich in mononuclear cells, however, the response of these cells to drugs with different mechanisms may contribute to the understanding of the cellular response to therapeutic agents in central as opposed to peripheral compartments.

**Aim:** To evaluate the effect of biologics used in the management of PsA on synovial fluid mononuclear cells (SFMCs) in vitro and to compare their modes of action to GCs, currently used to locally alleviate synovial inflammation.

**Methods:** SFMCs derived from PsA patients (n=11) were cultured in vitro in the presence of biologics with different mode of actions (adalimumab, infliximab, secukinumab and ustekinumab, 10ug/ml) and GCs (betamethasone and methylprednisolone, 1 ug/ml and 10ug/ml) or medium as control. Levels of the secreted TNF were measured by ELISA. Changes in %CD14$^+$CD16$^+$ monocytes were analyzed by flow cytometry.

**Results:** TNFi (adalimumab $p<0.01$, infliximab $p=0.0003$) and GCs (betamethasone and methylprednisolone at 1ug/ml $p<0.01$ and at 10ug/ml $p<0.04$) significantly reduced TNF levels in supernatants derived from SFMCs of PsA patients (n=8) compared to medium. None of the other biologics reduced TNF levels (Fig. 1A). Additionally, %CD14$^+$CD16$^+$ in SFMCs derived from PsA patients (n=11) were significantly reduced by TNFi ($p=0.0003$) compared to medium. However, other biologics and GCs did not display similar activity (Fig. 1B).

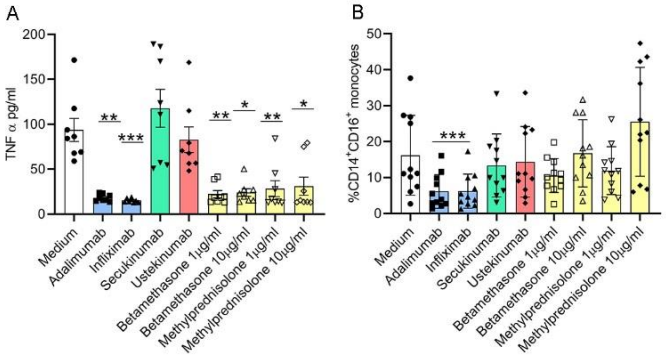


**Figure 1.** *TNFi and GCs block TNF secretion but exhibit different activity on inflammatory CD14$^+$CD16$^+$ monocytes derived from SFMCs of PsA patients*. SFMCs were co-cultured with adalimumab, infliximab, secukinumab and ustekinumab at 10ug/ml or with betamethasone and methylprednisolone at 1ug/ml and 10ug/ml or with medium alone. (A) Supernatants were analyzed for TNF levels (n=8). (B) Cells were analyzed for %CD14$^+$CD16$^+$ monocytes (n=11). All $p$ values were calculated by the non-parametric one-

way ANOVA Kruskal-Wallis test and Dunn's multiple comparison test, *$p$<0.04, **$p$<0.01 and ***$p$=0.0003.

**Conclusion:** TNFi and GCs suppress TNF secretion but only TNFi reduced the %$CD14^+CD16^+$ monocytes, none of the other biologics exhibit similar activity. These findings suggest an additional mechanism of action exerted directly by TNFi on synovial monocytes which differs from that of GCs.