

Interleukin-18 in Juvenile Idiopathic Arthritis Patients: a Marker of Disease Activity and Damage

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Objectives

- To measure IL-18 levels in the synovial fluid (SF) and serum of JIA patients
- To establish possible correlations between IL-18 levels and parameters of disease activity and severity as well as with other proinflammatory cytokines

To verify the importance of IL-18 in JIA pathogenesis



Patients and Methods

- 50 JIA patients who underwent knee steroid infiltration
- Type of disease onset: 13 systemic, 13 polyarticular
24 oligoarticular
- Mean age 11.6 years (6.6-22 y)
- Mean disease duration 6.9 years (0.2-20 y)
- 25 healthy matched controls (mean age-10.4 y)

Patients and Methods

- Clinical evaluation and review of medical records
- SF and blood collected simultaneously
- Quantification of cytokines (IL-1, IL-1Ra, IL-6, IL-18): ELISA
- Disease activity parameters: ESR, CRP, platelet count
- Radiological assessment: Steinbrocker method

| Treatment (%) | OLIGO (n=24) | POLY (n=13) | SYSTEMIC (n=13) |
|---------------------|-----------------|----------------|--------------------|
| NSAID | 70 | 15 | 0 |
| NSAID+DMARD | 25 | 69 | 23 |
| NSAID+DMARD+Steroid | 12 | 15 | 77 |

* $p < 0.05$

Results: IL-6

- Patients > controls
- Systemic onset patients ↑ ↑ levels of serum/SF IL-6
- Serum IL-6 correlated with:
 - Number of active and limited joints ($p < 0.006$)
 - C reactive protein ($p < 0.0001$) and ESR ($p = 0.004$)
 - Number of platelets ($p < 0.0001$)
 - Radiological score ($p = 0.006$)
- SF IL-6 correlated with:
 - IL-1 β ($p = 0.004$) and IL-1Ra ($p = 0.007$)
 - Number of SF leucocytes/PMN ($p < 0.0001$)





Results: IL-1 and IL1-Ra

- Patients > controls (serum) ($p=0.01$)
- SF levels > serum ($p<0.05$)
- Similar among types of onset (SF and serum)

- **No correlation with:**

- Number of active or affected joints
- Functional or radiological class
- ESR or CRP
- Parent and physician evaluation
- Disease duration
- Morning stiffness

Results: IL-18

- Patients > controls ($p=0.002$)

Patients: 963 ± 971 pg/ml Controls: 378 ± 192 pg/ml

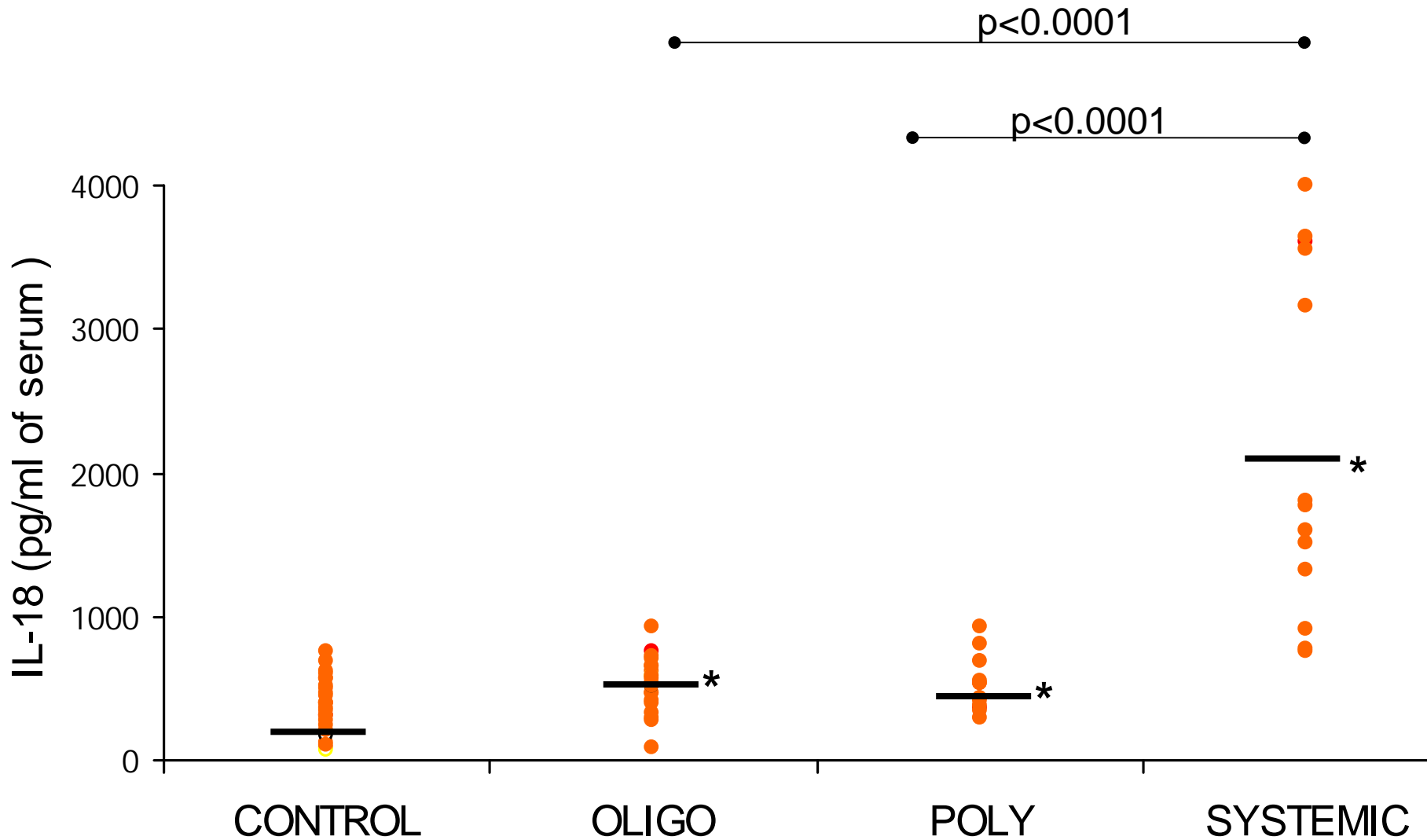
- Serum levels ~ SF

Serum: 963 ± 971 pg/ml SF: 947 ± 602 pg/ml

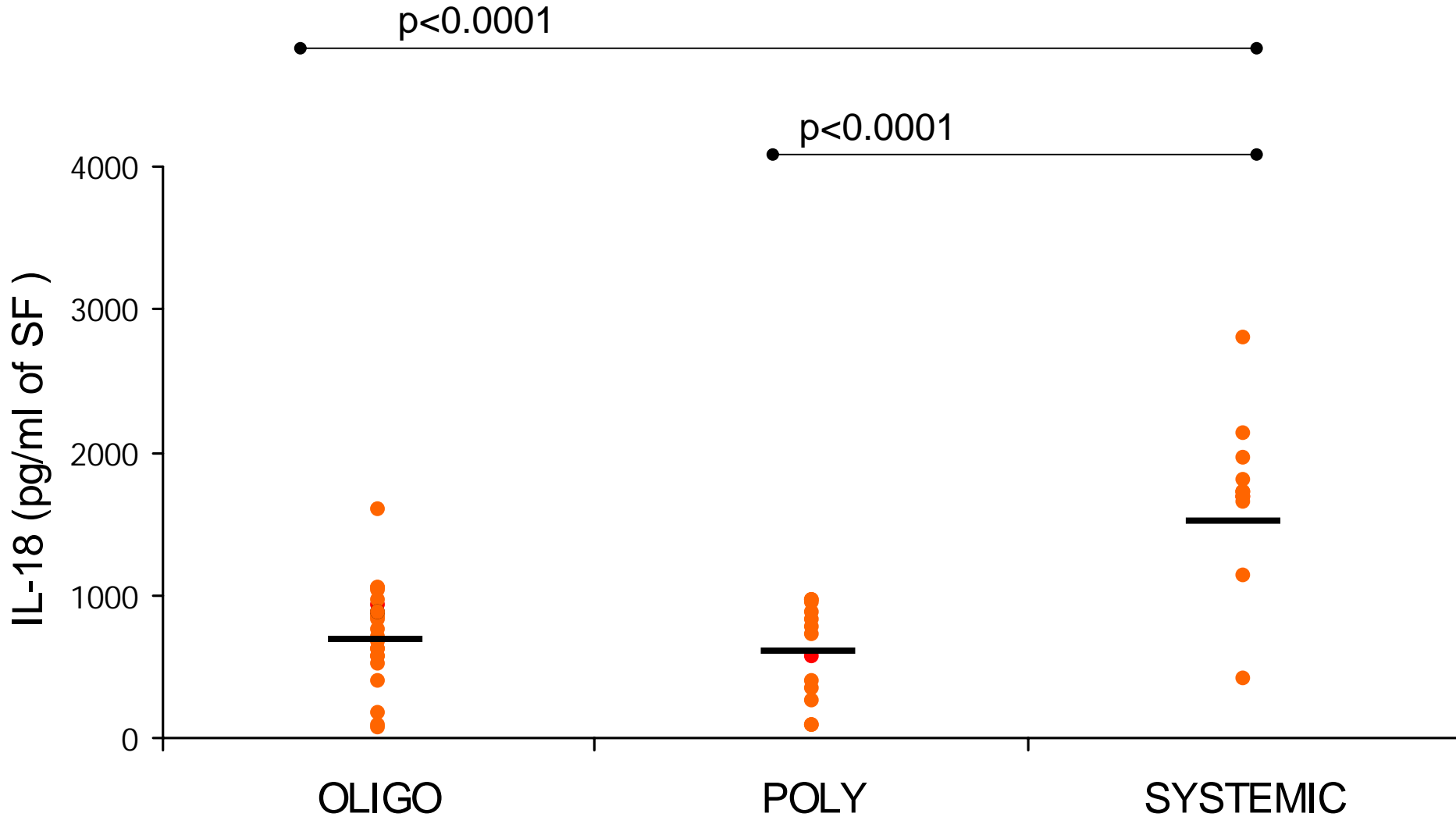
- Positive correlation between SF and serum ($r=0.68$, $p<0.0001$)




Results: serum IL-18



Results: SF IL-18



Results: IL-18



| | SERUM | | SF | |
|--------------------------------|----------|------------|----------|------------|
| Number of active joints | $r=0.50$ | $p<0.0001$ | $r=0.39$ | $p=0.03$ |
| CRP | $r=0.47$ | $p<0.0001$ | $r=0.48$ | $p<0.0001$ |
| Radiological score | $r=0.37$ | $p=0.008$ | $r=0.42$ | $p=0.003$ |
| IL-1 | $r=0.31$ | $p=0.04$ | $r=0.42$ | $p=0.003$ |
| IL-1Ra | $r=0.34$ | $p=0.025$ | $r=0.42$ | $p=0.002$ |
| IL-6 | $r=0.48$ | $p<0.0001$ | $r=0.33$ | $p=0.026$ |



Conclusions

- These results strongly suggest the participation of IL-18 in the pathophysiology of JIA.
- The positive correlation of this cytokine with several parameters of articular inflammation and disease severity suggests that IL-18 could be a new marker and possibly a better target for JIA treatment.