Investigation of the plasma cytokine/chemokine profile of the chronic constriction injury rat model of neuropathic pain: relevance to pharmacological reversal of allodynia.

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Introduction

Neuropathic pain (NeuP) describes heterogeneous group of chronic pain disorders arising from lesion or disease of the somatosensory system.

Two anticonvulsants: gabapentin (GBP) and pregabalin (PGB) are recommended as a first line of treatment in NeuP. Unfortunately, both are associated with poor efficacy and undesirable side-effects.

Chronic constriction injury (CCI) is one of the most widely used models

Identifying a plasma biomarker to track disease progression or predict pharmacological efficacy will facilitate drug discovery in NeuP.

The aim of this study was to investigate plasma cytokine/chemokine profile in the CCI model after NeuP induction followed by GBP and PGB treatment.

Methods

The CCI model was induced in male Sprague-Dawley rats (n=16) by unilateral ligation of the sciatic nerve.

Paw withdrawal threshold (PWT) mechanical allodynia was assessed using von-Frey hairs.

PWT was measured at: baseline (BL; day 0), day 20 following nerve ligation, 2hr and 24hr (day 27) post-GBP (100mg/kg, p.o.), 2hr and 24hrs (day 42/43) post-PGB (30mg/kg, p.o.).

Meso Scale Discovery (MSD) V-Plex mice Proinflammatory assay

Plasma samples from CCI rats were analysed using MSD platform:

IL-1β, IL-6, TNF-α, IFN-γ, IL-10, IL-5, IL-13, KC-GRO, IL-4

Results

Effect of Gabapentin on paw withdrawal threshold.

Effect of Pregabalin on paw withdrawal threshold.

IL-6 (pg/ml)

<table>
<thead>
<tr>
<th>Group</th>
<th>BL</th>
<th>NeuP</th>
<th>2hr post GBP</th>
<th>24hr post GBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>IL-4</td>
<td>1.86±1.11</td>
<td>2.25±0.14</td>
<td>2.41±0.14</td>
<td>2.59±0.13</td>
</tr>
<tr>
<td>KC/GRO</td>
<td>173.3±8.76</td>
<td>178.8±9.04</td>
<td>124.7±10.88</td>
<td>123.9±7.34</td>
</tr>
</tbody>
</table>

* p<0.05, ** p<0.01, *** p<0.001 vs. BL

+ p<0.05, ++ p<0.01, +++ p<0.001 vs. NeuP

Values are Mean ± SEM

Conclusions

- Reversal of increased plasma IL-5 following CCI induction was specific to GBP treatment only.
- IL-13 a cytokine associated with suppression of NeuP was actually increased by PGB consistent with its efficacy.
- The plasma cytokine/chemokine profile here suggests a complex interaction between NeuP, disease progression, pharmacological intervention and inflammatory signaling.
- This study identifies potential plasma markers of NeuP progression and treatment efficacy.

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