

Background

Naproxen sodium is a non-steroidal anti-inflammatory drug (NSAID) that is commonly used to manage pain and inflammation post dental implant surgeries. Acetaminophen is also widely used to manage pain.

Previous studies have shown that naproxen sodium has greater peak analgesic effects and a longer duration of action than acetaminophen following third molar surgery, but the effect of naproxen sodium and acetaminophen on postoperative levels of inflammatory cytokines has not been examined to date.

IL-8 and IL-1 β are inflammatory cytokines that are produced during tissue trauma. Quantification of IL-8 and IL-1 β in gingival crevicular fluid (GCF) is a marker for local inflammation levels.

The goal of the study was to compare the local anti-inflammatory effect of over-the-counter (OTC) doses of naproxen sodium and acetaminophen. The demographic data of the patients was analyzed to determine the possible correlations between local inflammatory level and personal traits.

Study Design

The subjects were 30 adult patients who received one or two adjacent dental implants. Patients with confounding pre-surgical conditions were excluded.

Blood, urine, and GCF samples, and subjects' demographic data were collected from the patients prior to surgery (t=Baseline), and after the surgery (t=0, 1, 2, 4, 6, 24, 72 h).

Subjects were assigned to naproxen sodium group and acetaminophen group in a double-blind, randomized manner (Table 1).

	Naproxen Sodium Group	Acetaminophen Group
Day One:		
Immediately post-surgery	220 mg x 2	500 mg x 2
6 hours post-surgery	Placebo x 2	500 mg x 2
12 hours post-surgery	220 mg x 1 plus placebo x 1	500 mg x 2
Day Two:		
On Awakening	220 mg x 1 plus placebo x 1	500 mg x 2
6 hours post dose one	Placebo x 2	500 mg x 2
8 hours post dose one	220 mg x 1 plus placebo x 1	Placebo x 2
12 hours post dose one	Placebo x 2	500 mg x 2
16 hours post dose one	220 mg x 1 plus placebo x 1	Placebo x 2
Day Three:		
On Awakening	220 mg x 1 plus placebo x 1	500 mg x 2
6 hours post dose one	Placebo x 2	500 mg x 2
8 hours post dose one	220 mg x 1 plus placebo x 1	Placebo x 2
12 hours post dose one	Placebo x 2	500 mg x 2
16 hours post dose one	220 mg x 1 plus placebo x 1	Placebo x 2

Table 1. Treatments of Naproxen Sodium and Acetaminophen Group

Methods

Local inflammation levels was accessed by quantifying proinflammatory cytokines IL-8 and IL-1 β in GCF.

GCF were collected from teeth adjacent to surgical site using Perio papers (Figure 1). After collection, the perio papers were placed in 100 μ l PBS at 4 degrees for 2 hours, then stored at -80 degrees until further analysis.

The level of IL-8 and IL-1 β in GCF were quantified using R&D Systems IL-8 and IL-1 β ELISA kits.

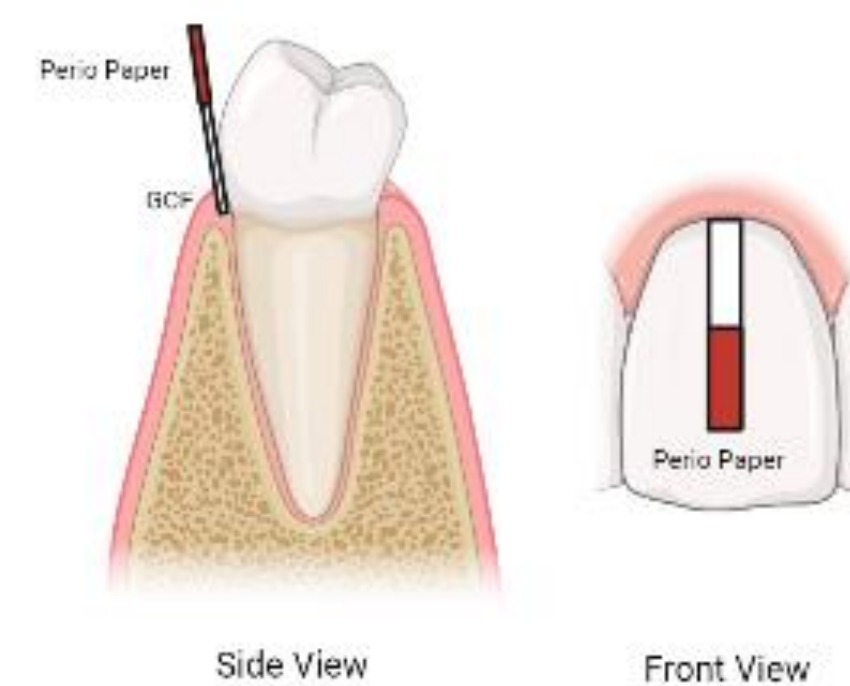


Figure 1. Illustration of Collecting GCF Using Perio Papers

Results

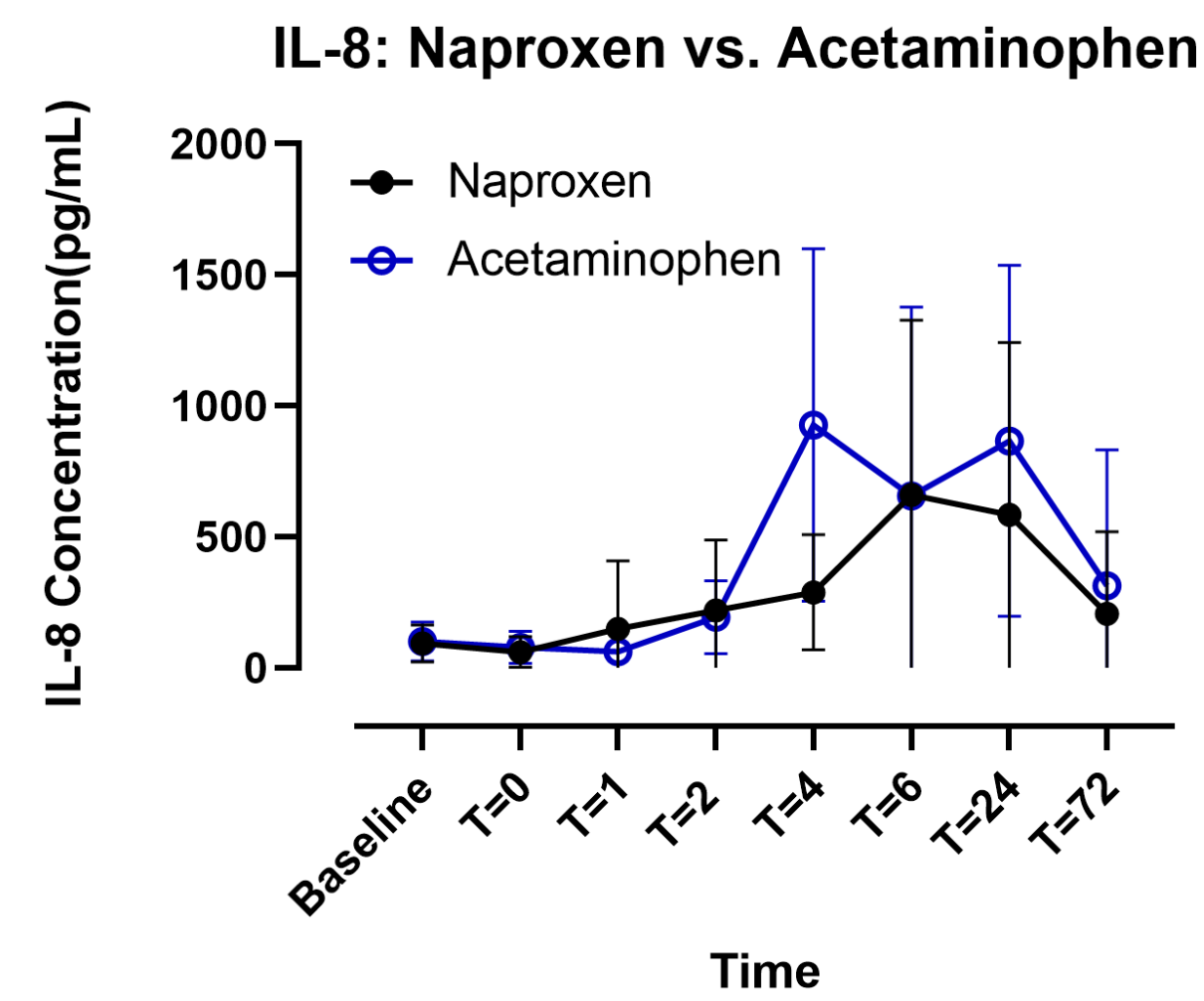


Figure 2a. Changes in IL-8 Concentrations in Patients Treated with Naproxen vs. Acetaminophen

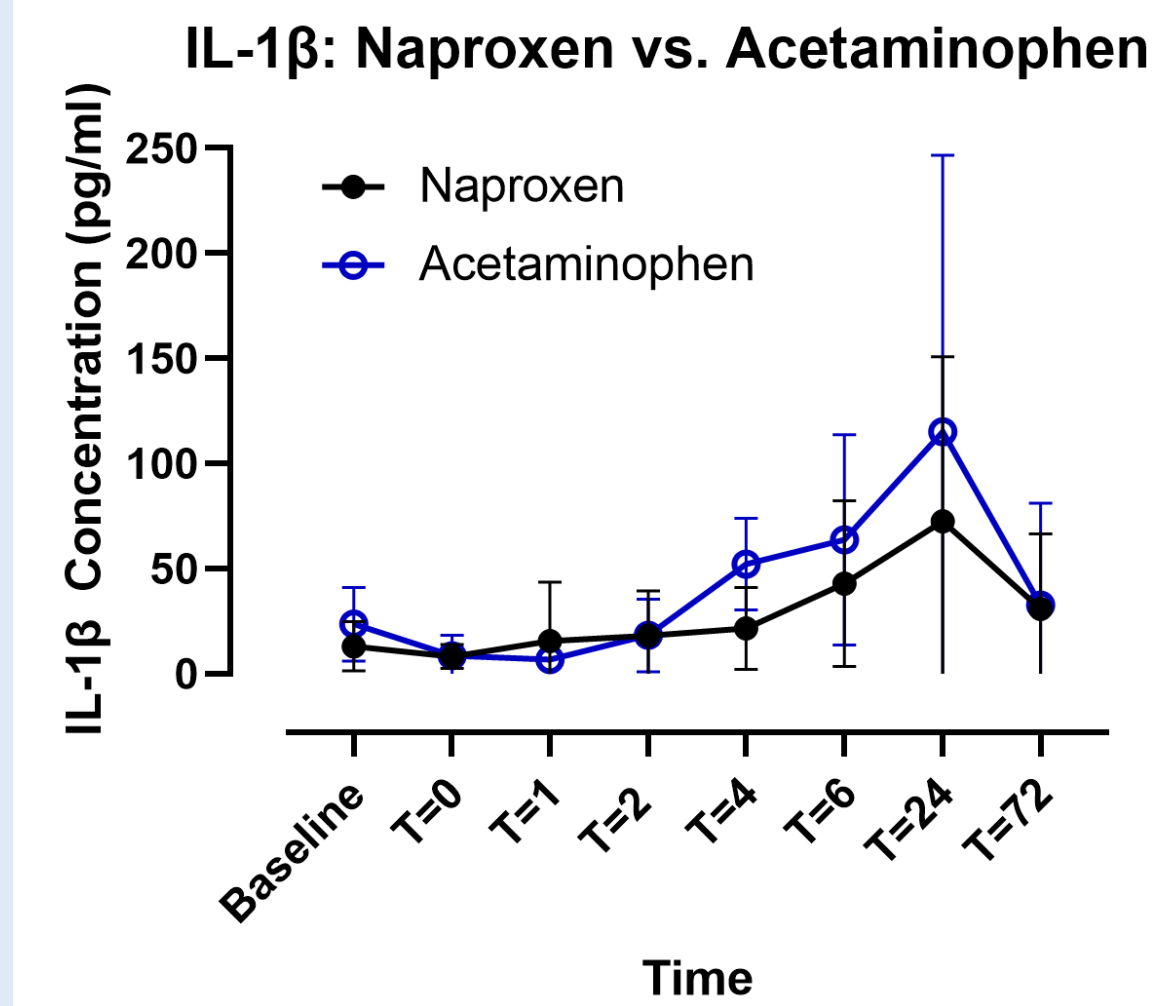


Figure 2b. Change in IL-1 β Concentrations in Patients Treated with Naproxen vs. Acetaminophen

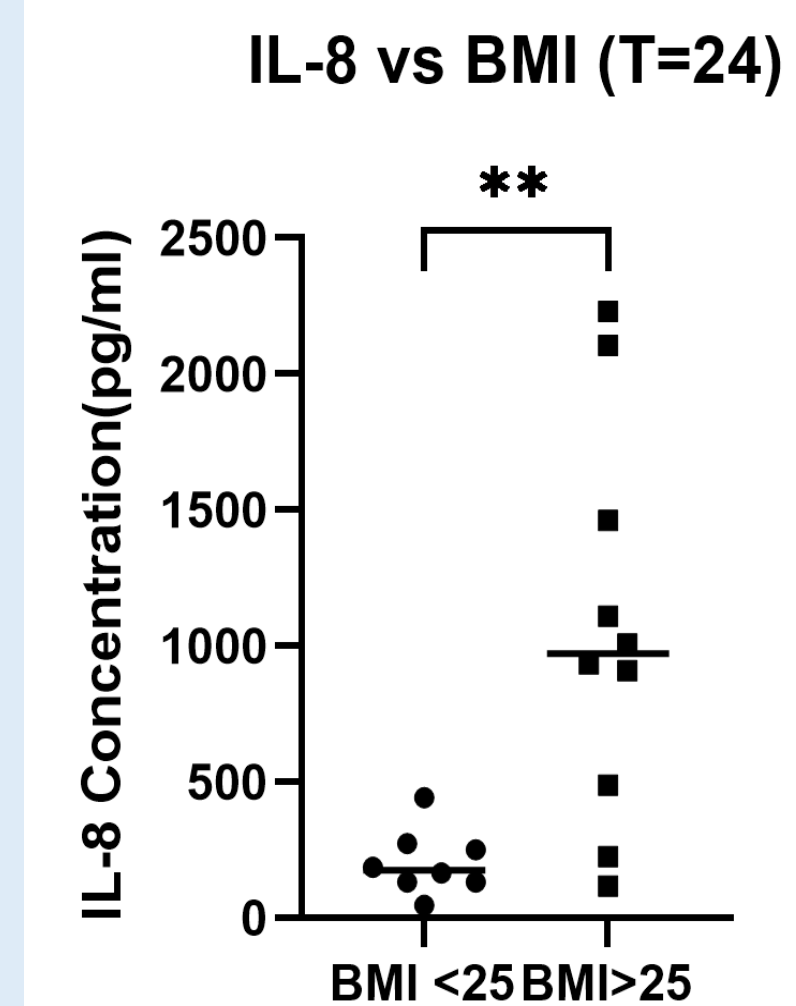
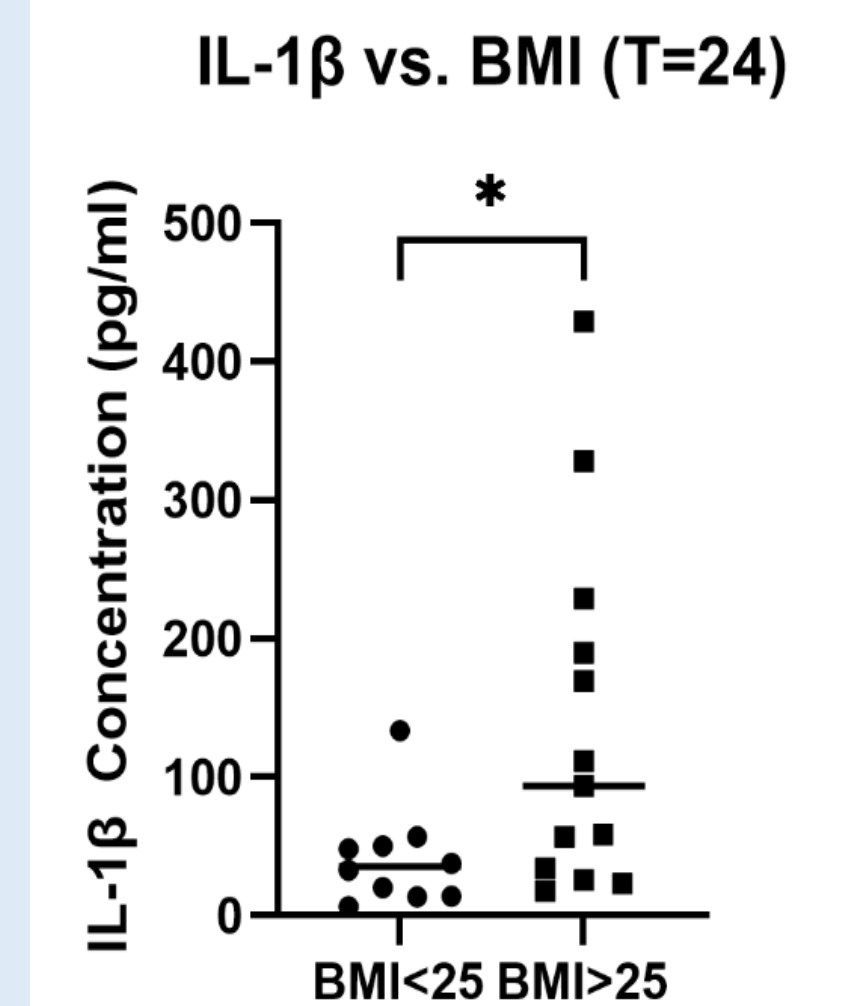


Figure 3a,b. IL-8/IL-1 β Concentrations in GCF collected at T=24 Amongst Subjects with Lower/Higher BMI



	Naproxen	Acetaminophen
n	13	13
Gender (F:M)	6:7	10:3
Age (Years)	44.4 \pm 14.5	45.0 \pm 15.2
BMI (Kg/m ²)	24.52 \pm 3.29	26.41 \pm 4.53
# implants (1 implant: 2 implants)	12:2	12:1
Surgery Length (mins)	74.9 \pm 36.1	81.1 \pm 28.7

Table 2. Demographic Data of Subjects

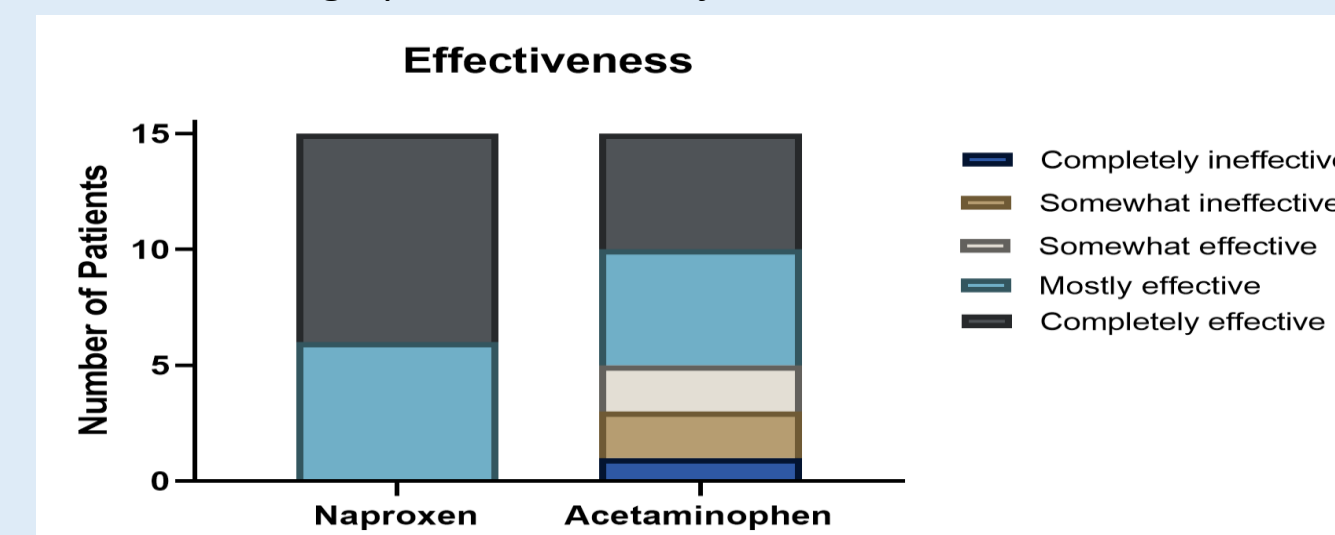


Figure 4. Subjects' Ratings of Effectiveness of Medication Received

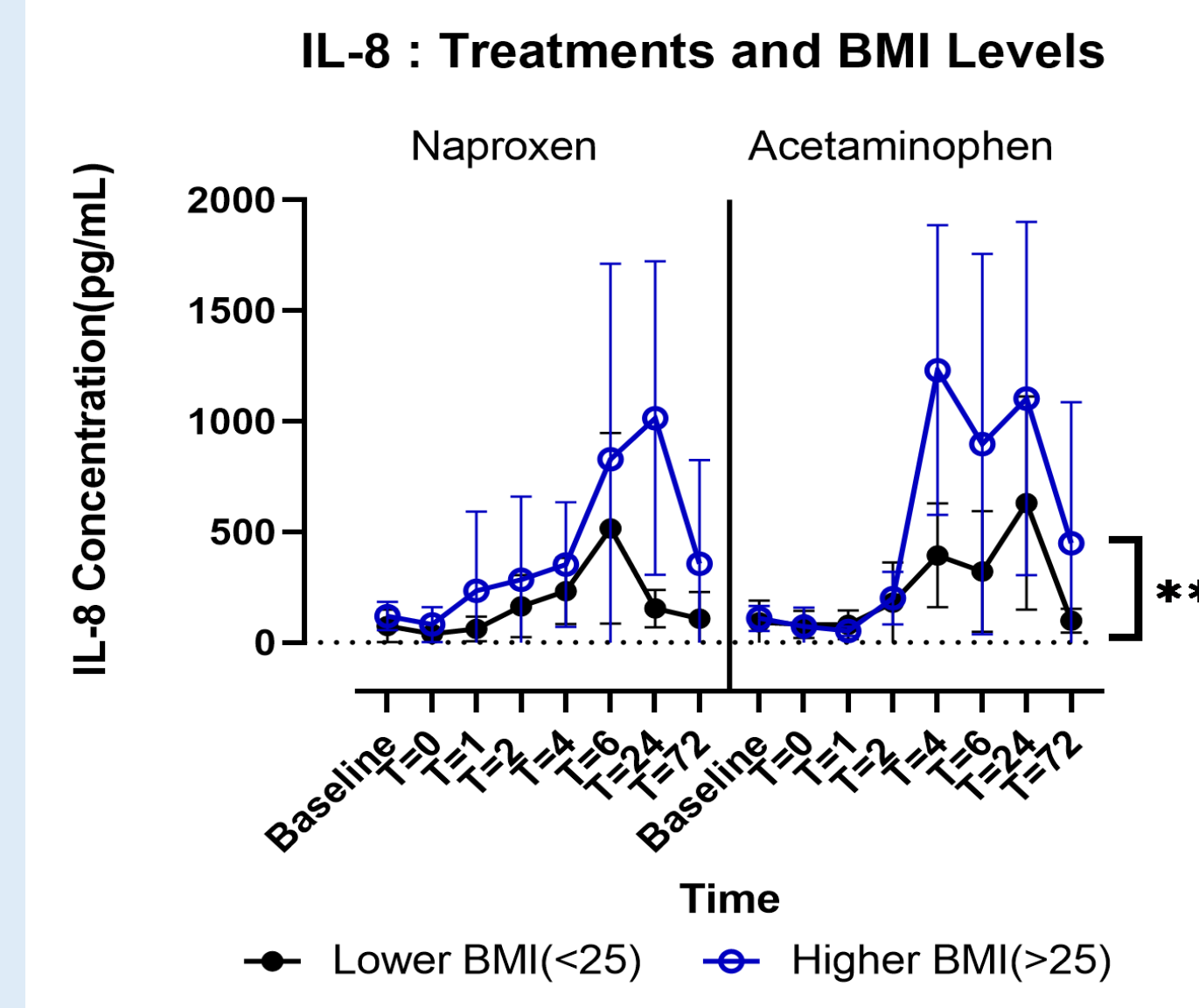
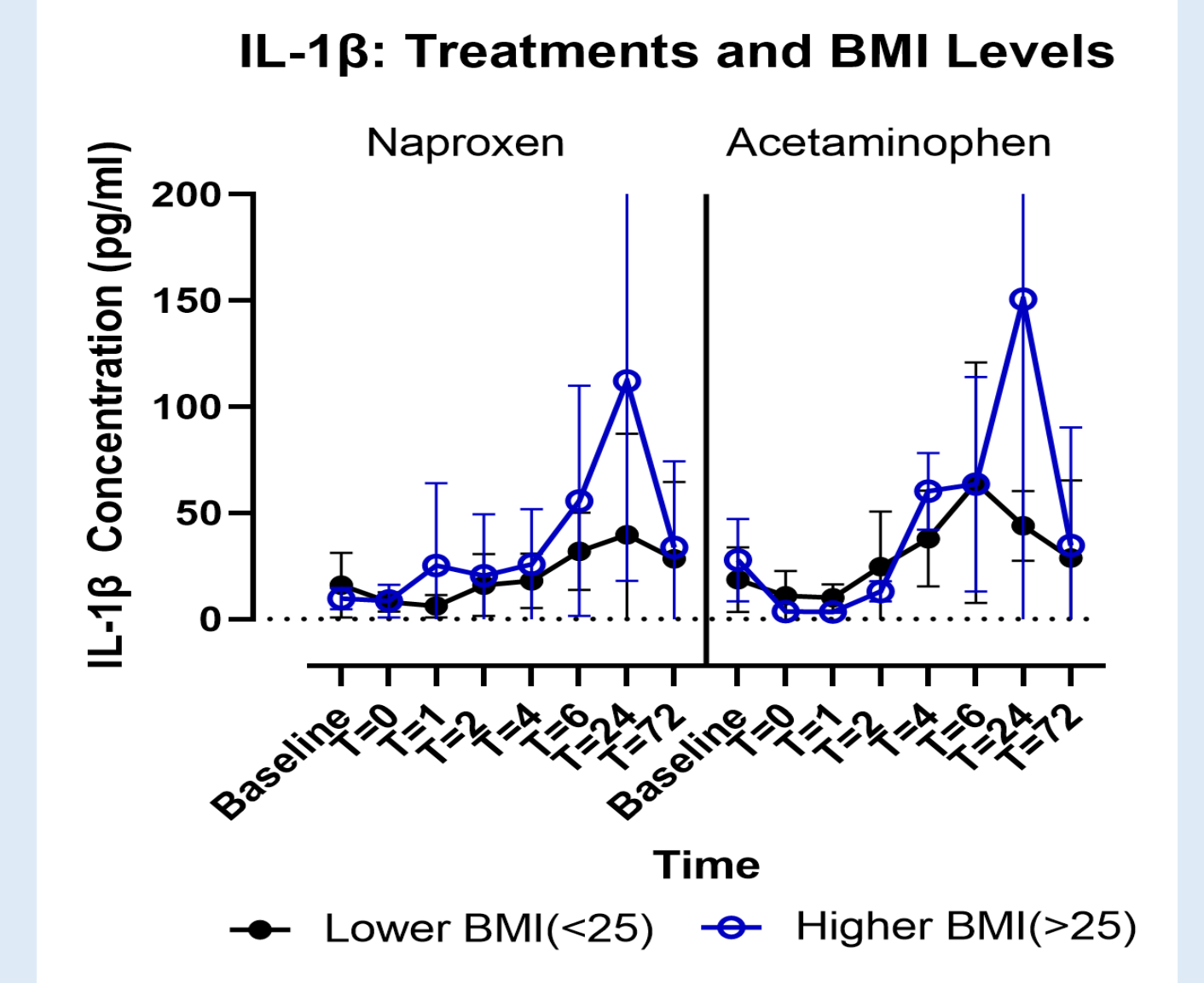


Figure 5a,b. Changes in IL-8/IL-1 β Concentrations in Subjects with High vs. Low BMIs and Treated with Naproxen vs. Acetaminophen



Conclusions and Future Work

These findings suggest that there was a trend toward greater suppression of IL-8 and IL-1 β levels in patients treated with naproxen sodium compared to acetaminophen, but the differences were not statistically significant.

BMI was a factor that significantly affected the post-implant local inflammation level. Subjects with higher BMI (>25) demonstrated higher levels of local inflammation compared to those with lower BMI (<25).

The correlation of other demographic traits, including gender, age, number of implants, surgery length, and patients' ratings on medicine effectiveness, with levels of inflammation were analyzed. The results were not statistically significant.

Investigation in changes in other inflammatory markers such as COX-1 and COX-2 activity and systemic inflammation levels will help promote a better understanding of naproxen sodium's effect on postoperative inflammation levels and improve predication of the most effective analgesic medications for each individual patient.

Acknowledgements

The work was supported by grants from Penn Undergraduate Research Mentoring Program (PURM) and Bayer Pharmaceuticals, LLC.