

TITLE: CHARACTERIZATION AND PREDICTION OF PLACEBO RESPONDERS IN PERIPHERAL NEUROPATHIC PATIENTS IN A 4-WEEK ANALGESIC CLINICAL TRIAL

Abstract

In analgesia randomized clinical trials (RCTs), the magnitude of the placebo response tends to increase with the year of trial completion, including in neuropathic pain trials. This placebo response phenomenon has a negative influence when testing the statistically significant superiority of active compounds compared to placebo.

In chronic pain, meta-analyses have already highlighted several clinical and demographic parameters influencing placebo response in RCTs, such as pain intensity, age, sex, pain duration and study design as well as the geographical location. On the other hand, mechanistic trials investigating properties of analgesic placebo had explored psychological predictors of placebo response. Unfortunately, those correlations between psychological traits and placebo response were mainly studied in healthy volunteers.

The main objective of this pilot study was to investigate the relationship between patient's characteristics and the placebo response. Forty-one patients with peripheral neuropathic pain (PNP) were enrolled and were blindly given a placebo in addition to their regular analgesic treatment during 4 weeks. The individual patient's characteristics were collected: medical and disease history, pain evaluation and personality traits using validated scales. The placebo response was determined with the average pain score (APS, 11 numeric scale ranging from 0 (no pain) to 10 (pain as bad as you can imagine) daily collected all along the study.

The mean APS at baseline was 5.3. In 12 patients, the APS score decreased by more than 20%, these patients were considered as placebo responders. Univariate as well as multivariate analysis found characteristics significantly correlated with the placebo response. Interestingly, those characteristics include demography, clinical history and psychological traits. Moreover, their combination in a multivariate predictive model was able to identify individual patient as placebo responders, with 80% accuracy. This make a step toward the characterization and the prediction of the placebo response, a major confounding factor, in RTCs.

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