NOCEBO in neurological disorders and headache

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Nocebo is the antipode of placebo and refers to adverse events a person manifests after receiving placebo. It has received sparse scientific and clinical attention but it has great importance in headache conditions illustrating the power of the human brain. Relevant mechanisms for nocebo contain prior conditioning and suggestions, expectation, anxiety modulation, and relative experiences. Nocebo submits more to the intervention than to the outcome and includes expected adverse events or, less frequently, nonspecific effects that cannot be substantiated referring to pharmacological action of the treatment. Information disclosure for potential side effects can itself contribute to producing adverse events, or detailed and extensive information by physicians can also trigger nocebo adverse events. Like placebo, nocebo shares key functions in pain conditions and headache. One meta-analysis showed that in RCTs for migraine prevention, eight out of 20 patients treated with placebo experience any adverse event and one out of 20 (5%) withdraw treatment because of adverse events. The same picture stands for tension-type headache and cluster headache, although data for these conditions are poor because of the limited number of RCTs. Other meta-analyses of RCTs revealed that nocebo varies significantly among neurological conditions. The percentage of patients who reported at least one adverse event and treated with placebo in RCTs changes from 43% in migraine prevention up to 67% in Parkinson disease and fibromyalgia. Dropout ratio because of adverse events in placebo-treated patients ranges from 2% in multiple sclerosis to almost 10% in Parkinson disease and fibromyalgia. Notably, in RCTs for depression nocebo was not increased, as someone may expect (dropout ratio 4.5%). In clinical practice, nocebo may be more prevalent than in RCTs. These data emphasize the need for minimizing nocebo to the extent possible by educating the patients and treating them appropriately. To capture patients with potential future nocebo responses a specific self-fulfilled questionnaire (Q-No) was evaluated with 71.7% specificity, 67.5% sensitivity, and 42.5% positive predictive value. Neurologists should acknowledge nocebo as a significant cofactor for treatment adherence and failure and plan techniques to border nocebo, such as patients' education and close follow-up. Positive suggestions and continuous support increase patient's compliance and decreases nocebo.