POEM

Placebo effect only found for continuous, patient-reported outcomes

Clinical question How effective is placebo?

Bottom line Although the authors argue against the existence of a placebo effect, this study does not rule out a small placebo effect, particularly for patient-reported continuous outcomes, such as scales for pain or nausea. It may never be possible to separate out completely the contribution of natural history, study bias, treatment effect and placebo effect to the health of our patients.

Synopsis Observed benefit in a treated patient may be caused by the natural history of disease, the treatment effect, study bias, or the oft-cited "placebo effect". The authors previously reported in a systematic review of 114 randomised controlled trials (RCTs) that included both placebo and untreated control groups that there was no such thing as a placebo effect, or at least that it could not be distinguished from biases inherent in the studies. This report updates that systematic review with the results of 42 additional such RCTs.

The authors first did a careful search of the literature for studies that had both a placebo and a no-treatment control group. They only included studies with concealed allocation, blinded outcome assessment, and a dropout rate of less than 50 per cent. Only the primary outcome of each study was extracted.

The identified RCTs studied a variety of problems, including pain, nausea, hypertension, jet lag and erectile dysfunction. The results of the 42 newer trials were similar to those originally reported by the authors, so the authors combined them. In total there were 156 studies with extractable data, 38 reporting binary outcomes (ie, treatment success or failure) and 118 reporting continuous outcomes (ie, a numerical rating of pain).

The authors began by drawing a funnel plot, which is a way to look for publication bias. Although the funnel plot is difficult to interpret, it is possible that smaller studies with negative outcomes for placebo were under-reported.

However, since looking for a difference between placebo and untreated controls was unlikely to be the intention of any of these studies, it is not clear why authors would choose to not submit smaller "negative" trials for publication. With this caveat in mind, the authors pooled the results. There was no benefit to placebo over no treatment for success/failure outcomes, although examination of individual topics and the confidence interval suggests that there is a possible trend in favour of placebo.

Regarding continuous outcomes, there was a small but significant benefit to placebo among all studies (standardised mean difference [SMD] = –0.24, 95 per cent confidence interval [CI] –0.31 to –0.17). The benefit was especially large among patient-reported continuous outcomes (SMD = –0.30, CI –0.38 to –0.21) and was of borderline significance for observer-reported outcomes (SMD = –0.10, CI –0.20 to 0.01). This benefit of placebo for trials with continuous outcomes persisted even when only the three highest quality studies were included. It was also consistent for all 10 topics studied with continuous outcomes (eg, pain, smoking, nausea): each had a point estimate of effect less than zero, consistent with benefit of placebo over no treatment. The authors argue that there may be a small placebo effect, but it is probably clinically insignificant and cannot be distinguished from the bias inherent in any study.

Level of evidence = 1a (systematic review, with homogeneity, of randomised controlled trials)

Reference Hrobjartsson A, Gotzsche PC. Is the placebo powerless? Update of a systematic review with 52 new randomised trials comparing placebo with no treatment. Journal of Internal Medicine 2004; 256:91–100.