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FILE: ▪Ginger (*Zingiber officinale*)
▪Blinding in Clinical Trials

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RE: Can Ginger be Blinded in Clinical Trials?

Zick S, Blume A, Normolle D, Ruffin M. Challenges in herbal research: a randomized clinical trial to assess blinding with ginger. *Complement Ther Med*. 2005;13:101-106.

The gold standard for clinical research is the randomized, double-blind, placebo-controlled trial. In this study design neither the researchers nor the volunteers know (double-blind) who received the active drug and who the placebo. This study design removes the potential effects of bias from the trial, because if researchers and volunteers knew who was taking placebo and who the active drug, it might consciously or unconsciously translate into a clinically relevant reaction. Blinding can be difficult for some medicines, especially those that contain volatile oils or other aromatic compounds, and most clinical trials do not test the effectiveness of their blinding strategies. Ginger (*Zingiber officinale*) is a pungent herb with a distinctive taste, which might make blinding difficult. The current study assessed if subjects could determine whether they received ginger capsules or placebo in a randomized, double-blind, parallel-arm (two trials with the same volunteers occurring simultaneously), placebo-controlled trial.

Eighty adult men and women, approximate age range 20 to 52 years, enrolled in the study which took place at the University of Michigan General Clinical Research Center. None had chronic illnesses or were taking any medications. Excluded from the trial were people with a history of peptic ulcer disease, gastrointestinal bleeding from ulcers, gastrin secreting tumors, or any skin cancer except basal and squamous cell carcinomas. Volunteers were randomly assigned to receive a size 0, red, animal gelatin capsule (Gallipot®) containing either 250 mg ginger (Pure Encapsulations®, Sudbury MA; 22:1 supercritical CO_2 extract standardized to 5% (6)-gingerol) or a lactose placebo. They were asked to "examine, smell and then swallow the capsule with water." They then attempted to identify whether they'd received ginger or placebo, by answering the following questions: "Was it taste?"; "Was it the smell?"; "Was it the way the capsule looked?"; "Was it the way the capsule worked?"

In the second arm volunteers received an identical-looking bottle filled with either ginger or placebo capsules. Within 15 minutes after examining the bottle visually and by smell,

volunteers attempted to identify whether they'd received a bottle containing ginger or placebo and why by answering the following questions: "Was it the smell?"; "Was it the way the capsules looked?" Adverse events (AE) for both arms were assessed by telephone and email at 24, 48, and 72 hours after receiving the active treatment or placebo.

The likelihood of volunteers correctly identifying receipt of a ginger capsule versus a placebo capsule was similar ($P < 0.01$). Of those receiving ginger, 77.5% (62–89% CI) correctly identified they had received ginger, compared to 82% (67.2–92.6%) in the placebo group who correctly identified they had taken a placebo capsule. None of the reasons given by volunteers for guessing was significantly associated with guessing the correct capsule. Correctly identifying the capsule was not associated with age, sex, race/ethnicity, or smoking status.

In the second arm a significantly greater percentage of participants were able to correctly identify receipt of a bottle containing ginger than those who received a bottle containing placebo (75% [62–88% CI, $P = 0.0016$] vs. 55% [40–70% CI, $P = 0.5271$], respectively). A significant 66% of volunteers claimed that smell was the reason they claimed that they had received a ginger or placebo bottle ($P < 0.04$). The bottle's appearance was not significantly associated with selecting correctly ($P = 0.68$). The earlier in the trial people were given their bottles, the more likely it was that they correctly guessed which bottle they'd received ($P < 0.01$). The authors believed this was due to dissipation of ginger's aroma over time. Four adverse events were reported in both arms and were not significantly different between groups.

This study showed that blinding with ginger is ineffective when ginger capsules are supplied in bottles. The authors concluded that future clinical trials using ginger should distribute the capsule in blister packs so volunteers cannot identify that they'd received ginger. This would minimize the aroma; however, the efficacy of blinding using ginger in blister packs has not yet been assessed in a clinical trial.

—John Neustadt, ND

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