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NAUSEA AND VOMITING

Getting to the root of the antiemetic effects of ginger

Ginger has been used since ancient times for the treatment of nausea and vomiting. More recently, short clinical trials have demonstrated the effectiveness of this herb in the treatment of nausea and vomiting during pregnancy and in chemotherapy-induced nausea and vomiting (CINV). Patients with functional gastrointestinal disorders, such as IBS and functional dyspepsia, might also benefit from treatment with ginger, although the evidence is less robust in this setting.

Studies have suggested that the antiemetic effect of ginger might be mediated via 5-HT_3 receptors. Most work in this field has been conducted in cell lines or gut samples from mice. "With our work, we wanted to unravel the mode of action of ginger in the human system," says Beate Niesler from the Department of Human Molecular Genetics, Institute of Human Genetics, Heidelberg, Germany. "It is well known that rodents differ from humans with regard to the 5-HT_3 receptor system."

Niesler and colleagues therefore used calcium influx assays and ligand binding studies to investigate the effect of ginger on homomeric 5-HT_3A and heteromeric 5-HT_3AB receptors in a human cell line (HEK293 cells) as well as in human submucous plexus material (in collaboration with Michael Schemann, Technical University, Munich, Germany).

"We could prove that ginger and its pungent components act in an antagonistic manner on human homomeric 5-HT_3A and heteromeric 5-HT_3AB as well as native 5-HT_3 receptors on enteric neurons from the submucous plexus," reports Niesler. Furthermore, the researchers demonstrated that the 5-HT_3 receptor binding site for the active constituent of ginger is different to that for the 'setrons' (for example, ondansetron and alosetron). The setrons are another class of agents that interact with 5-HT_3 receptors and are the gold standard for treatment of CINV. This finding means that the combination of ginger and a setron would exert an additive inhibitory effect on 5-HT_3 receptors. In fact, clinical trials involving patients with cancer receiving setrons for the treatment of CINV have demonstrated reduced incidence of nausea in patients who also received ginger.

The researchers hope that their findings might encourage longer clinical trials assessing the safety of ginger extracts in various settings. They are also interested in following up the mode of action of other natural compounds.

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Original article Walstab, J. *et al*. Ginger and its pungent constituents non-competitively inhibit activation of human recombinant and native 5-HT_3 receptors of enteric neurons. *Neurogastroenterol. Motil.* doi:10.1111/nmo.12107