

**Effectiveness and tolerability of repetitive transcranial magnetic stimulation for preventive treatment of episodic migraine: a single-centre, randomised, double-blind, sham-controlled phase 2 trial (Magnet-EM)**

ABSTRACT

Background: This is a phase II randomised, double-blind, sham-controlled trial to evaluate the effectiveness and tolerability of repetitive transcranial magnetic stimulation for preventive treatment of episodic migraine amongst migraine subjects. Methods: Subjects age 18 to 60 years will undergo a baseline evaluation to establish the diagnosis of migraine based on the International Classification of Headache Disorder 3rd Edition (ICHD-3). Those who fulfil the ICHD-3 criteria for episodic migraine and compliant to the headache diary during a month run-in period will be enrolled. A total of 76 subjects will be randomised to receive either transcranial magnetic stimulation or sham stimulation for 5 sessions within 2 weeks duration. Follow-up sessions will be conducted monthly for three consecutive months. Prior to treatment, subjects will be required to fill up questionnaires and undergo few procedures such as electroencephalography, transcranial Doppler ultrasound and biochemical analysis for serum serotonin, serum calcitonin gene-related peptide and serum beta-endorphin. These procedures will be repeated at month 3 after receiving the last treatment. The primary outcome measure of this study is the difference in mean monthly migraine days at baseline and at months 1, 2 and 3 after treatment sessions. Discussion: Following evidence from previous studies showing restoration of dorsolateral prefrontal cortex (DLPFC) activation to almost normal level, the rTMS intervention will target left DLPFC in this study. An intermediate duration of treatment sessions is selected for this study. It is set to five treatment sessions given within 2 weeks duration.

**Keyword:** Migraine; Repetitive transcranial magnetic stimulation (TMS); Randomised controlled trial