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Transcranial magnetic intermittent theta-burst stimulation for depression in pregnancy – A case series

To the Editor:

Anti-depressant treatment with selective serotonin reuptake inhibitors (SSRIs) is considered safe and effective during pregnancy, but response rates are fairly low, and compliance is often hampered by a subjective worry concerning the effects SSRIs may have on the fetus/newborn child [1]. Repetitive transcranial magnetic stimulation (rTMS) may be a suitable alternative treatment for depression during pregnancy, but there is a paucity of clinical data, restricted to one randomized controlled trial with 22 women, and case-reports and case-series [2,3].

Recent advances with efficient protocols of short duration such as intermittent theta-burst stimulation (iTBS) offers further feasibility of rTMS [4]. However, there is only one case-report of iTBS during pregnancy so far [5].

Here we report a case series of five consecutive cases of pregnant depressed women who were referred to the Brain Stimulation Unit at Uppsala University Hospital, Sweden, during 2019. The patients were referred via a well-developed collaboration between the Maternity Clinic and the Psychiatric Clinic in the University Hospital.

All five patients were assessed before, during, and after the iTBS course per clinical routine, and oral and written consent was obtained from all patients after completing their treatments, to collect relevant information from their medical records and to publish their data in this case-series.

The patients were first screened for rTMS safety with a modified translated version of the TASS (Rossi 2011). A resting motor threshold determination was performed through a standardized procedure, as was the localization of the treatment spot over the left prefrontal cortex (F3 in the 10–20 system).

The iTBS protocol consisted of triplet 50 Hz bursts, repeated at 5 Hz; 2 s stimulation and 8 s pause; 600 pulses per session; total duration of 3 minutes 12 seconds, applied at 120% of the RMT [4]. The stimulator output was gradually ramped up initially during the treatment course to increase tolerability. We used a MagPro R30 magnetic stimulator and a Cool-B65 figure-of-eight coil (MagVenture, Farum, Denmark).

Psychiatric assessment before iTBS included a clinical interview by an experienced psychiatrist (RB), collecting information for rating with the Montgomery Asberg Depression Rating Scale (MADRS) [6], Maudsley Staging Method for treatment resistant depression (MSM) [7], and Clinical Global Impression – severity (CGI-S) rated on a seven point Likert scale ranging from “normal” to “among the most extremely ill patients”. Symptom self-report was collected with MADRS-S [8], EQ Visual Analogue Scale (VAS) [9]. For further assessment of suicidal ideation, a short version of the Columbia-Suicide Severity Rating Scale (C-SSRS) was used as self-report including the items of frequency, duration, and controllability (total sum ranging from 0 to 15 points on a Likert scale) [10].

Subjective ratings of scalp-pain were recorded every treatment session and the symptom self-reports were repeated weekly. Subjective memory impairment was rated on a seven-point Likert scale, where 0 is none and 7 is total inability to remember things.

The mean (SD) age was 29 years (2). Two of the women had two children, two had one, and one had no children. All of them were married or had a co-habiting partner. All five women were on sick leave due to their current depressive episode. Gestational week at rTMS initiation for the five women was 24, 30, 32, 35, and 37.

All pregnancies ended in full term (range 38 + 6 to 41 + 1 weeks). Two of the women gave birth via elective cesarean section, three via spontaneous vaginal births. One of the infants was large for gestational age and was given short-term respiratory support immediately after parturition. One of the infants had meconium-colored amniotic fluid at birth, but no other complications. All the infants had an APGAR score of 10, 10 min after birth.

All five women had recurrent major depression, and two also had an attention deficit hyperactivity disorder. Citalopram 40 mg/day was used by two of the women while the rest had no current psychopharmacological treatment, but one had stopped sertraline treatment over a month ago due to a brief hypomanic reaction. Mean (SD) baseline MADRS was 30 (6), MSM 6 (1), and resting motor thresholds 55% (8%) of the magnetic stimulator output. The mean (SD) time to reach target treatment intensity was 7 (4) days.

One patient received accelerated iTBS with two treatments a day with at least 50 minutes apart and stopped after 11 treatments due to partus (patient C in Fig. 1). Another patient stopped iTBS after 16 treatments due to partus (patient A). Two patients stopped treatment after 16 and 21 treatments, respectively, due to remission of depressive symptoms (patients B and E). One patient switched from iTBS after six weeks to 1 Hz rTMS over the right frontal lobe (F4) due to only partial response and received further two weeks of treatment and then stopped due to partus (patient D).

The CGI-S, MADRS-S, EQ 5D VAS and Short CSSR scores of each patient are displayed in Fig. 1.

Apart from the scalp pain (which was reduced during the course of the treatment in all patients), the following side-effects were reported: initial post session fatigue (n = 3), head ache (n = 2), vertigo (n = 1), jaw twitching (n = 1). However, subjective memory impairment decreased in all patients.

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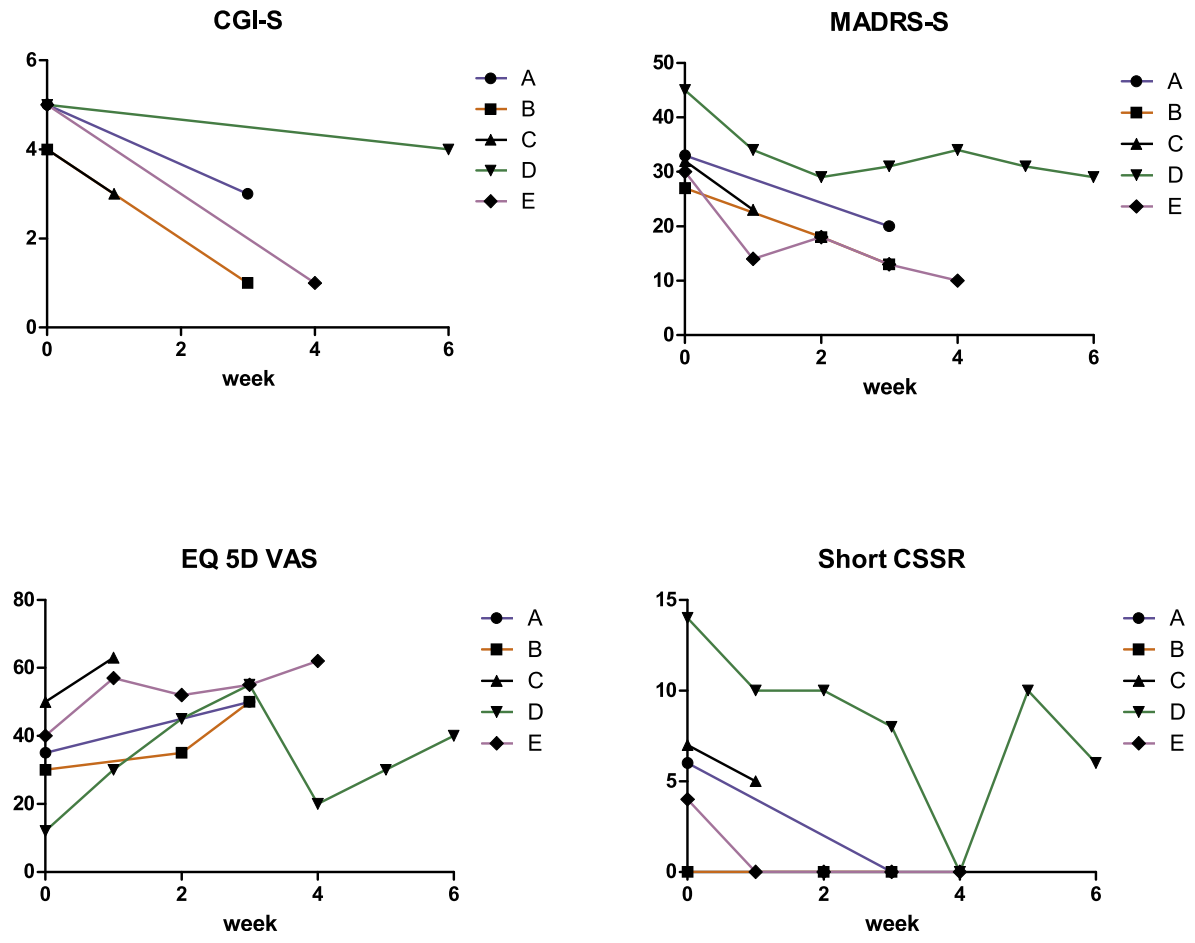

Fig. 1.

In five pregnant women receiving iTBS treatment for major depression, a decrease in MADRS-S score was observed in all patients, and two patients achieved remission. A decrease in suicidal ideation was noted, as well as a reduction in CGI-S score. No serious adverse events for mother or child were recorded during the study period.

These results point in the same direction as in the first case-study, that iTBS during pregnancy seems to have similar effects as iTBS in non-pregnant women [5], and also in line with the only RCT on rTMS with 1 Hz right frontal stimulation, reporting a 27% remission rate [2].

With all the inherent limitations of a case-series, our results calls for a randomized controlled trial of iTBS for depression during pregnancy.

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Authors contributions

RB and SS conceptualized the study, conducted the analyses, and drafted the manuscript. MG and AR participated in the discussion and consensus. All authors reviewed and approved the final manuscript.

Declaration of competing interest

None.

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