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CASE REPORT

Maintaining remission of depression with repetitive transcranial magnetic stimulation during pregnancy: a case report

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Abstract It is important to explore potential safe treatment options for the ongoing treatment of women's depression during pregnancy. One promising treatment is repetitive transcranial magnetic stimulation (rTMS). We report on the case of a woman who became pregnant while receiving regular maintenance rTMS combined with pharmacotherapy treatment for major depressive episode. The patient achieved remission following two acute courses of rTMS and continued with maintenance rTMS treatment over the course of 4 years, during which she became pregnant and gave birth to a healthy infant. Her remission was maintained over this time including during and after her pregnancy. There were no adverse effects to the patient or her infant during the pregnancy or in the post-natal period. Maintenance rTMS may be an effective and feasible treatment option for depression during pregnancy.

Keywords Transcranial magnetic stimulation · Maintenance therapy · Antenatal depression · Pregnancy

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Case report

Treatment of depression during pregnancy is a complex topic, and clinical decisions need to consider both the risks and benefits. There is general consensus that viable treatment options must be made available for pregnant women with depression (Richards and Payne 2013). Untreated antenatal depression can negatively impact both the mother and foetus/infant. Depression during pregnancy is associated with inadequate maternal weight gain (Bodnar et al. 2009), increased rates of preterm birth (Cripe et al. 2011; Yonkers et al. 2009; Li et al. 2009), preeclampsia (Kurki et al. 2000), lower infant birth weight (Grote et al. 2010) and higher rates of infant admission to neonatal care units (Chung et al. 2001). In addition, depression usually continues into the post-natal period (Soderquist et al. 2009), which can have adverse effects on maternal-infant bonding as well as the child's development (Deave et al. 2008). In order to provide the best care to pregnant women and their developing infant, it is important to consider risks of treatment in the context of illness severity, consequences of no treatment and undertreatment and individual treatment preferences.

One promising treatment option for pregnant women with depression is repetitive transcranial magnetic stimulation (rTMS) (Kim et al. 2011; Kim et al. 2009). The use of rTMS as an evidence-based treatment for depression has been increasingly recognised and accepted (Slotema et al. 2010; Fitzgerald et al. 2011). There have been several case reports and pilot studies published on the use of rTMS to treat depression in pregnancy with positive results (Kim et al. 2011; Zhang and Hu 2009; Tan et al. 2008; Zhang et al. 2010). However, to our knowledge, there is no published data on the effectiveness of a regular, scheduled maintenance rTMS programme in maintaining remission from depression in pregnancy.

We report on the case of a participant from a larger rTMS study (Galletly et al. 2012) who became pregnant while receiving regular maintenance rTMS combined with pharmacotherapy treatment for major depression.

History

Mrs. X is a 34-year-old woman with a tertiary-level education. She was first diagnosed with major depression in 2001 at age 21. There was a family history of bipolar disorder, post-traumatic stress disorder and depression. She had no other notable medical or psychological conditions. She has been in a very supportive and stable relationship for 15 years (married for 1.5 years) with Mr. X who is aged 36. She had no other previous pregnancies or children.

She was initially prescribed venlafaxine by her general practitioner, which was ineffective and produced the side effect of weight gain. She was then prescribed citalopram; however, she experienced some visual disturbances with this. In 2002, she was referred to a psychiatrist and diagnosed with bipolar II disorder. She has no history of manic episodes. Throughout 2003, she trialled a range of different antidepressant and antipsychotic medications, including reboxetine and sodium valproate, but they were either ineffective or had negative side effects. She found some benefit with mirtazapine and continued on a stable dose of this until 2005 when her mood deteriorated. Increasing the mirtazapine dose seemed to cause weight gain, so instead she was commenced on lamotrigine which improved her depressive symptoms. In 2008, significant work stressors led to her resignation from the organisation she was employed by. At that time, she was prescribed olanzapine and pregabalin for her comorbid anxiety symptoms. She was also prescribed lithium which had limited benefit in treating her depression. She had no history of inpatient treatment and had not received ECT.

rTMS acute courses

Mrs. X was first referred to our clinic and assessed as suitable for rTMS in September 2008 at age 29. She had her first acute course (3 days per week for 6 weeks, total of 18 treatments) of rTMS from October to November 2008. Repetitive TMS sessions were administered using a MagPro R30 machine and MCF B65 coil. We used sequential bilateral rTMS at 110 % motor threshold, with 15 min of intermittent high-frequency rTMS (10 Hz) to the left dorsolateral prefrontal cortex (DLPFC) followed by 15 min of continuous low-frequency (1 Hz) rTMS to the right DLPFC. She continued pharmacotherapy during her course which included lamotrigine 125 mg, thyroxine 75 μg, olanzapine 1.25 mg, mirtazapine 15 mg, pregabalin 75–180 mg and lithium carbonate 1,250 mg. She met DSM-IV (m.i.n.i neuropsychiatric interview) criteria for major depressive episode (MDE); however, she was only mildly depressed according to her 21-item Hamilton Depression Rating Scale (HAMD; Hedlund and Vieweg 1979) score of 13. She did not meet our study criteria for a clinical response (defined as a 50 % decrease in HAMD score), with a post-treatment HAMD score of 10, but this could be attributed to her already low baseline HAMD score. She did, however, meet criteria for a partial response (>25 % reduction in score) based on her Montgomery-Åsberg Rating Scale for Depression (MADRS; Montgomery and Åsberg 1979) results. At baseline, she had a score of 24 on the MADRS, and at follow-up, this had reduced to 16.

She relapsed in early 2009 and was referred for a second acute course of rTMS (5 days per week for 4 weeks, total of 20 treatments). She was moderately to severely depressed at baseline, according to her HAMD score of 24, and met DSM-IV criteria for MDE. At the time she was taking lamotrigine 125 mg, pregabalin 75–180 mg, lithium carbonate 1,250 mg and mirtazapine 15 mg. She had a full response and was in remission (score of 3 on HAMD) following her second course. At the recommendation of her psychiatrist, Mrs. X was referred for maintenance rTMS to maintain her remission.

This subject is a part of a larger clinical rTMS research study. Due to the open-label nature of the study, we accepted patients with a variety of psychiatric diagnoses including both bipolar (depressive phase) and major depressive disorder. While this subject had a diagnosis of bipolar II disorder, she met DSM-IV criteria for MDE prior to entry into the study. Throughout the 5 years she was treated at our clinic, she did not experience any hypomanic episodes.

Maintenance rTMS

Mrs. X began a maintenance schedule in August 2009 with one treatment per week. She was given sequential bilateral rTMS at the same parameters as the acute courses. At this time, she was taking lamotrigine 250 mg and pregabalin 75–180 mg. In September 2009, her treatments were spaced to one every 2 weeks, and in October, treatments were further spaced out to one every 3 weeks. At this point, she was assessed, and according to her HAMD score of 15, she had relapsed. On advice from her psychiatrist, it was decided to increase her maintenance rTMS frequency to one every 2 weeks, as any less than that seemed to result in relapse. Mrs. X has continued to receive maintenance rTMS with continued remission for the last 4 years. She has regular follow-up assessments, and her HAMD and Zung self-rated depression (Zung 1965) scores are reported in Table 1 and Fig. 1, respectively. During that time, she has remained on pharmacotherapy. Because of her success with the combination of pharmacotherapy and rTMS, she is reluctant to cease medication.

Table 1 HAMD scores over time

	Assessment date (stage)							
	6/04/2009 (post-acute course score)	6/10/2009 (8 weeks into maintenance programme)	10/3/2010	23/9/2010	20/4/2012	11/10/2012	27/6/2013 (2 weeks prior to birth)	29/8/2013 (6 weeks post-birth)
HAMD score	3	15	6	7	3	4	2	0

HAMD scoring categories 0–7 normal, 8–13 mild, 14–18 moderate, 19–22 severe

Maintenance rTMS during pregnancy

In 2010, Mrs. X wrote a letter to our rTMS committee detailing her desire to start a family with her husband in the future. She provided evidence to support her view that she should be able to continue on her maintenance rTMS treatment if she became pregnant. She felt the positive effects of pharmacotherapy and rTMS on her mood and stability outweighed any potential risk of harm to herself or the foetus.

Our TMS committee, in consultation with the patient, her psychiatrist, and our TMS colleagues at the Monash Alfred Psychiatry Research Centre, agreed with her request to continue with her maintenance rTMS if she was to become pregnant. Prior to this, our rTMS study had excluded pregnant women based on lack of evidence of the safety of its use in this population. However, in light of more recent evidence (Kim et al. 2009; Zhang and Hu 2009; Tan et al. 2008; Zhang et al. 2010), there did not seem to be any clear contraindication to the use of rTMS in pregnant women. Indeed, Wasserman (1998) guidelines on TMS noted that although pregnant patients are usually excluded from rTMS "exceptions may be made if the potential benefit of rTMS is more significant than the risk".

Mrs. X became pregnant in November 2012, and our rTMS unit was promptly notified. She continued her maintenance treatment as usual, having treatment once every 2 weeks. There were no antenatal complications and her foetus developed normally. She had her last treatment 2 weeks prior to giving birth and returned for treatment 2 weeks post-delivery. She remained in remission from depression throughout her pregnancy and did not develop post-natal depression (see HAMD and Zung results in Table 1 and Fig. 1).

In the last trimester of her pregnancy, it was noted the baby was in the breech position. She was scheduled for a lower section caesarean section delivery; however, she spontaneously went into labour at 39 weeks. A non-eventful caesarean section was performed resulting in the delivery of a healthy male infant weighing 3.44 kg. He measured 49 cm long with a head circumference of 35 cm. He had normal APGAR test scores at both 1 and 5 min post-delivery (8 and 9, respectively). Mother and baby were both discharged from hospital 1 week post-delivery, both healthy.

Mrs. X continues to have success with maintenance rTMS well into the post-natal period. Her last assessment was conducted 6 weeks post-delivery (results in Table 1).

Conclusions

This is the first documented case of a pregnant patient receiving long-term regular maintenance rTMS treatment for her depression. The patient did not show any adverse reaction to the treatment during or after her pregnancy, consistent with previous studies of rTMS in pregnancy. It is notable that the patient did not develop any post-natal depression.

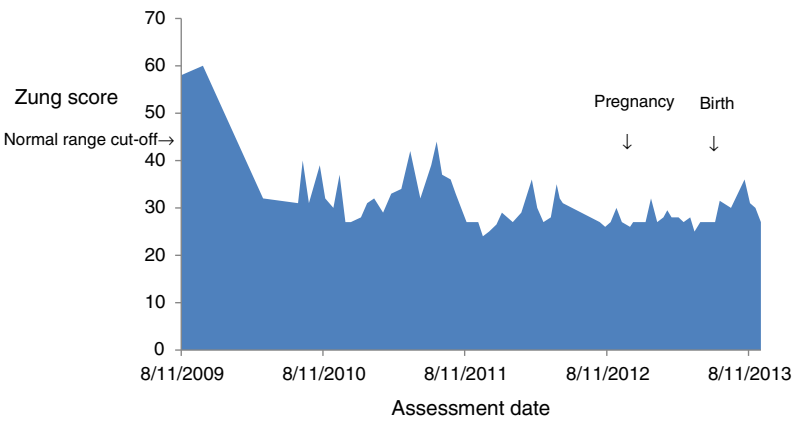

Fig. 1 Zung depression scores over time. Score categories 20–44 normal, 45–59 mild depression, 60–69 moderate depression

It appears that the combination of rTMS and her psychiatric medication was able to maintain her in remission throughout her pregnancy and subsequently. There was no harm caused to the developing foetus, and the baby continues to remain healthy. In theory, rTMS should be a safe treatment in depression. The strength of the magnetic field declines quickly as one moves further from the coil, in a logarithmic fashion. With a coil placed over the mother's scalp, the strength of the magnetic field in the uterus, and therefore the foetus, would be very low.

It should be noted that the rTMS parameters used in this study differ from those reported in previous studies, limiting comparison of our case report with previous findings. Future research is needed to determine optimal rTMS treatment parameters for use in pregnant women.

Repetitive TMS may be an effective and feasible treatment option for depressed women during their pregnancy; however, further research is needed. Indeed, if the efficacy and safety of rTMS are supported by future research, it may well prove to be the treatment of choice for antenatal depression.

References

Bodnar LM, Wisner KL, Moses-Kolko E, Sit DK, Hanusa BH (2009) Prepregnancy body mass index, gestational weight gain, and the likelihood of major depressive disorder during pregnancy. J Clin Psychiatry 70:1290–1296

Chung TK, Lau TK, Yip AS, Chiu HF, Lee DT (2001) Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. Psychosom Med 63:830–834

Cripe SM, Frederick IO, Qiu C, Williams MA (2011) Risk of preterm delivery and hypertensive disorders of pregnancy in relation to maternal co-morbid mood and migraine disorders during pregnancy. Paediatr Perinat Epidemiol 25:116–123

Deave T, Heron J, Evans J, Emond A (2008) The impact of maternal depression in pregnancy on early child development. Br J Obstet Gynaecol 115:1043–1051

Fitzgerald PB, Hoy K, Gunewardene R, Slack C, Ibrahim S, Bailey M, Daskalakis ZJ (2011) A randomized trial of unilateral and bilateral prefrontal cortex transcranial magnetic stimulation in treatment-resistant major depression. Psychol Med 41:1187–1196

Galletly C, Gill S, Clarke P, Burton C, Fitzgerald P (2012) A randomised trial comparing repetitive transcranial magnetic stimulation given three days/week and five days/week for the treatment of major depression: is efficacy related to the duration of treatments or the number of treatments? Psychol Med 42:981–988

Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ (2010) A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. Arch Gen Psychiatry 67:1012–1024

Hedlund JL, Vieweg BW (1979) The Hamilton rating scale for depression. J Oper Psychiatr 10:149–165

Kim DR, Gonzalez J, O'Reardon JP (2009) Pregnancy and depression: exploring a new potential treatment option. Curr Psychiatr Rep 11: 443–446

Kim DR, Epperson N, Paré E, Gonzalez JM et al (2011) An open label pilot study of transcranial magnetic stimulation for pregnant women with major depressive disorder. J Womens Health 20:255–261

Kurki T, Hiilesmaa V, Raitasalo R, Mattila H, Ylikorkala O (2000) Depression and anxiety in early pregnancy and risk for preeclampsia. Obstet Gynecol 95:487–490

Li D, Liu L, Odouli R (2009) Presence of depressive symptoms during early pregnancy and the risk of preterm birth: a prospective cohort study. Hum Reprod 24:146–153

Montgomery SA, Asberg M (1979) A new depression scale designed to be sensitive to change. Br J Psychiar 134:382–389

Richards EM, Payne JL (2013) The management of mood disorders in pregnancy: alternatives to antidepressants. CNS Spectr 18:261–271

Slotema CW, Dirk Blom J, Hoek HW, Sommer IEC (2010) Should we expand the toolbox of psychiatric treatment methods to include repetitive transcranial magnetic stimulation (rTMS)? A meta-analysis of the efficacy of rTMS in psychiatric disorders. J Clin Psychiatry 71:873–884

Soderquist J, Wijma B, Thorbert G, Wijma K (2009) Risk factors in pregnancy for post-traumatic stress and depression after childbirth. Br J Obstet Gynaecol 116:672–680

Tan O, Tarhan N, Coban A et al (2008) Antidepressant effect of 58 sessions of rTMS in a pregnant woman with recurrent major depressive disorder: a case report. Prim Care Companion J Clin Psychiatr 10:69–71

Wasserman EM (1998) Risk and safety of repetitive transcranial magnetic stimulation: report and suggested guidelines from the International Workshop on the safety of repetitive transcranial magnetic stimulation. Electroencephalogr Clin Neurophysiol 108:1–16

Yonkers KA, Wisner KI, Steward DE et al (2009) The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynaecologists. Obstet Gynecol 114:703–713

Zhang D, Hu Z (2009) rTMS may be a good choice for pregnant women with depression. Arch Womens Ment Health 12:189–190

Zhang X, Liu K, Sun J, Zheng Z (2010) Safety and feasibility of repetitive transcranial magnetic stimulation (rTMS) as a treatment for major depression during pregnancy. Arch Womens Ment Health 13:369–370

Zung W (1965) A self-rating depression scale. Arch Gen Psychiatry 12: 63–70