Abstract

Managing schizophrenia during pregnancy often presents a clinical dilemma. Although pharmacological interventions are mostly effective for these disorders during pregnancy, there are few drawbacks for this approach. The potential teratogenicity and long duration of interventions required to control the symptoms somehow limits its usage during pregnancy. Here we described a case report of treatment-resistant schizophrenia successfully treated with ECT without obvious complication to the mother and her baby. Conclusion: Electroconvulsive therapy is an ideal alternative treatment for a patient with schizophrenia during pregnancy. ECT also will eliminate the potential side effects of antipsychotic medications on the mother and teratogenicity effect to the fetus, especially during the first trimester.

Keywords: Pregnancy; Electroconvulsive therapy; Schizophrenia

Introduction

Schizophrenia is one of the major psychiatric illnesses that have a high incidence in Malaysian population. Data from National Mental Health Registry for schizophrenia revealed 7351 registered cases from 2003 to 2005. The prime onset for schizophrenia in women is during the childbearing years from ages 25 to 35 [1]. Fertility may be reduced in schizophrenic women, partly related to the illness itself and partly as side effects of typical antipsychotic medication [2,3]. However, with a better care and increased use of atypical (second generation) antipsychotic, 50-60% of the women with schizophrenia will become pregnant; 50% of these pregnancies will be unplanned or unwanted as women with chronic schizophrenia may not practice family planning and victims of sexually abused. These women are likely to be unmarried, have less social supports and they are at greater risk of being an incompetent mother and having the added burden of having to give up their children.

It is not uncommon to have patients with schizophrenia who is pregnant and these maternal schizophrenia require urgent attention and treatment, especially when there are potential adverse-effect of the psychotropic to the fetus. Hence, another method of therapy like ECT can be recommended to maternal schizophrenia who is disturbed mentally and physically. The aim of this report is to highlight the role of ECT as a safety intervention to treat a pregnant patient with schizophrenia in the second trimester.

Case Report

A 22-year-old Malay female was brought to Emergency
Department by her family members, as there were concerns from her family members that she was acting aggressively towards her mother and husband. Previously she was under the follow-up of psychiatric for her schizophrenia which was resistant to antipsychotic medication (treatment resistant schizophrenia). Currently her schizophrenia was controlled with oral haloperidol and lorazepam.

At this presentation in the Emergency Department, she was pregnant for her first child at 17 weeks period of gestation. Referral to psychiatric team was made and she was decided for admission to psychiatric ward. Subsequently, she was decided by the psychiatric team for electroconvulsive therapy for her schizophrenia.

Multidisplinary discussion was made between obstetrician, psychiatrist and anaesthetist prior to procedure. Gastric acid aspiration prophylaxis (iv Ranitidine 50 mg, mist Sod Citrate 30M, iv metachlopromide 10 mg) were given prior to procedures. The ECT was performed under general anaesthesia with rapid sequence induction (RSI) technique using propofol and suxamethonium and endotracheal tube intubation. Her general anaesthesia was supplemented with target controlled infusion of remifentany with the dose of 70 mcg/kg/hr. The obstetric team was requested to standby for every ECT sessions. Full symptomatic remission was achieved after 6 sessions of ECT (at 17th to 21st weeks of gestation). Her pregnancy progress was well and reached full term, and a healthy child was delivered via cesarean section.

Discussion

Psychiatric illness during pregnancy often presents a clinical delemma to psychiatrist and obstetrician. This is because pharmacologic interventions that are usually effective for these disorders have a teratogenic potential and therefore are almost contraindicated during pregnancy. Moreover, these pharmacologic therapies normally require weeks to stabilize the psychiatric illness.

During pregnancy, the risk to fetus and mother maybe substantial depending on the mental and psychologic condition of the mother, her ability to care for herself, and possible suicidality. In a crisis situation, in which the risk of untreated symptoms are extreme, the patient is known to be refractory to medications, or the medications may represent substantial risk to the fetus. Therefore, electroconvulsive therapy may represent a significant valuable alternative in pregnant women with a psychiatric illness.

As all antipsychotics cross the placenta, it has a potential to cause structural or functional dysgenesis of fetal organs and/or skeletal structures especially when exposure occurs in first trimester. However, with this potential risk of teratogenic to the fetus, discontinuation of certain antipsychotic medication is considered unavoidable during pregnancy. Discontinuation of antipsychotic medications among the schizophrenic patients will likely lead to relapse in schizophrenia illness. Review of relevant studies [4,5] has concluded that over the follow-up periods of up to two years, relapse in schizophrenia illness in those patients who have withdrawn from antipsychotic medications occur in around 50% of cases while for people who have continued on antipsychotic medications is about 15%. In other words, for those patients who discontinue antipsychotic medications, the risk of relapse is 2-3 times greater than that it would have been if they have stayed on medications. The risk of relapse is much greater with abrupt discontinuation of medications as compared to those who gradually withdraw the medications.

Specifically, untreated or uncontrolled maternal schizophrenia has been associated with multiple obstetric complications including low APGAR score, prematurity, low birth weights, small for gestational age babies, stillbirth and death [6]. It is unclear whether these outcomes are due to the psychiatric illness themselves or problems that might occur during pregnancy. More importantly, women with schizophrenia may fail to attend pre-natal appointments, eat poorly, smoke more and abuse alcohol or illegal drugs. Therefore, discontinuation of antipsychotic medications in pregnant schizophrenia women will increase multiple risk to the fetus and the mother.

Priority of ECT in the treatment of psychiatric disorders in general population including maternal schizophrenia can be divided into three categories [7] which include ECT as first-line treatment (in the case of severe depressive, schizophrenia psychosis, schizophrenia with life-threatening psychotic conditions or intolerable side-effects of psychopharmacological treatments, ECT as a second-line treatment in condition such as medication failures in depression, schizoaffective psychosis, schizophrenia, mania and depression or psychotic symptoms in case of organic diseases and ECT as a last-resort treatment is reserved for conditions such as treatment-resistant obsessive compulsive disorder (OCD), treatment-resistant dyskinesias, treatment-resistant Gilles de la Tourette syndrome and treatment-
In general, ECT is one of the best-tolerated biological therapies with low risk for severe complications, even lower than during the application of tricyclic antidepressant medications [7]. The mortality rate during ECT varies between 1: 50000 and 1: 25000 treatments [2,8]. In less than one in 10000 treatments severe complications are seen that warrant special attention [7]. ECT therefore is considered to be one of the safest medical procedures under anaesthesia.

Specific issues related to ECT in pregnancy are determined by period of gestation [9,10]. Issues related to anaesthesia are more significant during second and third trimester when the risk of aspiration of regurgitation gastric contents during anaesthesia related to ECT is significantly important as the gravid uterus getting bigger. Another important issue related to anaesthesia in ECT is the risk of aortocaval compression beyond 20 weeks of gestation. Therefore, certain measures need to be considered before anaesthezing a maternal for ECT therapy which include administrating of prophylaxis against aspiration of gastric content, performing rapid sequence induction with criciod pressure, using cuff endotracheal tube during intubation, and measuring to reduce aortocaval compression either by putting the maternal on slight lateral supine position or by putting wedge at patient's back to achieve left tilt position.

Issues related to pregnancy itself include the risk of abruptio placenta and abortion during the first trimester. During the second and third trimester, there is a significant risk of transient fetal bradycardia during ECT therapy and post-ECT uterine contractions and delivery.

ECT procedure itself exposes a specific issues to the mother and the fetal. As the electrical current is delivered, parasympathetic nervous system stimulation will results in maternal bradycardia, or rarely maternal asystole. Shortly thereafter, the sympathetic nervous system will be stimulated, which will lead to maternal tachycardia and hypertension lasting for 5 minutes or longer, exposing the mother to the risk of excessive hypertension and life-threatening cardiac arrhythmias. This risk will remain present during the first, second and third trimester of gestation. As for the fetal, especially during second and third trimester, surge of catecholamine from the activation of sympathetic nervous system will affect the circulation to the uterus. Intense vasoconstriction to the uterus circulation will decrease blood flow to the uterus and placental with a potential complications of causing fetal hypoxia and bradycardia.

As for outpatient, she was referred for ECT therapy at 18 weeks gestational age and required 6 cycles of ECT therapy. The first ECT therapy was performed at 18 weeks gestational age and the 6th ECT therapy was performed at 21 weeks gestational age. Seizure duration ranging from 35 seconds to 53 seconds and ECT doses ranging from 35 mc to 53 mc. No obvious complication was noted during the whole six episodes of ECT therapy. In managing this patient, the risk of pulmonary aspiration is the main concern together with the risk of compromised fetal condition and preterm delivery. For each ECT session, fetal well-being was monitored by the obstetrician who performed ultrasound fetal monitoring at pre- and post-ECT procedure.

As for her anaesthetic care during electroconvulsive therapy (ECT) procedures, Propofol was used as an anaesthetic agent for ECT therapy as recommended during pregnancy [10,11], due it rapid induction and fast recovery properties. Suxamethonium, the short acting depolarising neuromuscular blocking agent was given to facilitate rapid sequence induction and to prevent seizure induces injury [12]. Remifentanil is a potent short-acting opioid analgesic, and has been found to reduce blood pressure and heart rate when administered as an adjuvant to general anaesthesia and it does not affect the duration of ECT-induce seizure activity, does not prolong the recovery times or increase post-ECT rise effects [13]. However, remifentanil is classified as Category C by FDA, animal studies have failed to reveal evidence of teratogenicity. Until now, there are no controlled data study in human pregnancy.

Maintaining a good hemodynamic parameters is very important in order to prevent fetal hypoxia. Hemodynamic responses that occur during ECT procedure consist of generalised autonomic nervous system stimulation [14]. As the electrical current is delivered, parasympathetic nervous system stimulation will results in sinus bradycardia, or rarely asystole. Shortly thereafter, sympathetic nervous system will be activated, which lead to sinus tachycardia and hypertension lasting for 5 minutes or longer. This may lead to arrhythmias and increase catecholamine release which can affect circulation to the uterus [15]. Vasoconstriction induce by the release of catecholamine will decrease blood flow to the uterus and placenta and potentially lead to fetal hypoxia. Patient was positioned on a supine position with slight left lateral position by putting wedge on her left side.
of the body. This is important as aortocaval compression can further impaired maternal circulation to the uterus and placenta which can further worsen fetal hypoxia.

**Conclusion**

Electroconvulsive therapy is an ideal alternative treatment for schizophrenia patient during pregnancy. It can either be as a first-line treatment or as a second-line treatment where medications fail to control or possibility of medication resistant schizophrenia. Although ECT was proven to be a safe medical procedure during pregnancy, certain precautionary measures related to anaesthesia, pregnancy and procedure in ECT must be taken before proceeding to the therapy.

**Acknowledgements**

The authors would like to thank the Director General of Health Malaysia for his permission to publish this article. The authors would also like to thank all multidisciplinary members of the psychiatric teams, obstetrics team, and anaesthetics team for their dedications, efforts and support in managing this case.

**Compliance with ethics guidelines**

Abdul Karim O, Noraslawati R, Anisah J, and Syaratul Emma H declare that we have no conflict of interest. Patient anonymity was preserved and this article does not contain any animal studies with animal subjects performed by any of the authors.

**Funding**

No funding sources.

**Ethical approval**

Not required.

**NMRR approval**

Approved.

**References**

1. Leung A, Chue P. Sex differences in schizophrenia, a review of the literature. Acta Psychiatr Scand Suppl. 2000;401:3–38.
2. Howard LM. Fertility and pregnancy in women with psychotic disorders. Eur J Obstet Gynecol Reprod Biol. 2005 Mar;119(1):3–10.
3. Newport DJ, Calamaras MR, DeVane CL, Donovan Cur Op Gyn Obs, 1(1): 48-52 (2018).
4. Barnes TRE, Schizophrenia Consensus Group of British Association for Psychopharmacology. Evidence-based guidelines for the pharmacological treatment of schizophrenia: recommendations from the British Association for Psychopharmacology. J Psychopharmacol (Oxford). 2011 May;25(5):567–620.
5. Viguera AC, Baldessarini RJ, Hegarty JD, van Kammen DP, Tohen M. Clinical risk following abrupt and gradual withdrawal of maintenance neuroleptic treatment. Arch Gen Psychiatry. 1997 Jan;54(1):49–55.
6. Nilsson E, Lichtenstein P, Cnattingius S, Murray RM, Hultman CM. Women with schizophrenia: pregnancy outcome and infant death among their offspring. Schizophr Res. 2002 Dec 1;58(2–3):221–9.
7. Fink M, Sackeim HA. Convulsive therapy in schizophrenia? Schizophr Bull. 1996;22(1):27–39.
8. American Psychiatric Association Committee on Electroconvulsive Therapy. Weiner RD, Coffey CE, Folk J, Fochtman LI, Greeberg RM et al. The practice of electroconvulsive therapy. 2nd ed. Washington DC: American Psychiatric Association;2001.
9. Echevarría Moreno M, Martin Muñoz J, Sanchez Valderrabanos J, Vázquez Gutierrez T. Electroconvulsive therapy in the first trimester of pregnancy. J ECT. 1998 Dec;14(4):251–4.
10. Anderson EL, Reti IM. ECT in pregnancy: a review of the literature from 1941 to 2007. Psychosom Med. 2009 Feb;71(2):235–42.
11. Kuczkowski KM. Advances in obstetric anesthesia: anesthesia for fetal intrapartum operations on placental support. J Anesth. 2007;21(2):243–51.
12. Guay J, Grenier Y, Varin F. Clinical pharmacokinetics of neuromuscular relaxants in pregnancy. Clin Pharmacokinet. 1998 Jun;34(6):483.
13. Sebel PS, Hoke JF, Westmoreland C, Hug CC, Muir KT, Szlam F. Histamine concentrations and hemodynamic responses after remifentanil. Anesth Analg. 1995 May;80(5):990–3.
14. Ding Z, White PF. Anaesthesia for electroconvulsive therapy. Anesth Analg 2002;94:1351-64.
15. Mayo C, Kaye AD, Conrad E, Baluch A, Frost E. Update on anesthesia considerations for electroconvulsive therapy. Middle East J Anaesthesiol. 2010 Feb;20(4):493–8.
