Policy

Clinical Guideline

Psychotropic Medication during Pregnancy and Breastfeeding

Policy developed by: SA Maternal & Neonatal Community of Practice
Approved SA Health Safety & Quality Strategic Governance Committee on: 19 April 2016
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Summary	Clinical practice guideline on the use of psychotropic medication during pregnancy and breastfeeding
Keywords	Psychotropic medication during pregnancy and breastfeeding, clinical guideline, psychotropic medication, prescribe, therapeutic guidelines, depression, bipolar, anxiety, puerperal psychosis, LactMed, SSRIs, SNRIs, tricyclic antidepressants, antidepressants, benzodiazepines, mood stabilisers, antipsychotics
Policy history	Is this a new policy? **N** Does this policy amend or update an existing policy? **Y v2.0** Does this policy replace an existing policy? **N** If so, which policies?
Applies to	All SA Health Portfolio
Staff impact	All Staff, Management, Admin, Students, Volunteers All Clinical, Medical, Nursing, Allied Health, Emergency, Dental, Mental Health, Pathology
PDS reference	CG191

Version control and change history

Version	Date from	Date to	Amendment
1.0	30 Mar 2010	08 Jan 2013	Original version
2.0	08 Jan 2013	19 April 2016	Reviewed
3.0	19 April 2016	Current	

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Note

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:
The aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant women. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that Perinatal services prepare to respectively manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Introduction

> Both Australia and the United Kingdom have recently published well-researched and authoritative guidelines for use of psychotropics in the perinatal period (see below)

> In addition, new evidence is constantly being published which requires any guidelines to be regularly updated. For these reasons, this document does not attempt to provide a stand-alone set of guidelines. Rather, it identifies readily available existing resources which the prescriber can consult in any situation where psychotropic prescribing is being considered in relation to pregnancy or lactation. In addition, it summarises some fundamental practical points about each type of medication where some degree of consensus is now emerging. However, the reader needs to be aware that this document is attempting to provide prescribing advice in a rapidly developing area in which there continue to remain many uncertainties

To prescribe or not to prescribe?

> A comprehensive discussion of these issues, including the risks of not prescribing (taking account of recently discovered direct adverse impacts of maternal mental illness or fetus) is available in Therapeutic Guidelines, including a protocol for assessing risk

benefits which can be used to educate a woman and her family. All of the existing guidelines present a detailed discussion of the need for a risk-benefit analysis as part of the informed consent process.

> Note that the guidelines cited here emphasise the existence of various forms of psychotherapy as viable alternatives to medication in selected clinical situations

Aboriginal women should be referred to the aboriginal health professional to support their care

Existing guidelines **(for the use of psychotropic medication in pregnancy and lactation)**

> The existing perinatal psychotropic drug guidelines are (in order of currency of publication):

1 **NICE Guideline CG192: Antenatal and Postnatal Mental Health.** Published December 2014. National Institute for Health and Care Excellence, UK. Available from URL: http://www.nice.org.uk/guidance/cg192

2 **Therapeutic Guidelines: Psychotropic 2013.** This publication has had regular on-going updates since 1989. It is arguably the most "user friendly" of the recent guidelines. One chapter deals with psychotropic use in pregnancy and lactation. It includes up-to-date information on nicotine, caffeine and alcohol / other substance use in pregnancy and lactation, which are not usually covered in other guidelines.

3 **BeyondBlue / NHMRC Clinical Practice Guidelines.** Depression and related disorders – anxiety, bipolar disorder, and puerperal psychosis – in the peripartum period. A guideline for primary health professionals, February 2011. BeyondBlue website. Available from URL: http://www.beyondblue.org.au/index.aspx?link_id=6.1246&tmp=FileDownload&fid=1626

Other online sources for up-to-date prescribing information:

4 **Mother to Baby** is a service of the Organisation of Teratology Information Specialists. Available from URL: http://www.mothertobaby.org/

5 **LactMed** is a database concerning medication during lactation. It is updated monthly by the US National Library of Medicine. Available from URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT

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Prescribing in pregnancy

Antidepressants

Selective serotonin reuptake inhibitors/ Serotonin-noradrenaline reuptake inhibitors (SSRIs / SNRIs)

- Numerous large-scale case-control studies and a number of meta-analyses have attempted to address the question of malformation risk with SSRIs. Some have suggested an association with an increased risk of cardiac malformations; however some have found no association. At present there is no conclusive evidence of an increase in the malformation rate above 2-3 % likely association with non-life-threatening neonatal adaptation problems which are usually mild and self-limiting with a reported incidence of up to 30 % in those newborns with antenatal exposure – monitoring of the infant and access to a special care nursery are recommended by the NICE and Beyond Blue guidelines
- Possible association with preterm birth and small for dates infant, although conditions (e.g. chronic depression or stress) for which SSRIs are prescribed may also cause / contribute to the same outcomes
- Persistent Pulmonary Hypertension of the Newborn (PPHN) may be considered a potential major concern, as a result of a 2006 retrospective study. However, of seven subsequent studies, 4 have found an association with SSRI exposure and 3 have not. The most recent study documented a population risk of PPHN of 1.2 per 1,000, increasing to 3 per 1,000 with SSRI exposure. The rareness of this complication suggests it should have no particular influence on prescribing unless there are other clear risk factors present for the woman and fetus, as determined by an obstetrician or paediatrician / neonatologist
- Late gestation exposure to selective serotonin reuptake inhibitors has been associated with a significantly increased risk of PPH and postpartum anaemia, regardless of mode of delivery. Although women and their clinicians should be aware of the potential risks of PPH when making treatment decisions near the end of pregnancy, caution is advised against the routine cessation of antidepressants in late gestation until further research regarding optimal management strategies are available (Grzeskowiak et al. 2015)

Tricyclic antidepressants (TCAs)

- High toxicity in overdose
- No evidence of direct teratogenicity
- Withdrawal or Neonatal Adaptation Syndrome (NAS) is possible
- These are not considered first-line agents outside of the perinatal period, due to higher risk in overdose and higher side effect burden, and there is no reason to prefer them in the perinatal period either – TCAs should only be considered if known to be particularly effective for a specific patient, or as part of working through an algorithm for severe or treatment-resistant depression (refer to the guidelines for depression published by the Royal Australian and New Zealand College of Psychiatrists, available from URL: https://www.ranzcp.org/Publications/Statements-Guidelines.aspx#mood

Other antidepressants

- Including mirtazapine, moclobemide, irreversible MAOIs
- Limited / inadequate evidence. However no indication of increased abnormalities above the background rate

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Benzodiazepines

> Some early studies suggested a slight increase in oral clefting; however more recent research is more reassuring. High resolution ultrasound investigation may be warranted. Use just before birth may result in excessive neonatal sedation and respiratory depression

Mood stabilisers

Lithium

> The risk of cardiac teratogenicity is less than previously believed, estimated in one study to be 0.05-0.1%, or about 1 per 10,000 babies with lithium exposure in the first trimester

> Lithium can therefore be continued during pregnancy if the woman's individual risk-benefit analysis indicates that it is a good choice. Fetal echocardiography may be indicated

> Abrupt cessation is associated with a very high risk of relapse so should be avoided in favour of a slow taper if cessation is chosen

> The NICE and Beyond Blue guidelines provide specific advice concerning monitoring of lithium during pregnancy and management during labour and delivery

Antiepileptics

> Where antiepileptics have been the preferred mood stabiliser, their use in a pregnancy should be carefully reviewed, preferably before conception

> Valproate and carbamazepine should be used only where there is a strong indication in view of the unacceptably high risk of neural tube defects, and in addition with valproate, adverse effects on cognitive function / intelligence quota in children (Nadebaum C et al. 2012)

> High dose folate (5 mg per day) is widely advocated to reduce risk in exposed pregnant women based on animal data, but human studies are mainly lacking

> Lamotrigine clearance may be increased in pregnancy, leading to a reduction in lamotrigine concentrations and potential loss of efficacy[7]

> Lamotrigine levels should be monitored in pregnancy and the dose adjusted accordingly[7]

> To date data suggest that lamotrigine has not been shown to increase the risk of major birth defects, however there are conflicting reports of an association with an increased risk of oral facial clefts

> Atypical antipsychotics and lithium are generally preferred as mood stabilisers in pregnancy however this relative preference needs to be weighed with other factors in the individual woman's risk-benefit analysis

Antipsychotics

First-generation

> No substantial evidence of teratogenicity

Second-generation antipsychotics

> No convincing evidence of teratogenicity

> Clozapine and olanzapine have particularly been associated with increased weight gain and gestational diabetes. Clozapine has a theoretical potential to cause toxicity in the f

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neonate

- There is insufficient data to fully assess the risks of clozapine in pregnancy and hence the manufacturer states it is contraindicated. However, optimal maternal treatment is necessary, and after a thorough risk-benefit analysis the treating psychiatrist may decide its use is justified. Clozapine is usually considered to be unsafe in breastfeeding
- At present no antipsychotic shows clear superiority in terms of safety in pregnancy, so the selection of medication should be made based on personal history of best response and/or usual choice for the presenting psychiatric syndrome

Prescribing during lactation

- All existing guidelines present a risk-benefit analysis. Therapeutic Guidelines provides a protocol for assessing risk and providing patient education
- If the mother is using psychotropic drugs that are associated with drowsiness, monitor the breastfed baby for prolonged sedation, disinterest in feeding and inadequate weight gain, and ensure the mother is informed of safe sleeping practices
- Monotherapy is preferred as this represents less challenge to the baby's immature capacity to metabolise drugs
- For further information regarding the use of specific psychotropic medications in breastfeeding contact the WCHN Medicines and Drug Information Centre – 08 8161 7222 Mon-Fri (9am-5pm)
- For other resources regarding psychotropics and breastfeeding refer to:
    - LactMed at URL: http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
    - Perinatal Psychotropic Medicine Information Service (PPMIS) http://www.ppmis.org.au/medicine_profiles_index/
    - Motherisk at URL: www.motherisk.org

Antidepressants

- There is no substantial evidence (with the possible exception of doxepin) that breast-feeding on either tricyclics or SSRIs pose a significant risk
- Breastfeeding should generally be encouraged

Benzodiazepines

- Longer half-life benzodiazepines (e.g. diazepam) may accumulate if the infant is preterm or jaundiced. Time-limited use of short half-life benzodiazepines is probably acceptable for the mother of a healthy infant

Mood stabilisers

Lithium

- On balance, breast-feeding should be avoided if possible. Very detailed accounts of the pros and cons (as well as dosage changes and suggested infant monitoring) are in existing therapeutic guidelines

Antiepileptics

- As antiepileptic drugs are excreted in breast milk only in low concentrations encour

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breastfeeding

- With lamotrigine there is a theoretical risk of Stevens-Johnson Syndrome in the breastfed infant (based on high dosages in epileptic women). For further breastfeeding advice for women taking antiepileptics, see 'Epilepsy in pregnancy' in the A to Z index at www.sahealth.sa.gov.au/perinatal

Contraception in combination with antiepileptic drugs

- The oral progestogen-only pill or progesterone implant (Implanon®) should not be used for women on the enzyme-inducing anticonvulsants
- Medroxyprogesterone acetate depot injection and Levonorgestrel IUD (Mirena) provide reliable contraception
- Combined pills containing at least 50 micrograms of oestrogen may be appropriate contraception for some women, however specialist advice should be sought. Contact the WCHN Medicines and Drug Information Centre – 08 8161 7222 Mon-Fri (9am-5pm)
- For further information on contraception advice for women on antiepileptics, see 'Epilepsy in pregnancy' in the A to Z index at www.sahealth.sa.gov.au/perinatal

Antipsychotics

First-generation

- Evidence is sparse, but not contraindicated

Second-generation

- Clozapine should be regarded as contraindicated in breast-feeding
- No replicated reports have emerged on risk / benefits of the other second-generation antipsychotics in breast feeding

See: LactMed at URL: http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm

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References

1. National Institute for Health and Care Excellance (NICE). Antenatal and Postnatal Mental Health. NICE Guideline CG192, December 2014. National Institute for Health and Care Excellence, UK. Available from URL: http://www.nice.org.uk/guidance/cg192
2. Clinical Practice Guidelines. Depression and related disorders – anxiety, bipolar disorder, and puerperal psychosis – in the peripartum period. A guideline for primary health professionals, February 2011. Available from URL: http://www.beyondblue.org.au/index.aspx?link_id=6.1246&tmp=FileDownload&fid=1626
3. Psychotropic Expert Group. Therapeutic guidelines: psychotropic. Version 6. Melbourne: Therapeutic Guidelines Limited; 2013. Available from URL: http://www.tg.org.au/index.php?sectionid=48
4. Boyce P, Galbally M, Snellen M, Buist A. Pharmacological treatment of major depression in pregnancy. Chapter in Galbally M, Snellen M and Lewis A, eds. *Psychopharmacology and Pregnancy*. Springer-Verlag, Heidelberg Berlin, 2014.
5. RANZCP Available at URL: http://www.ranzcp.org/Publications/Clinical-Practice-Guidelines.aspx
6. Grigoriadis S, Vonderporten EH, Mamisashvili, L, Roerecke M, Rehm J, Dennis CL, et al. The effect of prenatal antidepressant exposure on neonatal adaptation: a systematic review and meta-analysis. J Clin Psychiatry. 2013;74(4):e309-20. Doi:10.4088/JCP.12r07967.
7. Kieler H, Artama M, Engeland A, Ericsson O, Furu K, Gissler M et al. Selective serotonin reuptake inhibitors during pregnancy and risk of persistent pulmonary hypertension in the newborn: population-based cohort study from the five Nordic countries. BMJ. 2012;344:d8012.
8. Cohen LS, Friedman JM, Jefferson JW, Johnson EM, Weiner ML. A re-evaluation of risk of in utero exposure to lithium. JAMA. 1994;271:146-50.
9. Harden C, Pennell P, Koppel B et al. Practice Parameter update: Management issues for women with epilepsy – Focus on pregnancy (an evidence-based review): Vitamin K, folic acid, blood levels and breastfeeding: Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society. Neurology. 2009; 73; 142-149
10. Boden R, Lundgren M, Brandt L, Reutfors J, Kieler H. Antipsychotics during pregnancy: Relation to fetal and maternal metabolic effects. Arch Gen Psychiatry 2012; 69: 715-21.
11. Nadebaum C; Anderson V; Vajda F; Reutens D; Wood A, Neurobehavioral consequences of prenatal antiepileptic drug exposure, Developmental Neuropsychology 2012; Vol. 37 (1), pp. 1-29.
12. Kulkarni J, Storch A, Baraniuk A, Gilbert H, Gavrilidis E, Worsley Expert Opin Pharmacother. 2015 Jun;16(9):1335-45. doi: 10.1517/14656566.2015.1041501. Antipsychotic use in pregnancy.
13. Grzeskowiak LE, McBain R, Dekker GA, Clifton VL. Antidepressant use in late gestation and risk of postpartum haemorrhage: a retrospective cohort study. BJOG 2015; DOI: 10.1111/1471-0528.13612.

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Abbreviations

ACOG	American College of Obstetrics and Gynecology
DVD	Digital versatile disc
ECT	Electroconvulsive therapy
etc	et cetera meaning 'and so on'
NHMRC	National Health and Medical Research Council
NICE	National Institute for Clinical Excellence
O & G	Obstetrics and Gynaecology
OTIS	Organisation of Teratology Information Specialists
PPHN	Persistent Pulmonary Hypertension of the Newborn
RANZCP	Royal Australian and New Zealand College of Psychiatrists
SNRIs	Serotonin-Noradrenaline Reuptake inhibitors
SSRIs	Selective Serotonin Reuptake Inhibitors
TCAs	Tricyclic Antidepressant
UK	United Kingdom
URL	Uniform Resource Locator

Version control and change history

PDS reference: OCE use only

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