South Australian Paediatric Clinical Guidelines

Psychotropic medication during pregnancy and breastfeeding: A guide to guidelines

Introduction

- A substantial number of well-researched and authoritative guidelines for use of psychotropics in the perinatal period have recently been published (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 on the fetus) is available in Therapeutic Guidelines, including a protocol for assessing risk benefits which can be used to educate a woman and hopefully her partner. All of the existing guidelines present a detailed discussion of risk-benefit analysis
- Most of the guidelines emphasise the need to consider various forms of psychotherapy as a possible alternative to medication

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

- The existing (or forthcoming) perinatal psychotropic drug guidelines are (in order of currency of publication):

1 *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*. A scholarly review with particular emphasis on the actual "hard" evidence, and using little reference to "expert opinion". Many existing guidelines rely quite heavily on the latter. Available from the BeyondBlue website at http://www.beyondblue.org.au/index.aspx?link_id=6.1246&tmp=FileDownload&fid=1626

2 *Guidelines of the American Psychiatric Association and the American College of Obstetrics & Gynecology (2009).* The authors are Kimberly Yonkers, Katherine Wisner, Nada Stotland, Donna Stewart et al. all of whom are world authorities in this area. These **deal very comprehensively with pregnancy, but not breast feeding**. Their focus is only on depression and they do not include mood stabilisers. The main strength of these guidelines is that they present a number of algorithms for common

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clinical scenarios which are very practical and include those for women contemplating pregnancy, those already pregnant etc. They also cover ECT. They were published simultaneously in:

General Hospital Psychiatry: 2009; 31 (5): 403-413

Obstetrics and Gynecology 2009; 114 (3) 703-713

3 *Therapeutic Guidelines: Psychotropic (2009).* 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. Therapeutic Guidelines have recently won a highly prestigious international award for the best e-publication in a professional area. Many institutions have purchased a Therapeutic Guidelines site license. Individuals can purchase the DVD for laptop or desktop, or Mini-TG (for Smart Phone or hand held computer). All versions include the entire Therapeutic Guidelines suite (covering all specialties including Psychiatry)

4 *MotherRisk Guidelines* (Can J Clin Phar 2009; 16, (1). This whole issue of the journal is a very comprehensive set of guidelines covering pregnancy and breastfeeding

5 *A full set of guidelines* published in: Clinical O&G, 2009; 52 (3). It comprises the whole issue of the journal and covers pregnancy and breastfeeding

6 *American College of O & G Guidelines* (updated April 2008) and published in full in O & G; (4) 111:1001-20). This is a comprehensive set of guidelines with an emphasis on obstetric and neonatology complications of psychotropics. However, being at least 18 months old, it must now be considered out-dated

7 *RANZCP guidelines sections on bipolar and major depression* (2009) Available at URL: http://www.ranzcp.org/Publications/Clinical-Practice-Guidelines.aspx

8 Organisation of Teratology Information Specialists. Available from URL: www.otispregnancy.org

9 Perinatal Psychotropic Medicine Information Service (PPMIS) – Royal Women's Hospital, Melbourne. Available from URL: http://www.ppmis.org.au/

10 LactMed. Available from URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT

Prescribing in pregnancy

Antidepressants

Tricyclics

- High toxicity on overdose
- No evidence of direct teratogenicity
- Withdrawal or Neonatal Adaptation Disorder is possible

SSRIs / SNRIs

- No evidence of teratogenicity and earlier concerns about paroxetine have not been substantiated in more recent publications. For further information, refer to URL: http://www.otispregnancy.org/pdf/paroxetine
- Likely association with non-life-threatening neonatal adaptation problems which are

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usually mild and self-limiting with a reported incidence of 20 % in those newborns exposed

- 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 in Neonate (PPHN) may be considered a potential major concern, as a result of a 2006 retrospective study. However these concerns have not been confirmed in more recent studies. Risk factors for the development of PPHN include smoking, obesity and preterm birth which occur more often in mothers with depression than those who are not depressed, making it difficult to distinguish between SSRI drug effects and the impact of depression. (Malam 2012)

Other antidepressants

- Including mirtazapine, moclobemide, irreversible MAOIs
- Limited/inadequate evidence. However no indication of increased abnormalities above the background rate. For further information refer to URL:
  - http://www.otispregnancy.org/hm/inside.php?id=41
  - http://www.ppmis.org.au/medicine_profiles_index/

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. For further information refer to URL: http://www.otispregnancy.org/pdf/benzodiazepines
- 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 and some authorities suggest that, if a mood stabiliser is necessary in pregnancy, lithium may well be the drug of choice. For further information, see URL: http://www.otispregnancy.org/pdf/lithium

Antiepileptics

- 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[8]

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- 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 with valproate, adverse effects on cognitive function / intelligence quota (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

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 fetus or 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

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
- 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 is breastfeeding refer to:
  - LactMed at URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~3AIcfo;
  - Perinatal Psychotropic Medicine Information Service (PPMIS) http://www.ppmis.org.au/medicine_profiles_index/
  - Motherisk at URL: www.motherisk.org

Antidepressants

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- 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 encourage 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 chapter 66 Epilepsy in pregnancy at URL: http://www.health.sa.gov.au/PPG/Default.aspx?tabid=101#2685

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 sort. 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 chapter 66 Epilepsy in pregnancy at URL: http://www.health.sa.gov.au/PPG/Default.aspx?tabid=101#2685

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

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- See: LactMed at URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT

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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
RANZCP	Royal Australian and New Zealand College of Psychiatrists
URL	Uniform Resource Locator

Version control and change history

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