UNIT NO. 6

SPECIAL POPULATIONS

Dr Chua Tze-Ern

ABSTRACT

Age and other physical attributes may affect the presentation and management of depressive and bipolar disorders. Three of these populations are discussed in this paper.

In young patients, mood symptoms are less clear-cut than in adults, and pharmacological treatment, if used, should be prescribed at low doses, with close observation for side effects.

In the perinatal population, the diagnosis of depression hinges more on emotional than physical symptoms, as the latter may be a consequence of the gravid state. Treatment of mood disorders in this population is a delicate balance between the timely amelioration of harmful symptoms and the prevention of medication side effects in the child.

In the elderly, sensitivity to the possible existence of depression is important for those who present primarily with chronic illnesses or recent bereavement. Mood symptoms may masquerade as physical complaints and medications should be used with care because of age-retarded drug metabolism.

Keywords: Children, adolescents, perinatal, elderly

SFP2011; 37(4): 31-34

INTRODUCTION

Major depressive and bipolar disorders sometimes affect patients who, by virtue of age or other physical attributes, present with different variants of symptoms, or require different forms of treatment. Three special populations are discussed in this paper:

1. Children and adolescents.
2. Women during the perinatal period.
3. Elderly patients.

It is unlikely for the full range of therapeutic options to be provided in the primary care setting, given its restrictions in terms of allied health resources and the need for psychotropic medications. Most of these patients will be more effectively managed by specialised psychiatric care providers. Nonetheless, the following discussion may be used to facilitate the recognition, initial treatment and psychoeducation of mood disorders in these populations by the family physician.

CHUA TZE-ERN, Associate Consultant, Kandang Kerbau Women's & Children's Hospital

I. CHILDREN AND ADOLESCENTS

Assessment

Very young patients will probably require the presence of their parents, while older ones may prefer a private consultation. The style of communication should be tailored to suit the patient's age and attention span.

Assessment should include the patient's parents, partly because a positive family history of mood disorders raises the likelihood of a diagnosis, and also because it may contribute to a difficult home environment that is not conducive to recovery.

Depression

As opposed to adult patients, depression in the young may manifest as irritability (instead of tearfulness and despondency) and failure to make expected weight gains (instead of outright weight loss)[1].

In many cases, the provision of a professional listening ear in a safe environment will prove therapeutic, as will advice recommending regular and adequate nutrition, rest and exercise. The next line of treatment is psychological therapy, which usually comprises cognitive behavioural therapy, family therapy and/or interpersonal therapy[2].

Antidepressants are effective in severe cases but they must be used with caution because of an association with suicidal thoughts. The US Food and Drug Administration's (FDA) medication guide[3] highlights an analysis that revealed that 4% of young patients on antidepressants developed treatment-emergent suicidal thoughts, compared to 2% on placebo[4]. This finding led to black box warnings on all prescription antidepressants and an FDA-issued public health advisory on their safety risk in young adults up to the age of twenty-five.

These developments imposed restrictions on the management of depression, which, by itself, definitely increases the risk of suicide. They also caused controversy because the highlighted analysis examined a limited number of antidepressants, and none of the patients studied actually committed suicide. However, these warnings serve as a timely reminder that there are drawbacks as well as advantages to using antidepressants in young patients. They do not mean that medication can never be used in this population. On the contrary, it can be (and has been) successfully employed in conjunction with cautious measures, such as small doses, frequent follow-up and careful observation for side effects.

There are indeed some pharmacological options – such as tricyclic antidepressants[5] – that are best avoided in young patients. Among the rest, fluoxetine has emerged as the one FDA-approved antidepressant that produces more benefit than harm in children. National Institute of Health and

Clinical Excellence (NICE) guidelines recommend a starting dose of 10mg daily, with an increase to 20mg daily after one week if necessary, and with consideration of lower doses for smaller children. Another FDA-approved option for patients aged twelve and above is escitalopram (Lexapro). Patients and their parents should be advised of the characteristic delay in the onset of antidepressant effect, in addition to possible side effects. Subsequent follow-up should take place every one to two weeks for a few months, to monitor for symptom progress, side effects and treatment-emergent suicidal thoughts.

Bipolar disorder

Bipolar disorders – especially bipolar II disorder – are more difficult to diagnose as they may manifest as mixed or psychotic symptoms[6]. There may be other explanations for disordered mood and behaviour, such as social stressors, physical illness, substance use, learning difficulties or attention deficit hyperactivity disorder.

Pharmacological treatment of acute mania comprises the same medications as in adult patients, but at lower doses and with close observation for side effects. Patients taking atypical antipsychotics should have their weight and prolactin levels monitored. If possible, valproate should be avoided in young female patients because of its possible long-term impact on fertility[7].

II. WOMEN DURING THE PERINATAL PERIOD

Antenatal depression

Overlaps exist between depressive symptoms and the physiological changes of pregnancy, particularly in terms of sleep patterns, weight and energy levels. Therefore, the diagnosis of antenatal depression, which occurs in 12.2% of local women[8], hinges largely on emotional symptoms, such as anhedonia, negative cognition and suicidality. These symptoms usually have multiple causes, such as the physical demands of pregnancy, stress and anxiety from preparing for the baby's arrival and changes in relationship, career and financial priorities.

A depressed mother may eat or rest poorly, default antenatal follow-up and self-medicate with alcohol, cigarettes or other substances. In addition, her low mood may impair her ability to form an attachment to her unborn child. Antenatal depression is also associated with risks of impaired fetal growth and premature labour, and is a major risk factor for subsequent postnatal depression9. In rare cases, a severely depressed pregnant woman may develop psychotic symptoms and contemplate harmful acts.

Fortunately, prompt recognition usually results in good response to treatment. Patients with milder episodes often recover with psychological support and therapy to help them make sense of their difficult experience. Severely depressed patients may benefit from treatment with antidepressants, but these must be used with caution. Selective serotonin reuptake inhibitors (SSRIs), for example, have been linked to persistent pulmonary hypertension of the newborn and neonatal behavioural syndrome, particularly when administered in late gestation[10]. Paroxetine, in particular, should be avoided in the first trimester because it is associated with odds ratios of 1.46 for cardiac defects and 1.24 for aggregated congenital defects[11]. Antidepressants, if used, should therefore be prescribed at the lowest dose possible, especially during early pregnancy, and patients taking them should be reviewed regularly and often.

Postnatal depression

Although DSM-IV-TR diagnostic criteria define the onset of postnatal depression as four to six weeks post-delivery, emerging evidence suggests it may actually occur as soon as two weeks, or as much as one year, after birth[12].

As with antenatal depression, its causes are multiple. A new mother can become fatigued and overwhelmed by the burden of infant care, especially as it may not allow her sufficient sleep. She is also undergoing physical changes, such as hormonal and weight fluctuations and recovery from the birthing process, and these may affect her self-esteem and libido. At the same time, she often has to manage shifts in her relationship, career and financial priorities, in addition to other events that may unexpectedly crop up, such as breastfeeding problems and illness in the baby.

As many as two out of three mothers may experience baby blues[13], which is a mild state of tearfulness and anxiety very soon after giving birth, because of tiredness and self-doubt about the new maternal role. Fortunately, this state lasts only a few days and resolves without formal medical treatment, especially if the mother has a supportive family.

Postnatal depression, which affects 6.8% of local mothers[8], is different from baby blues because it is more severe and of longer duration (at least two weeks). Left untreated, it may persist and impair the bonding between mother and baby, putting the child at risk for behavioural and emotional problems in the future[9]. Furthermore, because a depressed mother may not provide sufficient stimulation for her child, the cognitive development of the child may be affected. In rare cases, a severely depressed mother may become psychotic and start having suicidal or infanticidal thoughts. Yet, women with postnatal depression may find it difficult to acknowledge their difficulties and their need for help. In such cases, the use of a screening tool, such as the Edinburgh Postnatal Depression Scale, may be helpful in identifying and quantifying their symptoms.

Medication, when required for cases of greater severity, should be used with caution in breastfeeding mothers as a small percentage may be excreted into the breast milk. The milk/plasma drug concentration ratios for tricyclic antidepressants and SSRIs are generally low, although fluoxetine and sertraline are exceptions[14] and should be avoided if possible. Most cases of postnatal depression respond well to supportive therapy and low-dose antidepressants.

Bipolar disorder

Medication is crucial in the treatment of bipolar disorder but it may affect fertility and pregnancy. Carbamazepine and lamotrigine are known to inhibit the desired effect of oral contraceptives[15]. On the other hand, antipsychotics and some antidepressants may cause hyperprolactinemia, and valproate, in comparison to other mood stabilisers, increases the relative risk of oligomenorrhea with hyperandrogenism by over seven-fold[16].

When taken during pregnancy, mood stabilisers increase the risk of fetal malformations and perinatal complications. In particular, sodium valproate is associated with neural tube defects and neurodevelopmental abnormalities, while lithium carbonate is associated with Ebstein's anomaly[17]. Supplemental folate, taken from the periconceptional period, reduces the incidence of neural tube defects but does not prevent other ill-effects[18].

Unfortunately, bipolar relapse is as likely to happen during pregnancy as in any other time, as shown by a study in which 52% of pregnant women and 58% of non-pregnant women with the illness relapsed when taken off medication, there being no statistical difference between the two groups[19]. Furthermore, pregnant women who stop taking their maintenance mood stabilisers experience over twice the risk of recurrence compared to those who continue taking medication[20]. In addition, stopping medication during the postnatal period results in a 70% relapse rate, as this appears to be a time of particular vulnerability to mood disorders[19].

Because of these complications, the decision regarding management of bipolar disorder in pregnancy must be carefully discussed with the patient and her partner. Some patients may choose to stop taking mood stabilisers during pregnancy while others may opt to reduce or maintain their doses. If mood stabilisers are to be reduced or stopped, this should be done gradually, as abrupt discontinuation (i.e. over a fortnight or less) more than halves the time to 25% recurrence[19].

Instead of mood stabilisers, antipsychotics – such as chlorpromazine, haloperidol and quetiapine – may be used to treat bipolar episodes[21]. Reviews of small studies and case reports support their efficacy, although the use of atypical antipsychotics will necessitate monitoring of the patient's weight, blood sugar and blood pressure[22]. Another alternative is electroconvulsive therapy, which is effective for the same indications as in non-pregnant patients. Furthermore, it has relatively few side effects and it has not been implicated as a causal factor of congenital malformations[21].

III. ELDERLY PATIENTS

Depression

Life events that occur with the passage of time – such as the death of a spouse, existential issues or health problems – may precipitate depression, as can medications such as beta-blockers and steroids. Because situations like these are not unexpected in the twilight years, elderly patients may come to think that depression is a natural part of aging, particularly if they also happen to be socially isolated or homebound. Therefore, sensitivity to the possible existence of depression is important in the management of elderly patients who present primarily with chronic illnesses or recent bereavement.

Depression may manifest in an oblique manner in elderly patients; instead of outright sadness, they are more likely to present with physical complaints, self-neglect, poor energy and concentration, memory problems and feelings of hopelessness and anxiety. It may even resemble dementia in some cases – the term for cognitive impairment caused by depression is pseudodementia. Unlike actual dementia, however, it is of abrupt onset and resolves when the depression is treated.

When prescribed, medication should be initiated at lower doses and increased more slowly to compensate for slower drug metabolism. There is some evidence linking SSRIs to increased incidence of bone loss[23] and falls, and trazodone, mirtazapine and venlafaxine to higher risks of all-cause mortality. On the other hand, low-dose tricyclic antidepressants showed weaker associations with these adverse outcomes[24]. However, it is difficult to apply these results to real life with absolute certainty because such studies may suffer from the confounding effects of depression and other medical conditions and medication.

In cases of severe depression, the patient may require additional treatment options, such as an antipsychotic, mood stabiliser or electroconvulsive therapy[25].

Bipolar disorder

Mania in the elderly may, in addition to classical symptoms, produce signs suggestive of neurologic impairment, confusion and disorientation. Because of this, clinical examination and investigations are necessary for the exclusion of dementia and delirium.

Medication is generally crucial to the treatment of bipolar disorder, but it can be difficult to prescribe because of the paucity of guidelines in this particular population. As in the younger adult population, lithium, valproate, lamotrigine, carbamazepine, antipsychotics and antidepressants exert beneficial effects on the relevant symptoms, and polypharmacy may be necessary, depending on each patient's individual presentation. However, as in depression, starting doses should be lower and upward titration should take place more slowly. Refractory cases may require electroconvulsive therapy or psychotherapy[26].

CONCLUSIONS

Although general concepts of management apply to the special populations of children and adolescents; women in the perinatal period; and the elderly, certain modifications are necessary in order to provide treatment that is safe as well as effective. Because of the intensity of care that is therefore required, prompt referral to specialised psychiatric care is often beneficial, particularly for patients who are severely unwell.

REFERENCES

1. NIMH guideline on depression. US Department of Health & Human Services, National Institutes of Health. NIH Publication No. 11-3561, revised 2011.
2. NICE guideline on clinical management and service guidance – depression in children and young people. The British Psychological Society and The Royal College of Physicians, Sept 2005.
3. FDA medication guide about using antidepressants in children and teenagers, revised 2005. http://www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/UCM161646.pdf
4. Hammad TA. Review and evaluation of clinical data: relationship between psychotropic drugs and pediatric suicidality. Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and Pediatric Advisory Committee, Sept 13-14, 2004.
5. Geller B, Reising D, Leonard HL, Riddle MA, Walsh BT. Critical review of tricyclic antidepressant use in children and adolescents. J Am Acad Child Adolesc Psychiatry 1999; 38(5): 513-6.
6. McClellan J, Kowatch R, Findling R. Practice parameter for the assessment and treatment of children and adolescents with bipolar disorder. J Am Acad Child Adolesc Psychiatry 2008; 1: 107-25.
7. NICE guideline on clinical management and service guidance – bipolar disorder. The British Psychological Society and The Royal College of Physicians, Jul 2006.
8. Chee CYI, Lee DTS, Chong YS, Tan LK, Ng TP, Fones CSL. Confinement and other psychosocial factors in perinatal depression: a transcultural study in Singapore. J Affect Disord 2005; 89: 157-66.
9. Leigh B, Milgrom J. Risk factors for antenatal depression, postnatal depression and parenting stress. BMC Psychiatry 2008: 8: 24; DOI: 10.1186/1471-244X-8-24.
10. Tuccori M, Testi A, Antonioli L, Fornai M, Montagnani S, Ghisu N, Colucci R, Corona T, Blandizzi C, Del Tacca M. Safety concerns associated with the use of serotonin reuptake inhibitors and other serotonergic/noradrenergic antidepressants during pregnancy: a review. Clinical Therapeutics 2009; 31, Theme Issue.
11. Wurst KE, Poole C, Ephross SA, Olshan AF, First trimester paroxetine use and the prevalence of congenital, specifically cardiac, defects: a meta-analysis of epidemiological studies. Birth Defects Research (Part A) 2010; 88:159-70.
12. Gaynes BN, Gavin N, Meltzer-Brody S, Lohr KN, Swinson T, Gartlehner G, Brody S, Miller WC. Perinatal depression: prevalence, screening accuracy, and screening outcomes. Evidence Report/Technology Assessment No. 119. AHRQ Publication No. 05-E006-2. Rockville, MD: Agency for Healthcare Research and Quality, 2005 Feb
13. Beck CT, Reynolds MA, Rutowski P. Maternity blues and postpartum depression. J Obstet Gynecol Neonatal Nurs 1992; 21: 287-93.
14. Eberhard-Gran M, Eskild A, Opsjordmoen S. Use of psychotropic medications in treating mood disorders during lactation. CNS Drugs 2006; 20(3): 187-98.
15. Gaffield ME, Culwell KR, Lee CR. The use of hormonal contraception among women taking anticonvulsant therapy. Contraception 2011; 83: 16-29.
16. Joffe H, Cohen LS, Suppes T, McLaughlin WL, Lavori P, Adams JM, Hwang CH, Hall JE, Sachs GS. Valproate is associated with new-onset oligoamenorrhea with hyperandrogenism in women with bipolar disorder. Biol Psychiatry 2006; 59: 1078-86.
17. Galbally M, Roberts M, Buist A, Perinatal Psychotropic Review Group. Mood stabilisers in pregnancy: a systematic review. Australian and New Zealand Journal of Psychiatry 2010; 44: 967-77.
18. De-Regil LM, Fernandez-Gaxiola AC, Dowswell T, Pena-Rosas JP. Effects and safety of periconceptional folate supplementation for preventing birth defects. Cochrane Database of Systematic Reviews 2010, Issue 10. Art No: CD007950; DOI: 10.1002/14651858.CD007950.pub2
19. Viguera AC, Nonacs R, Cohen LS, Tondo L, Murray A, Baldessarini RJ. Risk of recurrence of bipolar disorder in pregnant and nonpregnant women after discontinuing lithium maintenance. Am J Psychiatry 2000; 157: 179-84.
20. Viguera AC, Whitfield T, Baldessarini RJ, Newport DJ, Stowe Z, Reminick A, Zurick A, Cohen LS. Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabiliser discontinuation. Am J Psychiatry 2007; 164: 1817-24.
21. Yonkers KA, Wisner KL, Stowe Z, Leibenluft E, Cohen L, Miller L, Manber R, Viguera A, Suppes T, Altshuler L. Management of bipolar disorder during pregnancy and the postpartum period. Am J Psychiatry 2004; 161: 608-20.
22. Gentile S. Antipsychotic therapy during early and late pregnancy: a systematic review. Schizophrenia Bulletin 2010; 36(3): 518-44.
23. Diem SJ, Blackwell TL, Stone KL, Yaffe K, Haney EM, Bliziotes MM, Ensrud KE. Use of antidepressants and rates of hip bone loss in older women. Arch Intern Med 2007; 167: 1240-5.
24. Coupland C, Dhiman D, Morriss R, Arthur A, Barton G, Hippisley-Cox J. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. BMJ 2011; 343:d4551
25. Alexopoulos GS, Streim J, Carpenter D, Docherty JP; expert consensus panel for using antipsychotic drugs in older patients. J Clin Psychiatry 2004; 65(2): 5-99.
26. Aziz R, Lorberg B, Tampi RR. Treatments for late-life bipolar disorder. Am J Geriatr Pharmacother 2006; 4(4): 347-64.

LEARNING POINTS

- **Mood symptoms in children are less obvious than in adults, and should be elicited using age-appropriate communication, with parental involvement.**
- **In young patients, antidepressants should be used with caution because of their association with suicidal thinking, while anti-manic agents should be prescribed at low doses in conjunction with close observation for side effects.**
- **Perinatal depression is common, and is potentially harmful to both mother and baby.**
- **With psychological support and judicious pharmacotherapy, perinatal mood disorders often resolve satisfactorily.**
- **In the elderly, mood symptoms may manifest as physical discomfort and neurological symptoms, and may even be mistaken as a natural component of old age.**
- **Medications for mood disorders in the elderly should be initiated at low doses and increased slowly if needed.**
- **Mood disorders in all these populations frequently warrant prompt referral to specialised psychiatric care in view of the need for intensive treatment.**