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ARTICLE

Perimenopausal depression – an under-recognised entity

SUMMARY

There is a high rate of suicide in women aged 45–54 years. This may be related to the biological changes associated with the menopause.

Perimenopausal depression may present with symptoms that differ from those of typical depression.

Management can include psychotherapy and other non-drug interventions. If drug treatment is indicated, it may be hormone replacement therapy, an antidepressant or both.

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Introduction

Mental health disorders can have devastating impacts on women as they approach menopause. This phase of a woman's life, typically between 42 and 52 years of age, is known as the 'perimenopause' and mental illness is very prevalent, in women at this stage. The risk of serious depression is significantly increased in perimenopausal women.[1] The adverse impact also affects her family and society.

Research specifically targeting the mental health of perimenopausal women is lacking. There is a gap in the recognition and provision of appropriate treatments for middle-aged women experiencing depression related to the hormonal changes of the menopause.

Epidemiology

Australian statistical data[2] show that the highest age-specific suicide rate for females in 2015 was in the 45–49 age group with 82 deaths (10.4 per 100 000). The second highest rate of suicide was in women aged between 50 and 54 years. These suicides should alert us to think about contributing factors, including biological changes in the gonadal hormones associated with the transition to menopause as well as social and psychological stresses in the midlife period.

In the 2007 National Survey of Mental Health and Wellbeing, the Australian Bureau of Statistics identified that 43% of women aged 18–65 years had a mental health problem at some point in their lives. In the preceding year, twice as many women compared to men suffered from mood disorders and four times more women experienced anxiety disorders. Among those with a mental illness in the preceding year, women had higher rates of suicidal thoughts and plans, compared to men. This shows that women clearly carry a high burden of mental illness and suicidality.

The Australian Bureau of Statistics has estimated that the economic cost of depression and anxiety in women (from lost productivity) could be as high as $22 billion per year. As outlined in an Australian Health Policy Collaboration Paper,[3] current funding for mental health from the Australian Government was 'neither effective nor efficient'. The paper highlighted that 'the lack of a gender lens, leading to gender-blind data and gender-blind proposals for reform, is problematic'. Furthermore, the social and psychological costs of depression and anxiety in women are extraordinarily high, when one considers the impact on families, communities and workplaces where women have vital roles. In addition to their many roles in the workforce, women commonly provide much needed care for children, partners and parents.

Diagnostic difficulties

The World Health Organization defines the perimenopause as 'the time immediately preceding the menopause, beginning with endocrine, biologic and clinical changes, and ending a year after the final menstrual period'. The diagnosis of perimenopausal depression is therefore often made retrospectively. To complicate matters the physical symptoms of the menopause often present much later (up to five years) than the psychological symptoms. This delay can make the diagnosis of perimenopausal depression very difficult. It is important for health professionals to consider whether women who experience depressive and anxiety symptoms for the first time in their mid-40s are actually experiencing depression related to the perimenopausal hormone fluctuations. Similarly, women who experience an exacerbation of a previously well-controlled depression may also be experiencing a perimenopausal relapse.

Symptoms

Perimenopausal depression includes a wide range of symptoms. Some are seen in the 'typical depression' that men and younger women experience, while other symptoms are unusual. Perimenopausal symptoms can fluctuate in severity, thus adding to the diagnostic difficulty. The common symptoms in perimenopausal depression (see Box) are detailed in a questionnaire called the MENO-D.[4] In particular, the cognitive symptoms, paranoia and irritability are marked in perimenopausal depression compared to symptoms of major depressive disorders seen in men or younger women.

Management of perimenopausal depression

The course of mental illness in women differs from that of men and is greatly influenced by biological, psychological and social changes over the life cycle. However, most treatments for mental illnesses have been developed and trialled in the 'typical' male patient which may not be the optimal treatment for women with mental ill health related to the menopause.

It is vital to investigate the physical health of a woman presenting with perimenopausal depression to rule out other causes for her symptoms, such as thyroid disorders and autoimmune disorders. This also establishes a good physical baseline for the woman as she embarks on menopausal changes and possibly hormone treatments. Having ruled out other causes of the symptoms, the treatment of perimenopausal depression needs to take a holistic biopsychosocial approach.

Psychosocial treatments

If the woman's perimenopausal depression is clearly related to work or relationship problems, then psychotherapy is an important intervention. Other useful interventions for general well-being include education about menopause, regular exercise, mindfulness techniques, yoga and dietary advice. Minimising alcohol intake is very important for the patient's mental and physical health.

Drug or 'biological' treatments

Treatments for perimenopausal depression usually include antidepressants and gonadal hormones. Often, the order in which they are used depends on the clinician's particular expertise or medical specialty.

Hormone therapy alone may be appropriate for recent onset depression, without suicidality, in otherwise healthy women experiencing other perimenopausal symptoms. The hormone therapy chosen must be tailored for each patient. Recommendations by the International Menopause Society, updated in 2016,[5] are a useful, comprehensive set of evidence-based practice guidelines.

Tibolone is a synthetic steroid with a mixed hormonal profile which has shown benefit in treating perimenopausal depression.[6] Tibolone can cause minor intermenstrual bleeding, but does not cause increased breast density.[6]

Bioidentical hormones are compounds synthesised to resemble ovarian hormones. There are limited safety and dosing data on these compounds which are not recommended by the International Menopause Society.[5]

Antidepressant treatment for perimenopausal depression usually begins with a selective serotonin reuptake inhibitor. If this approach is not effective, serotonin noradrenaline reuptake inhibitors are often second-line drugs. However, both classes can have agitating adverse effects and a woman with prominent perimenopausal insomnia, irritability and anxiety may experience exacerbation of these symptoms with drugs such as fluoxetine. Agomelatine is a newer antidepressant with positive sedative impact and fewer adverse effects in women with perimenopausal depression.[7]

Combining hormone therapy and antidepressant therapy may be required for perimenopausal women with depressive symptoms that do not respond to either treatment alone. In such cases, the adverse effects of combined treatment need to be monitored carefully.

Box Symptoms of perimenopausal depression

- Low energy
- Paranoid thinking
- Irritability or hostility
- Decreased self-esteem
- Isolation
- Anxiety
- Somatic symptoms
- Sleep disturbance
- Weight gain
- Decreased sexual interest
- Problems with memory and concentration

Conclusion

Most women with perimenopausal depression respond to treatment. It is important to recognise the special symptoms of perimenopausal depression as well as the serious nature of this depression. Clinicians need to provide a tailored management approach for these women. It is not appropriate to deem this

type of depression as minor or presume that, once the hormonal fluctuations settle, the depression will improve. The process of menopause can take many years, during which the patient's quality of life and that of her family, may deteriorate irreparably. Tragically, suicide in middle-aged women is becoming a more common occurrence. <

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REFERENCES

1. Clayton AH, Ninan PT. Depression or menopause? Presentation and management of major depressive disorder in perimenopausal and postmenopausal women. Prim Care Companion J Clin Psychiatry 2010;12::e1-13. https://doi.org/10.4088/PCC.08r00747blu
2. Australian Bureau of Statistics. 3303.0 - Causes of Death, Australia, 2015. Canberra: Australian Bureau of Statistics; 2016 Sep 28. www.abs.gov.au/AUSSTATS/abs@.nsf/allprimarymainfeatures/2ABFC8DC5C3C53A9CA2581A7001599A3?opendocument# [cited 2018 Nov 1]
3. Duggan M. Investing in women's mental health: strengthening the foundations for women, families and the Australian economy. Australian Health Policy Collaboration Issues paper no. 2016-02. Melbourne: Australian Health Policy Collaboration; 2016. https://www.vu.edu.au/australian-health-policy-collaboration/publications [cited 2018 Nov 1]
4. Kulkarni J, Gavrilidis E, Hudaib AR, Bleeker C, Worsley R, Gurvich C. Development and validation of a new rating scale for perimenopausal depression – the Meno-D. Transl Psychiatry 2018;8:123. https://doi.org/10.1038/s41398-018-0172-0
5. Baber RJ, Panay N, Fenton A; IMS Writing Group. 2016 IMS recommendations on women's midlife health and menopause hormone therapy. Climacteric 2016;19:109-50. https://doi.org/10.3109/13697137.2015.1129166
6. Kulkarni J, Gavrilidis E, Thomas N, Hudaib AR, Worsley R, Thew C, et al. Tibolone improves depression in women through the menopause transition: a double-blind randomized controlled trial of adjunctive tibolone. J Affect Disord 2018;236:88-92. https://doi.org/10.1016/j.jad.2018.04.103
7. Krüger S, Tran T. EPA-1061 – Agomelatine in the treatment of perimenopausal depression - a pilot study. Eur Psychiatry 2014;29 Suppl 1:1. https://doi.org/10.1016/S0924-9338(14)78345-2