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The pregnancy and postpartum period appear to be a time of heightened vulnerability for the development of major depression in some women. The treatment of depressive disorder during pregnancy is an important but complex clinical topic. This article provides a systemic review of treatments for depressive disorder during pregnancy and lactation: Psychotherapy, Pharmacotherapy, Electroconvulsive therapy and other effective treatments.

PubMed and EMBASE were searched using terms with regard to the treatment of depressive disorders during pregnancy and lactation. Reference lists of related reviews and studies were searched. In addition, relevant SUDFWLFHJXLGHOLQHVZHUHVHDUFKHGXVLQJWKH3XE0HGDQGLGHQWLÀHGFOLQLFDOOLWHUDWXUHZHUHUHYLHZHGDQGVXPPDUL]HG in a narrative manner.

The treatment option for depressive disorders during pregnancy and lactation depends on the severity of depressive illnesses of the individual patient. For mild to moderate depression, the non-pharmacological treatment VKRXOGEHFRQVLGHUHGÀUVW)RUPRGHUDWHWRVHYHUHGHSUHVVLRQSKDUPDFRWKHUDS\VKRXOGEHDGPLQLVWHUHGLQDGGLWLRQ to the psychosocial treatment. ECT is recommended for depressive disorder of severe intensity. Treatment strategies are described according to the point of time of pregnancy or lactation. FDA categories for antidepressants during pregnancy and lactation are described. In addition, issues regarding to the electroconvulsive therapy and psychosocial treatment are discussed.

Treatments during pregnancy and lactation requires a comprehensive assessment of the risks DQGEHQHÀWVRIWUHDWPHQWIRUERWKPRWKHUDQGLQIDQWV)XUWKHUPRUHQWH5HFHQWWKHUHLVJURZLQJHYLGHQFHWKDWWKHXVHRI

Keywords: Depression; Pregnancy; Lactation;Antidepressant; er-apeutic approach

Introduction

About 70% of pregnant women experience depressive symptoms during their gestation period and the prevalence rates of the major depressive disorders during pregnancy range from 10% to 16% [1]. ese imply that pregnancy cannot protect women from depression. e factors that increase the depression risk of pregnant women include a history of depression and premenstrual syndrome, motherhood at a young age or single motherhood, lack of social support, multiple births, couple con ict, and ambivalent emotions on pregnancy [2]. When depression during pregnancy is not treated, various problems such as nutritional de ciency and sleep disorder occur. In addition, depressive mothers may not comply with medical instructions, and their risks of smoking/drug addiction and of committing suicide may increase. Moreover, problems such as fetal growth retardation, premature birth, low birth weight, di cult labor, low Apgar scores, increase in the death rate, mental retardation associated with severe neurological or cognitive function disorders, and insu cient attachment formation may develop [2,3]. us, mothers have the important task of understanding major depressive disorders during pregnancy, which cover the elds of obstetrics, internal medicine, and psychiatry.

e prevalence rate of major depressive disorder a er childbirth is estimated as 10-15% [4]. Major factors of depressive disorders that develop during the perinatal period include a history of postpartum depression and depressive disorders, and a family history of depression, particularly of postpartum depression. Additional factors include low social support, negative life events, an unstable marital relationship, motherhood at a young age, unexpected pregnancy, ambivalent emotions, and newborn health problems, acute or chronic health problems of the mother, insu cient ability to react, and domestic abuse or violation. In minor-age mothers, the prevalence rate of postpartum depression reaches as high as 26% [5].

In principle, medication is avoided during pregnancy. However, in a study [6] that monitored pregnant women with a history of depression, since their pregnancy without depression, 43% of the subjects experienced recurrent depression during their gestation period. e recurrence rate (68%) in the women who stopped taking antidepressant medications was signi cantly higher than that (26%) in the women who continued taking the medication. Clinicians are o en caught in a situation that requires them to choose between discontinuing the prescription of antidepressant medications to pregnant women and prescribing such medications for new depressive pregnant women. Clinicians may be hesitant or reluctant to decide in such a situation. Despite these concerns, many mothers had been reported to have been taking antidepressant medications [7]. According to the report, 42% of the mothers who stopped taking antidepressant medications due to pregnancy resumed their intake of such medications during

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severe depression or with a high risk of recurrence of depression, both psychosocial treatments and pharmacotherapy are essential [6]. When the risk of committing suicide is high, or if the patient cannot undergo pharmacotherapy or does not respond to the aforesaid therapies, electroconvulsive therapy (ECT) can be considered [10,11]. e details of a depression treatment strategy are as follows.

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e decision to discontinue or continue taking antidepressant medications is based on the severity of the symptoms [12]. When the patient has been free from the symptoms for the past six months a er only one depressive episode, it is recommended that she stop taking medications before pregnancy, and to start or maintain psychotherapy [6]. When there is a history of severe repetitivedepressive episodes, a su cient dose of antidepressant medications is maintained during

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Women with a risk of postpartum depression require close monitoring during their pregnancy and a er childbirth. e 7 to 10 days of temporary depressive symptoms a er childbirth, the so-called 'postpartum blues,' does not require a pharmacotherapy [4]. e patient is informed that the depression is temporary with a good prognosis. In cases with a history of postpartum depression, preventive treatments such as taking antidepressant medications are necessary, and if discontinued due to pregnancy, must be resumed a er childbirth [13]. When mothers want lactation, the bene t of pharmacotherapy and their potential e ects on newborn babies are su ciently explained to the mother before she decides on lactation. e short- or long-

prenatal drug toxicity or to the withdrawal symptoms. It is di cult to recognize these symptoms because the behavior of newborn babies is not yet well understood, and these symptoms are hardly di erentiated from the e ects of other internal diseases, obstetric problems, and drug e ects. TCA withdrawal syndrome or neonatal withdrawal symptoms are understood to be associated with the noradrenalin and dopamin channels, which are related to cholinergic rebounds [26]. Since SSRI does not a ect the choline and adrenalin receptors, no withdrawal symptoms were expected in newborn babies. However, according to recent studies [27], SSRI could cause neonatal abstinence syndrome.

e analysis of the frequency of neonatal abstinence syndrome and convulsions of newborn babies showed that the paroxetine frequency, two-thirds, was the highest, followed by the uoxetine, sertraline, and citalopram frequencies. is may be because paroxetine strongly combines with muscarinic receptors, unlike other SSRIs. Regarding neonatal abstinence syndrome, we advise mothers not to take paroxetine during pregnancy; but if it is unavoidable, we suggest the lowest e ective dose. Among new antidepressant medications, venlafaxine reportedly causes neonatal abstinence syndrome. e syndrome disappears within one to 14 days, but clinicians may need to consider gradually reducing the dose of antidepressant medications 10 to 14 days before childbirth to prevent these withdrawal symptoms. A er childbirth, the dose is restored to the pre-pregnancy level [2].

D g ea en d ing lac a ion: e US FDA has a separate drug safety grading system during the lactation period [28]. Category L1 includes drugs that have had no reported side e ects a er many lactating mothers took them, and no side e ects in their newborn babies and in controlled studies, did not increase the risk in newborn babies. Category L2 drugs were investigated with a limited number of lactating mothers, and no side e ects were reported in their newborn babies. Category L3 drugs are used for newborn babies only when their bene ts outweigh their hazards, and there has been no controlled study on them. Category L4 drugs have been reported as hazardous to newborn babies through lactation, but their bene ts for mothers outweigh their hazards to babies, so they can be used on a case-by-case basis. Category L5 drugs are clearly understood as hazardous to newborn babies, besides which their hazards outweigh any bene ts, so they are contraindicated for lactating mothers.

TCA is usually secreted through the breast milk in a low concentration. Amitryptyline, imipramine, nortriptyline, desipramine, and clomipramine are Category L2 drugs, and trimipramine is Category L3. Since doxepine has metabolites with long half-lives, it is accumulated in newborn babies and is thus classi ed as Category L5. Fluoxetine is an SSRI and has nor uoxetine, a metabolite with a long half-life, which is accumulated in newborn babies. Its risk to newborn babies is too high, so it is classi ed as Category L3, and Category L2 for older infants. Fluvoxamine, paroxetine, and setraline are Category L2, and citalopram, L3. Among atypical antidepressants, trazodone is Category L2, and buproprion, maprotiline, nefazodone, and venlafaxine, L3. In the Canadian Guidelines [10], TCA and SSRI are not contraindicated in the preliminary results due to the lack of data on the long-term e ects of antidepressant drugs secreted during the lactation period on infant development.

O he a ea en : Electroconvulsive therapy can be considered for patients with severe depression, psychotic symptoms, no response to medications, severe side e ects that have stopped pharmacotherapy, preference for electroconvulsive therapy a er understanding its bene ts and risks, and the risk of committing suicide or infanticide. However, the critical point on convulsion can change due to pregnancy, and no prospective controlled study has been conducted yet. In a study on electroconvulsive therapy for 300 women during their gestation period [29], 9.3% of the fetuses showed arrhythmia as a side e ect. To reduce this ratio, a modi ed standard-type electroconvulsive therapy is used three times a week for one to three weeks according to the individual responses.

e transcranial magnetic stimulation (TMS) technique usually has less signi cant treatment e ects than electroconvulsive therapy,

medications. e medications must be used based on the available information, and the lowest dose that can produce treatment responses must be selected and changed according to the gestation period. Over the past 10 years, the safety of using SSRI during pregnancy and lactation