

Buprenorphine and Methadone for Opioid Addiction During Pregnancy

Ellen L. Mozurkewich, MD, MS*, William F. Rayburn, MD, MBA

KEYWORDS

• Buprenorphine • Methadone • Pregnancy opioid addiction • Neonatal • Abstinence

KEY POINTS

- Opioid substitution therapy with methadone or buprenorphine during and after pregnancy, and postpartum, improves maternal and neonatal outcomes.
- It is expected that the physiologic changes of pregnancy, such as increases in maternal weight, intravascular volume, and renal elimination of drugs will necessitate increased dosage of opioid substitution medications during the second and third trimesters.
- Methadone therapy may be associated with higher treatment satisfaction and treatment retention in comparison with buprenorphine therapy.
- The only well-recognized adverse effect of opioid substitution therapy is the neonatal abstinence syndrome, which is common but not dose dependent. Compared with methadone therapy, buprenorphine therapy reduces duration and severity of neonatal abstinence syndrome.

INTRODUCTION

About 4% of pregnant women in the United States report current illicit drug use.¹ Opioid use during pregnancy has been reported to range between 1% and 21%.¹ Buprenorphine and methadone are opioid-receptor agonists used as opioid substitution therapy to limit the detrimental effects of illicit opioid use.² Opioid substitution therapy with buprenorphine or methadone is used during pregnancy to limit the exposure of the fetus to cycles of opioid withdrawal and reduce risk of infectious comorbidities of illicit opioid use.^{1,2}

Most authorities do not recommend detoxification to abstinence-based recovery during pregnancy because of theoretical risks to the fetus posed by intrauterine opioid

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Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, University of New Mexico School of Medicine, MSC 10 5580, 1 University of New Mexico, Albuquerque, NM 87131, USA

* Corresponding author.

E-mail address: emozurkewich@salud.unm.edu

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withdrawal and the high risk for relapse to illicit opioids.^{3,4} When undertaken as part of a comprehensive care plan, opioid substitution therapy may result in improved access to prenatal care, reduced illicit drug use, reduced exposure to infections associated with intravenous drug use, improved maternal nutrition, and improved infant birth weight.²

Substitution therapy must aim for an appropriate buprenorphine or methadone dose regimen to encourage patient adherence to the treatment program.² In making dosage adjustments, clinicians should be guided by patient-reported craving and withdrawal symptoms.² The requirement for increased doses during pregnancy is expected because of physiologic maternal increases in weight, intravascular volume, and increase in renal elimination during the second and third trimesters.² The objective of this review is to describe differences in patient selection between the two drugs, their relative safety during pregnancy, and changes in daily doses as a guide for prescribing clinicians.

METHADONE

Dosing Regimen and Precautions

The authors have previously reported experience with 139 consecutively chosen patients requiring methadone; about one-fifth were already taking methadone before pregnancy, while dosing during pregnancy began at the following gestational weeks: 4 to 8 weeks, 25 (18%); 9 to 16 weeks, 46 (33%); 17 to 24 weeks, 36 (26%); and 25 weeks, 3 (2%).² Although it is the authors' practice to admit all patients to the antepartum hospital ward as early as possible for methadone initiation, other authorities believe that hospital admission is not necessary.^{3,4} If patients are already receiving care in a methadone treatment program, pregnancy need not interrupt this therapy.¹ Methadone is available as an injectable solution or tablet, but is most often used as an oral solution.

Sonographic confirmation of a viable intrauterine pregnancy is often a prerequisite for acceptance to a methadone treatment program tailored specifically to pregnant women.¹ The initial evaluation includes a variety of tests. The authors suggest baseline tests for hepatitis B and C as well as liver function tests. Counseling regarding testing for human immunodeficiency virus (HIV) should be provided, and testing recommended using an opt-out approach. An electrocardiogram is recommended before beginning methadone because the drug can prolong the QT interval and cause torsades de pointes.⁵

The starting daily dose of methadone is as a single oral dose of 20 mg.¹ An additional 5 to 10 mg is given every 3 to 6 hours as needed for any signs or symptoms of withdrawal. Once withdrawal symptoms are suppressed, the dose should be increased no more frequently than every 3 to 5 days, to avoid overdose resulting from the long half-life of methadone (20–35 hours).¹ On the second day of treatment, the total dose of methadone given in the previous 24 hours is provided as the new morning dose. The patient's condition is considered to be stable when no remarkable symptoms or signs (dysphoria and restlessness, rhinorrhea and lacrimation, myalgias and arthralgias, nausea, vomiting, abdominal cramping, and diarrhea) are evident within 24 hours after her last dose. If the patient has been hospitalized for methadone initiation, she may receive the same single morning methadone dose as dispensed at the clinic pharmacy. Take-home doses are allowed over Sundays or holidays unless a random urine drug screen, performed at least monthly, is positive for other substances.

The authors' experience regarding daily maintenance dose ranges is similar to that of others.² The mean initial maintenance dose is 69 mg (range 8–160 mg) while the mean dose at delivery is 93 mg (range 12–185 mg). Nearly half require a low daily

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