Comparative Effectiveness Review
Number 263

Management of Postpartum Hypertensive Disorders of Pregnancy

Executive Summary

Main Points

- **Home Blood Pressure Monitoring (HBPM)**
  - Probably increases the likelihood of obtaining blood pressure (BP) measurements during recommended time intervals (63% met reporting recommendations) (moderate strength of evidence [SoE]) and may increase the number of BP measurements obtained overall (low SoE).
  - Most patients may be satisfied with care related to HBPM (≥87%) (low SoE)
  - HBPM may not affect initiation of BP treatment (low SoE, no evidence of difference)
  - HBPM may reduce unplanned hypertension (HTN)-related readmissions (low SoE)
  - HBPM probably decreases disparities between non-Black and Black patients in adherence to recommended BP surveillance (moderate SoE)
- **Pharmacological Treatment of Postpartum Hypertension**
  - Oral furosemide may shorten the duration of HTN in postpartum patients with preeclampsia (or gestational HTN) (low SoE)
  - There is insufficient evidence regarding comparative benefits and harms of other antihypertensive medications to treat postpartum HTN
- **Magnesium Sulfate Regimens**
  - *Shorter-duration* magnesium sulfate ($MgSO_4$) regimens (<24 hour), compared with standard (>24 hour) regimens:
    - Reduce the duration of urinary catheterization (high SoE), the time to ambulation (High SoE), and probably the time to start breastfeeding (moderate SoE)
    - May shorten time from delivery to contact with infant (low SoE)

Continued on page 2

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        - May lower rates of absent deep tendon reflexes, a sign of magnesium toxicity (low SoE)
        - Loading dose only regimens, compared with standard 24-hour regimens, probably increase the risk of recurrent seizures in patients with eclampsia (moderate SoE)
        - There is insufficient evidence regarding the risk of maternal mortality, and infant morbidities with different durations of $MgSO_4$ regimens
    - *Lower-dose* $MgSO_4$ regimens, compared with standard dose regimens:
        - May increase the risk of recurrent seizures among patients with eclampsia (low SoE)
        - May not affect mortality among patients with eclampsia (low SoE, no evidence of difference)
        - May not affect 5-minute Apgar scores among infants of patients with preeclampsia with severe features (low SoE, no evidence of difference)
        - Lowers the rate of absent deep tendon reflexes (a sign of magnesium toxicity) (high SoE)
    - There is insufficient evidence regarding whether nifedipine or other antihypertensive medications affect the rate of adverse events when administered with $MgSO_4$

Background and Purpose

Hypertensive disorders of pregnancy (HDP) affect up to 10 percent of pregnancies, and encompass a spectrum of disorders that include preexisting chronic HTN, gestational HTN, preeclampsia with and without severe features, eclampsia (seizure), and HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. Rates of HDP are rising in the United States,[1, 2] likely due to increased prevalence of pre-existing HTN, obesity, diabetes, older age at delivery, and use of artificial reproductive technologies.[3] Historically, it was believed that HDP was cured by delivery of the placenta, but it is now understood that HDP can persist, worsen, or develop *de novo* after delivery, and may result in severe morbidity or mortality due to eclampsia and stroke. Recent innovations in healthcare delivery—specifically, remote monitoring—show promise in improving early detection of postpartum HTN while also improving the patient experience by increasing the convenience of care and decreasing the need for clinical encounters.

HDP and its sequelae disproportionately affect minority and marginalized communities.[4, 5] There are substantial disparities across income and racial/ethnic minority groups in terms of who is affected and their outcomes. The prevalence of HDP is highest in non-Hispanic Black, American Indian, and Alaska Native individuals.[2] Overall, Black individuals are three times more likely than non-Hispanic White individuals to die of pregnancy-related conditions, both around the time of delivery and up to 1 year postpartum.[5] A higher percentage of these deaths are attributable to HDP (8.2% in Black individuals versus 6.7% in non-Hispanic White individuals).[5]

Some individuals require multiple antihypertensive agents, or large doses of antihypertensives, to control their BP postpartum. More evidence is needed regarding which medication(s) are most effective for outpatient postpartum BP management and have the fewest side effects, while not interfering with breastfeeding.

Individuals who develop preeclampsia with severe features are given $MgSO_4$ to prevent eclamptic seizures. However, there is uncertainty regarding optimal $MgSO_4$ regimens, particularly regarding the necessary treatment duration and dose.

This systematic review aims to inform clinical practice guideline developers, policymakers, and obstetricians/gynecologists, midwives, maternal fetal medicine specialists, family medicine clinicians, primary care physicians, nurse practitioners, nurses, other providers of care for peripartum and postpartum individuals and patients. The systematic review addresses three Key Questions (KQs) and a Contextual Question (CQ):

KQ 1: What are the effectiveness, comparative effectiveness, and harms of **home blood pressure monitoring/telemonitoring** in postpartum individuals?

KQ 2: What are the effectiveness, comparative effectiveness, and harms of **pharmacological treatments** for hypertensive disorders of pregnancy in postpartum individuals?

KQ 3: What are the comparative effectiveness and harms of alternative **$MgSO_4$ treatment regimens** to treat preeclampsia with severe features during the peripartum period?

CQ: How are race, ethnicity, and social determinants of health related to disparities associated with incidence and detection of HDP, as well as access to care, management, follow-up care, and clinical outcomes in individuals with postpartum hypertensive disorders of pregnancy?

Methods

In this systematic review, we used methods consistent with those outlined in the Agency for Healthcare Research and Quality Evidence-based Practice Center Program Methods Guidance (https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview). Our searches targeted comparative studies (i.e., randomized controlled trials [RCTs] and nonrandomized comparative studies [NRCSs]) for all three KQs from database inception to December 9, 2021. For KQ 1, we included single-arm studies. We extracted study data into the Systematic Review Data Repository Plus (SRDR+). With input from technical experts and key informants, we identified ten prioritized outcomes for each KQ. Where there was sufficient evidence without an unacceptable amount of

heterogeneity, we conducted pairwise meta-analyses. We assessed the risk of bias and evaluated the SoE using standard methods. The PROSPERO protocol registration number is CRD42022313075.

Results

We found 73 primary studies that enrolled 13,532 participants combined. Twenty-three studies were conducted in the United States, 2 in the United Kingdom, and 48 in a variety of other low- and middle-income countries. Summary conclusions are displayed in Tables A and B.

Postpartum home blood pressure monitoring: We found 13 studies (3 RCTs, 2 NRCSs, and 8 single-arm studies). Based on one RCT and one NRCS, there is moderate-strength evidence that HBPM probably doubles adherence to recommended BP surveillance, from about 44 to 60 percent to about 92 to 94 percent. Evidence from 5 single-arm studies indicates that most patients submit BP measures when given HBPM devices (e.g., 63% meet American College of Gynecologist [ACOG] recommendation for BP reporting). Two of three RCTs that reported on BP management provided low-strength evidence of no difference in the rate of initiation of antihypertensive medications (reported adjusted odds ratio [OR] and relative risk [RR] = 1.0; other measures of BP management were sparsely reported). Three single-group studies provided low-strength evidence that most patients with postpartum HDP (≥87%) were at least very satisfied with remote monitoring (no studies compared satisfaction with care with versus without HBPM). One RCT and one NRCS provided low-strength evidence that HBPM may reduce HTN-related hospital admissions (risk difference −3.5%, 95% confidence interval [CI] −6.9 to −0.1; adjusted RR 0.12, 95% CI 0.01 to 0.96; respectively). One RCT, supported by a single arm study and a NRCS, provided moderate strength evidence that use of HBPM may reduce racial disparities in BP ascertainment (in the RCT, the relative RR was 0.51, 95% CI 0.33 to 0.78, implying a halving of the disparity between Black and non-Black patients; in the NRCS, the gap in adherence to a postpartum BP check decreased from 24.6% to 0.4%; in the single arm study, both Black and non-Black patients reported BP measurements with HBPM). There was insufficient evidence regarding the effect of HBPM on whether patients felt “in control” of managing their HDP. There was no evidence regarding the effect of HBPM on other prioritized outcomes, including maternal morbidity or mortality, quality of life, anxiety or depression, or length of postpartum hospital stay.

Pharmacological treatment of postpartum HDP: We found 17 RCTs that compared various pharmacological treatments for postpartum HTN. Five RCTs evaluated postpartum hospitalized patients with acute, severe HTN. Five RCTs evaluated oral diuretics for early postpartum HTN. Five RCTs compared oral antihypertensive treatments for persistent postpartum HTN. Two RCTs specifically evaluated end-organ protective effects of two antihypertensive drugs in patients with postpartum HDP. Because the studies evaluated a large variety of specific drugs and evaluated disparate outcomes, we had sufficient evidence to make only two conclusions. One RCT found that treatment with the diuretic furosemide (compared to placebo) in postpartum patients may reduce the likelihood of persistent HTN by more than half (adjusted RR 0.40, 95% CI

0.20 to 0.81, and RR 0.31, 95% CI 0.11 to 0.88). There was insufficient evidence regarding the comparative benefits and harms of other parenteral or oral antihypertensive medications to treat postpartum HTN (due to inconsistent findings or the existence of only single trials). There was also insufficient evidence related to maternal morbidity and mortality (among two small studies that evaluated different drugs), length of postpartum hospital stay (reported in only one study), and adverse events (due to sparseness of data per drug). There were no eligible studies that evaluated satisfaction with care, quality of life, anxiety or depression, reduction in health disparities, or severe infant morbidities.

Comparative effects of $MgSO_4$ regimens: Twenty-one RCTs compared shorter-duration (<24 hour) $MgSO_4$ regimens with standard (24 hour) treatment, 15 RCTs compared different doses of $MgSO_4$, 2 RCTs compared intramuscular with intravenous administration, 1 RCT evaluated the effect on uterine bleeding of interrupted versus continuous $MgSO_4$ administration during cesarean section, and 1 RCT evaluated the addition of nifedipine to the $MgSO_4$ regimen.

Shorter duration $MgSO_4$ regimens decrease urinary catheterization time (4 RCTs, high SoE), time to ambulation (2 RCTs, high SoE), time to breastfeeding (2 RCTs, moderate SoE), and time from delivery to contact with the infant (1 RCT, low SoE). For morbidity and mortality outcomes, despite numerous RCTs with thousands of patients (and infants), poor clinical outcomes were sufficiently rare that summary effect estimates were highly imprecise; thus, there is insufficient evidence regarding the effect of using shorter duration $MgSO_4$, regimens on seizure in patients with preeclampsia with severe features (16 RCTs, summary OR 1.09, 95% CI 0.49 to 2.39). However, in patients with eclampsia, loading dose only regimens probably increase the odds of recurrent seizure (4 RCTs, summary OR 2.04, 95% CI 1.21 to 3.46). Shorter duration regimens may result in fewer instances of magnesium-related toxicities (as manifested by loss of deep tendon reflexes; summary OR 0.52, 95% CI 0.32 to 0.84; low SoE due to inconsistency) (4 RCTs). Due to sparse or inconsistent reporting across studies, there was also insufficient evidence related to satisfaction with care. There were no eligible studies that addressed quality of life, psychosocial distress, reduction in health disparities, or adverse drug reactions.

In six RCTs that enrolled patients with preeclampsia with severe features and *compared lower versus higher dose regimens*, no seizures were reported, regardless of $MgSO_4$ dose. In the two RCTs reporting maternal mortality, there were no maternal deaths (insufficient evidence). In the seven RCTs that enrolled patients with eclampsia, the odds of experiencing a recurrent seizure with lower dose regimens were 2-fold higher (OR 2.06, 95% CI 0.99 to 4.31, low SoE). There was no evidence of a difference in mortality (6 RCTs, summary OR 0.60, 95% CI 0.26 to 1.35; low SoE). Patients treated with lower dose $MgSO_4$, regimens have lower rates loss of deep tendon reflexes, an early indicator of magnesium toxicity (5 RCTs, summary OR 0.16, 95% CI 0.09 to 0.28; high SoE). There is no evidence of a difference in 5-minute Apgar scores (mean difference [MD] 0.15, 95% CI –0.21, 0.51) in infants of patients with preeclampsia with severe features treated with lower dose MgSO4 regimens. Due to imprecision related to rare events, evidence was insufficient for other infant morbidities. No eligible studies reported on breastfeeding outcomes, satisfaction with care, quality of life, postpartum recovery

(e.g., urinary catheterization and time to ambulation), maternal-neonatal bonding, psychosocial distress, reduction in health disparities, or adverse drug reactions.

Four studies evaluated other different $MgSO_4$ regimens (one with concomitant oral nifedipine) with disparate reported outcomes. The studies provided insufficient evidence to allow conclusions.

Limitations

Although we found a sizable evidence base overall (73 primary studies), we were able to make only a limited number of conclusions, largely because the studies were generally small and reported a heterogeneous collection of intermediate outcomes. Few studies reported subgroup data or statistically evaluated whether the effect of the intervention differed among subgroups (i.e., heterogeneity of treatment effects). Many of the prioritized outcomes were either not reported in any included study for specific comparisons or were reported in an insufficient number of studies to allow meta-analyses or merit conclusions (i.e., they provided insufficient evidence).

Implications and Conclusions

HBPM probably improves overall BP ascertainment in the early postpartum period, largely through greater adherence with reporting of BP measures (Moderate SoE) and probably decreases disparities (between Blacks and non-Blacks) in achieving recommended BP surveillance standards (Moderate SoE). HBPM may reduce unplanned hypertension related readmissions (low SoE) but may not affect the likelihood of initiating treatment for hypertension (Low SoE). There is insufficient evidence regarding the effect of HBPM on clinical outcomes.

Postpartum treatment with the diuretic oral furosemide (vs. no furosemide) may reduce the duration of postpartum HTN (Low SoE). Evidence is insufficient or lacking regarding the comparative benefits and harms of other antihypertensive medications.

The evidence regarding the effect of different $MgSO_4$ regimens on serious clinical outcomes (seizures, death) remains mostly insufficient primarily, due to the rarity of these events with any $MgSO_4$ treatment. Nevertheless, although more evidence is needed to confirm this finding, for patients with eclampsia, loading dose-only $MgSO_4$ regimens probably increase the risk of recurrent seizures (Moderate SoE) but not the risk of death (Low SoE). Loss of deep tendon reflexes (a clinical sign of Magnesium toxicity) may be reduced with shorter duration regimens (Low SoE) and is reduced with lower dose regimens (High SoE). There is no evidence of a difference in 5-minute Apgar scores in infants of patients with preeclampsia with severe features treated with lower dose MgSO4 regimens (low SoE). Shorter duration $MgSO_4$ regimens reduce the duration of urinary catheterization (High SoE), time to ambulation (High SoE), time to breastfeeding (Moderate SoE), and time from delivery to contact with the infant (Low SoE). There is insufficient evidence regarding whether nifedipine or other antihypertensive medications affect the rate of adverse events when administered with $MgSO_4$.

Overall, the evidence base remains incomplete regarding the indications for and implementation of HBPM. Further evidence is needed to determine whether HBPM can reduce the occurrence of adverse clinical outcomes, such as eclamptic seizures, stroke, and pregnancy related deaths. In some settings, hospital readmissions might reflect improved ascertainment of HDP.

The evidence for comparative benefits and harms of available antihypertensive medication is scant. Trials are needed for the numerous antihypertensive drugs commonly used in practice to allow better decision making in choice of treatment. Both successful control of hypertension and effect on clinical event outcomes are important outcomes to be further studied.

Evidence from large pragmatic trials, augmented by analysis of real-world data, is needed to the optimal (i.e., lowest effective dose to minimize unpleasant side effects and toxicity, and shortest effective duration) $MgSO_4$ regimen(s) for individuals with preeclampsia with severe features.

Table A. Overall summary of evidence identified regarding Key Questions 1 (home monitoring) and 2 (hypertension treatment)

Outcome Category	Outcome	HBPM in PP Individuals	Pharmacological Treatments for HDP in PP Individuals
BP reporting (adherence)	BP measurements obtained during recommended time intervals	✓✓ HBPM probably improves BP reporting	N/A
	Number of BP measurements obtained	✓ May increase the number of BP measurements obtained overall	N/A
Antihypertensive treatment	Treatment initiation, adjustment, or discontinuation	✓ No evidence of difference in initiation	N/A
mBP control	Persistent HTN on PP Day 7	No eviden	✓ Oral furosemide for 5 days PP may reduce the rate of persistent HTN on PP Day 7: No conclusions for other medications
	Need for rescue medication	No evidence	No conclusions
	Days to resolution of HTN	No evidence	No conclusions
Severe maternal outcomes	Maternal morbidity and mortality	No conclusions	No evidence
Patient-reported outcomes	Satisfaction with PP care	✓ Most patients may be satisfied with care related to HBPM	No evidence
	Quality of life	No evidence	No evidence
	Anxiety/depression	No evidence	No evidence
Healthcare utilization	Length of PP hospital stay	No evidence	No evidence
	Unplanned readmission	✓ HBPM may reduce unplanned hypertension related readmissions	No evidence
	Unplanned obstetrical triage area, clinic visits or emergency department visits	No conclusions	No evidence
Infant-related outcomes	Breastfeeding	N/A	No evidence
	Severe infant morbidities	N/A	No evidence
Adverse events	Severe adverse events	N/A	No evidence
Reduction (or generation) of health disparities	Reduction of disparities in BP surveillance	✓✓ HBPM probably reduces disparities (non-Black vs. Black) in adherence to BP surveillance	No evidence

Abbreviations: BP = blood pressure, HBPM = home blood pressure monitoring, HDP = hypertensive disorders of pregnancy, HTN = hypertension, N/A = not applicable, PP = postpartum, SoE = strength of evidence, XR = extended release

✓ = Low SoE, ✓✓ = Moderate SoE, ✓✓✓ = High SoE (no instances in this table)

Color legend: High strength of evidence (green) (no instances in this table), Moderate strength of evidence (blue), Low strength of evidence (orange), Insufficient strength of evidence/no conclusions (unshaded/white), No evidence or not applicable (N/A) (gray). The colors do not provide unique information compared with the text and symbols.

Table B. Overall summary of evidence identified for Key Question 3 (alternative MgSO4 regimens)

Outcome Category	Outcome (Population)	Shorter Versus Standard Duration $MgSO_4$ Regimens for Preeclampsia With Severe Features During Peripartum	Lower Versus Higher Dose $MgSO_4$ Regimens for Preeclampsia With Severe Features During Peripartum
Severe maternal outcomes	Maternal morbidity and mortality	No conclusions (rare event)	No conclusions (rare event) for patients without prior seizure ✓ No evidence of a difference in mortality among patients with prior eclamptic seizure
	Seizure (preeclampsia with severe features)	No conclusions (rare event)	No conclusions (rare event)
	Recurrent seizure (eclampsia)	✓✓ Loading dose only $MgSO_4$ regimens probably result in increased risk of recurrent seizure	✓ Lower dose $MgSO_4$ regimen may result in increased risk of recurrent seizure
Infant-related outcomes	Breastfeeding	✓✓ Shorter duration $MgSO_4$ regimen probably yields shorter time to start breastfeeding	No evidence
	Infant morbidity	No conclusions (rare event)	✓ No evidence of a difference in 5-minute Apgar score in infants of patients with preeclampsia with severe features
Patient-reported outcomes	Satisfaction with PP care	No conclusions	No evidence
	Quality of life	No evidence	No evidence
	Anxiety/depression	No evidence	No evidence
Postpartum recovery time	Duration of urinary catheter placement	✓✓✓ Shorter duration $MgSO_4$ regimen yields shorter duration of urinary catheterization	No evidence
	Time to ambulation	✓✓✓ Shorter duration $MgSO_4$ regimen yields shorter time to ambulation	No evidence
Maternal-neonatal bonding	Time from delivery to contact with infant	✓ Shorter duration $MgSO_4$ regimen may yield shorter time from delivery to contact with infant	No evidence
Reduction (or generation) of health disparities	Reduction of disparities in BP surveillance	No evidence	No evidence
Harms	Magnesium-related toxicity	✓ Shorter duration $MgSO_4$ regimen may lower risk of magnesium toxicity	✓✓✓ Lower dose $MgSO_4$ regimen lowers the risk of magnesium toxicity
	Other clinically important adverse events	No conclusions	No conclusions

Abbreviations: PP = postpartum, BP = blood pressure, $MgSO_4$ = magnesium sulfate, SoE = strength of evidence.

✓ = Low SoE, ✓✓ = Moderate SoE, ✓✓✓ = High SoE
Color legend: High strength of evidence (green), Moderate strength of evidence (blue), Low strength of evidence (orange), Insufficient strength of evidence/no conclusions (unshaded/white), No evidence (gray). The colors do not provide unique information compared with the text and symbols.

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