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REVIEW ARTICLE

Chronic kidney disease in pregnancy

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ABSTRACT
Parturients with renal insufficiency or failure present a significant challenge for the anesthesiologist. Impaired renal function compromises fertility and increases both maternal and fetal morbidity and mortality. Close communication amongst medical specialists, including nephrologists, obstetricians, neonatologists and anesthesiologists is required to ensure the safety of mother and child. Pre-existing diseases should be optimized and close surveillance of maternal and fetal condition is required. Kidney function may deteriorate during pregnancy, necessitating early intervention. The goal is to maintain hemodynamic and physiologic stability while the demands of the pregnancy change. Drugs that may adversely affect the fetus, are nephrotoxic or are dependent on renal elimination should be avoided.

Keywords: Obstetrical anesthesia; Renal failure; Epidural anesthesia; Pregnancy

Introduction

Chronic kidney disease (CKD) is diagnosed in 0.03–0.12% of pregnancies.[1] The low incidence may be a direct effect of renal disease on fertility, or represent underreporting of the condition. The impact of maternal renal disease on perinatal outcome will depend on the degree of renal insufficiency and co-morbid conditions at the time of presentation.[2] A recently published systematic review included 13 observational studies with over 26 000 pregnancies.[3] Parturients with CKD had up to a five-fold higher incidence of morbidity, including gestational hypertension, preeclampsia, eclampsia and maternal mortality, when compared to parturients with normal pregnancies. Similarly, the risk of adverse fetal outcome was two times greater in women with CKD.[3] However, there are limited data regarding the peripartum management of these patients. The purpose of this review is to examine the peripartum anesthetic management of parturients with underlying CKD presenting to the labor and delivery unit.

Anatomical and physiological changes in renal system

Several anatomical and physiological changes occur in the maternal renal system during pregnancy. The limited ability of diseased kidneys to adapt to the normal physiological changes of pregnancy may cause perinatal complications. The changes occur in response to the increased filtration and elimination demands associated with carrying the fetus during pregnancy. Kidney size increases by 1 cm in parturients and is associated with an increase in kidney volume by up to 30%,[4] and dilatation of the renal calyces, pelvis and ureters.[5] The morphologic changes result in stasis, which predisposes parturients to asymptomatic bacteriuria that may progress to pyelonephritis.[5] Vasodilatation, including the renal vessels, occurs by six weeks of gestation leading to a fall in blood pressure and an increase in cardiac output, renal plasma flow and glomerular filtration rate (GFR); these changes persist until late gestation (Table 1).[5]

Urinary protein excretion increases substantially due to both an increased GFR and increased permeability of the glomerular basement membrane. The upper limit of normal for urinary protein excretion in non-pregnant patients is 150 mg/dL; in pregnant women it is 300 mg/dL.[5]

GFR and creatinine clearance increase by 40–65% with no change in creatinine production, therefore serum creatinine concentrations fall to 0.4–0.6 mg/dL (35–55 μmol/L).[2] Parturients with a serum creatinine concentration >0.8 mg/dL (70 μmol/L) and a blood urea nitrogen (BUN) concentration >13 mg/dL (6 mmol/L) are considered to have renal insufficiency.[5]

Fluid and electrolyte changes during pregnancy

Total body water increases by 6–8 L during pregnancy. Plasma volume increases 1.1–1.6 L, resulting in a plasma volume of 4.7–5.2 L, 30–50% above that in non-preg-

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Table 1 Renal changes during pregnancy

Function	Change	Manifestation
Acid–base regulation	Increased bicarbonate secretion	Reduced serum bicarbonate to 20–24 mEq/L
Water metabolism	Reduced plasma osmolality	Reduction of 5–10 mOsmol/kg compared to non-pregnant
Volume regulation	Increased extracellular fluid	Total body water increase by 6–8 L. Plasma volume increase by 50%
Sodium metabolism	Sodium retention, reduced serum sodium concentration	Weight gain. Normal serum sodium concentration 135 mmol/L
Tubular transport	Proteinuria and glycosuria	Normal proteinuria up to 300 mg/day. Positive glucose on urine dipstick

nant women. This is accompanied by retention of 900–1000 mEq sodium which contributes to the mild edema seen in most pregnant women.[5] Serum osmolality decreases by 10 mOsm/L and serum [Na^+] decreases by 5 mEq/L (mmol/L), the latter attributed to relaxin, a peptide hormone of the insulin family secreted by the corpus luteum, which is responsible for osmoregulatory changes, increases in GFR and vasodilation in early pregnancy.[5] Parturients are considered hypernatremic when serum [Na^+] exceeds 140 mEq/L.[6]

Serum [K^+] is normal despite increased serum aldosterone, perhaps due to the potassium-sparing effects of elevated progesterone levels in pregnancy. Total serum calcium concentration falls in pregnancy due to reduced serum albumin, but ionized [Ca^{2+}] remains normal. Due to increased GFR in pregnancy, the tubular transport maximum is exceeded and reabsorption is decreased, causing increased excretion of glucose, amino acids, calcium, and urinary protein.

Respiratory changes in pregnancy

Elevated progesterone levels stimulate hyperventilation and cause mild respiratory alkalosis, resulting in a slight increase in arterial pH and a fall in plasma bicarbonate concentrations by about 4 mEq/L. A compensatory response occurs in the kidney, with greater bicarbonate excretion and a decline in serum bicarbonate concentration.[5] These acid–base alterations have two principal consequences. First, the reserve buffering capacity of the blood is reduced, with an impaired ability to compensate for a metabolic acidosis.[6] Second, since $PaCO_2$ falls during pregnancy, hypercapnea may occur when $PaCO_2$ is within the normal non-pregnant adult range; for example, a $PaCO_2$ of 40 mmHg is an indication of carbon dioxide retention in a pregnant woman at term.[6]

Hematological changes in pregnancy

Red blood cell mass increases 20–30% by the end of pregnancy, but the proportionally greater increase in intravascular volume results in the dilutional anemia of pregnancy. If this physiological anemia is superimposed on anemia secondary to renal disease, maternal reserve is substantially reduced. The primary cause of anemia in chronic renal failure is deficiency of erythropoietin, but other factors include blood loss, shortened red cell life span, vitamin deficiencies, uremia, iron deficiency and inflammation.[7] Anemia during pregnancy is associated with an increased incidence of preterm births, and higher infant mortality rates.[8] A positive correlation between maternal hemoglobin and a successful pregnancy has been documented in hemodialyzed parturients.[9]

Pathophysiology

The pathophysiology by which pregnancy exacerbates renal disease is unknown. Pre-existing renal disease may be a precursor for platelet aggregation, formation of fibrin thrombi, microvascular coagulation, and endothelial dysfunction in the kidney. The superimposition of a preeclamptic microangiopathy on kidneys with pre-existing dysfunction may lead to poorly reversible or persistent renal damage.[10] There are many causes of CKD or end-stage renal disease, each with its own pathophysiologic disease mechanism. More common causes include type 1 diabetes mellitus, glomerulonephritis, hypertension, lupus nephritis, immunoglobulin A (IgA) nephropathy, and polycystic kidney disease.[2] The effects of renal failure and anesthetic implications are shown in Table 2.

Effect of pregnancy on CKD

Parturients with intrinsic renal disease, especially with baseline azotemia and hypertension, suffer rapid deterioration in renal function after conception. Conversely, the course of renal disease may influence the pregnancy outcome. In general, as kidney disease progresses and function deteriorates, the ability to sustain a healthy pregnancy declines.[5]

Maternal complications with CKD include miscarriage, placental abruption, anemia, infection, premature rupture of membranes, polyhydramnios, pre-term birth, uncontrolled arterial hypertension, preeclampsia/eclampsia, hemorrhage, the need for cesarean delivery, and maternal death.[11] Fetal complications include re-