

Pregnancy and Renal Function

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Goal

Review the effects that pregnancy has on the pathophysiology of the renal system.

Objectives

1. Identify the anatomical and physiological changes to the renal system related to pregnancy
2. Describe the management of renal impairment during pregnancy
3. Discuss the implications that renal disease has on pregnancy

Introduction

Pregnancy has complex effects on the anatomy and physiology of the renal system and urinary tract. These effects are designed to provide a suitable environment for the growing baby as well as maintaining the health of the mother. Conversely, renal impairment has significant effects on the woman's ability to conceive as well as maintain the pregnancy. Thus, it is important to understand the effects of pregnancy on normal renal function and the consequences that renal disease has on pregnancy. This supplement will address the effects of pregnancy on the renal system and, in addition, address the effects that renal impairment has on pregnancy.

Anatomical changes in normal pregnancy

The urinary and reproductive systems are closely related and conditions affecting one system influence the other. Some of the changes seen in pregnancy are the kidney's increased size (can increase up to 2cm in length), increased vascular volume, increased interstitial space and increased glomerular size (not number). The greatest changes are seen in the collecting system, where calyces, renal pelvises and ureters dilate and elongate.

These changes are evident by the 3rd gestational month and persist until the 12th week post partum (Levine 1997, Paller 2004).

Pregnancy induces increased synthesis of prostaglandin E2 (PGE2) which inhibits ureteral peristalsis and may be responsible for the hypomotility and distension. Increased oestrogen and progesterone production causes muscular and hypertrophic changes in the urinary tract resulting in hypomotility of the urinary tract. Increased production of chorionic growth hormone may cause some renal hypertrophy.

Mechanical obstruction by the enlarged uterus can contribute to ureteral distension as well as changes to surrounding structures (Paller 2004).

Functional changes

The above anatomical changes have a considerable effect on renal physiology and hence on fluid balance, solute clearance and the other functions of the kidneys.

Early in pregnancy increased renal blood flow (RBF), secondary to increased cardiac output (CO) and renal vasodilatation, is seen. This has been shown to be up to 40% above non-gravid values. In contrast, there is no increase in cerebral or hepatic blood flow. The increase in CO, in part related to a 50% increase in blood volume, is not accompanied by a rise in blood pressure. Usually a decrease in systolic pressure is seen, due to the decrease in vascular resistance from vasodilation. This increased RBF is reflected in a subsequent increased glomerular filtration rate (GFR). This begins during the first few weeks after conception, is at its greatest at the beginning of the 2nd trimester and remains until after delivery.

Creatinine, urea and uric acid clearances increase, therefore serum levels decrease during pregnancy.

Acid base regulation is altered causing a decrease in the bicarbonate threshold. Early morning urine specimen is more alkaline. Pregnant women tend to hyperventilate and subsequently mild alkalosis is often present.

Glucose, water-soluble vitamins, protein and amino acids are excreted during normal pregnancy. This is attributed to the increase in GFR which causes the filtered load of nutrients to surpass the reabsorptive capacity of the kidney, therefore these substances spill into the urine. Intermittent glycosuria is normal and makes screening for diabetes more difficult.

Volume regulation in normal pregnancy is characterised by a gradual accumulation and retention of water and sodium. Most healthy women gain an average of 12.5 kilograms and most of this is fluid. The plasma volume doubles and this results in a fall in the plasma sodium concentration (dilution). Therefore, osmolarity levels decrease. This would normally stimulate a diuresis by suppressing ADH. However, in pregnancy this does not appear to happen. It appears as though the osmoreceptors are 'reset' at a lower level to avoid a continuous diuresis.

Blood pressure (BP) regulation is affected in pregnancy. The mean BP decreases by around 10 mmHg in early pregnancy due to the decrease in peripheral vascular resistance which is the result of the effects of progesterone (smooth muscle relaxant).

Renin concentration is 5 - 10 times greater in pregnancy, however the pregnant woman is extremely resistant

to the vasoconstriction effects of angiotensin II. This is related to elevated levels of aminopeptidase which destroys angiotensin II.

Erythropoietic activity increases during pregnancy which is unrelated to tissue hypoxia. This is possibly due to an increase in erythropoietin levels from an increase in renal tissue (Molzahn & Butera 2006, Goody & Ulmans 2004, Paller 2004, Levine 1997, Richard 1986).

Renal investigations

In the majority of pregnancies renal disorders are asymptomatic. However, during pregnancy renal disease may be diagnosed by abnormal urinalysis or the onset of hypertension. It is important that all patients with hypertension or proteinuria must be further investigated for renal disease.

Methods of evaluation are limited during pregnancy due to the presence of the baby. Methods of evaluation include history, examination, urinalysis, laboratory and radiological investigations. The interpretation of laboratory results may be complex due to the physiological alterations that normally occur during pregnancy as discussed above.

Renal complications of pregnancy

Urinary Tract Infections

The rate of asymptomatic bacteriuria (ASB) is similar to non-pregnant females (6-8%), but progression to symptomatic urinary tract infection (UTI) and/or pyelonephritis is much higher. Approximately 30-40% of pregnancies with untreated ASB will progress to frank pyelonephritis. Thus detection and treatment are important. Contributing factors to maternal bacteriuria include physiological changes such as increased stasis of urine in collecting system and increased glucose and protein in urinary tract, both of which enhance bacterial growth. The management of ASB includes single dose amoxicillin,

investigate recurrence via ultrasound and investigation 6 months post-partum.

Acute Pyelonephritis

The incidence of acute pyelonephritis is 1-2% of all pregnancies and was the leading cause of maternal death in pre antibiotic era. Now approximately 3% of pregnant women with pyelonephritis progress to septic shock. Pyelonephritis causes a marked decrease in GFR and impaired concentrating ability. The management is aggressive, usually with hospital admission, IV antibiotics, oral antibiotics for 6 weeks and re-screen urine regularly for remainder of pregnancy.

Hypertension

Hypertension complicates up to 10% of all pregnancies. Hypertension in pregnancy can be classified into pre-eclampsia, chronic hypertension or transient hypertension of (late) pregnancy.

Pre-eclampsia is a disorder unique to pregnancy. It is characterised by hypertension, proteinuria, oedema and coagulopathy. It usually occurs after the 20th gestational month, most frequently near term. Renal changes show characteristic lesions unique to pre-eclampsia. The resultant effect of these changes is a decreased capillary lumen and is seen in around 75% of pre-eclampsia. These changes appear to be reversible with time.

Functional changes associated with pre-eclampsia are decreased GFR, approx. 25% (still higher than non gravid), excessive sodium and water retention and increased serum uric acid. These changes are relative to the severity of pre-eclampsia, renal lesion and foetal outcome. Abnormal proteinuria also occurs which correlates with intra uterine growth retardation and foetal loss.

Treatment of pre-eclampsia involves the urgent hospitalisation. Foetal maturity is assessed and if mature

and near term, induction is therapy of choice. If not, adequate bed rest, blood pressure control and further investigation and observation of maternal and foetal status are commenced. Signs of impending eclampsia, headache, vomiting, hypertension, cerebral or visual disturbances, oliguria and epigastric pain, must be followed up.

Chronic Hypertension

Most women with essential hypertension have uncomplicated pregnancies. However, they do have an increased risk of developing pre-eclampsia in addition to other complications such as acute renal failure, placental abruption and foetal growth retardation. Women over 30 years or those who have evidence of end organ damage due to hypertension are at greatest risk of developing complications.

Transient Hypertension

These women probably represent a diversity of underlying diagnoses. They typically present in the third trimester with non-proteinuric hypertension that normalises by 10 days post-partum. Most of these women seem destined to have essential hypertension later in life (Levine 1997, Richard 1986).

Pregnancy in women with existing renal disease

Renal disease was formerly considered a contraindication to pregnancy. As severity of renal failure increases so does the inability to conceive and maintain a viable pregnancy. Pregnancy outcomes seem to depend on preconception renal function and presence or control of hypertension. With increasing renal failure there is seen a worsening of neonatal outcome, worsening maternal hypertension and proteinuria (risk of superimposed preeclampsia is increased to about 25%) with the possibility of irreversible loss of renal function. Foetal survival is still significantly decreased and prematurity and growth retardation is increased with maternal renal disease

and/or hypertension (BP > 170/110). Conception rates in dialysis dependent women of childbearing age is estimated to be <1% per year. Studies show a higher rate of conception in patients on haemodialysis compared to peritoneal dialysis. The likelihood of a successful live birth in recent data is 55% with low maternal morbidity (Goody & Umans 2004, Paller 2004).

Management of renal failure during pregnancy

The major thrust for management of the pregnant woman who is dialysis dependent is to increase the dose of dialysis. This usually means daily dialysis with increased time. Many ongoing changes and adjustments to the patient's ideal weight and dialysate need to be made. The goal is to maintain as near as possible normal biochemistry, fluid balance and blood pressure. Table 1

covers the suggested changes to dialysis prescription.

Conclusion

Pregnancy remains uncommon in dialysis patients, although the frequency of conception and successful births is increasing. This is in part due to close cooperation among all health professionals involved with the pregnant woman on dialysis. As obstetric care and renal care continue to improve outcomes for the pregnant woman should also be better. Data on long term outcomes after birth are still scant and further research is required in this area.

References

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Questions (Reflective)

1. What have you learnt about pregnancy and the effect on renal function?
2. How will this information affect your clinical practice?
3. How would you respond to a client on dialysis who asked for your opinion on whether to conceive while on dialysis?

Modification	Rationale
Increase Dialysis to 6-7 days Aim to keep pre urea < 15mmol/L Avoid large fluid shifts (high UFR) & hypotension	>20 hours/week appears to improve infant outcome. Prevents placental hypoperfusion
Increase IBW as assessed weekly	To mimic the usual physiological volume expansion of normal pregnancy
Monitor and adjust the dialysate composition based on biochemistry (Na+, K+, Ca++, HCO3-)	To adjust for daily dialysis and other characteristic physiological changes in pregnancy
Increase erythropoietin to maintain Hb > 110g/L	EPO sensitivity is decreased and anaemia, per se, leads to poor outcome
Maintain transferrin saturation >25%	Normal pregnancy requires ^a 1g of Fe
Monitor serum P and adjust oral P and phosphate binders	Daily dialysis and increased utilisation may lead to hypophosphataemia
Review medications	To avoid any teratogenic effects or foetal toxicity

Table 1: Suggested Dialysis Prescription Modifications During Pregnancy (adapted from Goody & Umans, 2004)