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Pyelonephritis in Pregnancy
Treatment Options for Optimal Outcomes

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Contents

Abstract

Acute pyelonephritis is one of the most common indications for antepartum hospitalisation. When acute pyelonephritis is diagnosed, conventional treatment includes intravenous fluid and parenteral antibacterial administration. There are limited data by which to assess the superiority of one antibacterial regimen over the other in terms of efficacy, patient acceptance and safety for the developing fetus. There is a small body of evidence to support the ambulatory treatment of pregnant women with pyelonephritis in the first and early second trimesters.

Acute pyelonephritis is one of the most common indications for antepartum hospitalisation, complicating 1 to 2% of all pregnancies. Asymptomatic bacteriuria (ASB), traditionally defined as a urine culture from mid-stream collection with a single isolate of more than 100 000 colony-forming units (cfu) of a uropathogen,[1] precedes pyelonephritis in approximately 20 to 40% of patients.[2] Pyelonephritis in pregnancy occurs mostly prior to delivery, although it also occurs postpartum.[2,3]

Numerous physiological changes predispose the pregnant woman to urinary tract infection. Ureteral peristalsis slows under the influence of progesterone and the enlarging uterus compresses the ureters. Mechanical compression of the bladder and decreased detrusor tone lead to increased capacity and incomplete emptying of the bladder. Increases in glomerular filtration with resultant elevations in urinary glucose levels, and alkalisation of urine facilitate bacterial growth. All of these factors contribute to ureteral dilatation and urinary stasis.

Women with urinary tract anomalies such as incompetent vesicourethral valves, renal calculi and medical conditions including diabetes mellitus, sickle cell disease or trait, and neurological problems such as paralysis from spinal cord injury, are at increased risk for acquiring pyelonephritis in

pregnancy. Pyelonephritis is also more likely to occur in women of low socioeconomic status.[4,5]

Clinical signs and symptoms of acute pyelonephritis include: fever, shaking chills, flank pain, nausea and vomiting, costovertebral angle tenderness (CVAT) and, less commonly, symptoms of cystitis such as dysuria and increased frequency.[3] Urinary dipstick testing for the presence of leucocyte esterase and nitrites may be positive.[6,7] The diagnosis is confirmed by urine culture, obtained usually by midstream clean-catch, but occasionally by suprapubic aspiration or urethral catheterisation. To obtain a proper clean-catch specimen, the patient should be instructed to wipe her introitus from front to back prior to micturition in order to avoid contamination with periurethral bacteria. According to the Infectious Diseases Society of American consensus definition of pyelonephritis, colony counts of greater than or equal to 10 000 cfu/ml from clean-catch voided specimens are acceptable for use in antimicrobial treatment studies, and provide a sensitivity of 90 to 95%.[8] One or two bacteria per high-power field on an unspun catheterised urine specimen, or more than 20 bacteria per high-power field on spun urine, closely correlates with greater than 100 000 cfu/ml bacteria on urine culture.[9] Pyuria or the presence of leucocyte casts are also consistent with the diagnosis.

Uropathogens responsible for pyelonephritis are taxonomically the same as those that cause ASB and cystitis. The most common uropathogen is *Escherichia coli*, which is cultured from approximately 85% of patients.[2,3] Other Gram-negative uropathogens include *Klebsiella*, *Enterobacter*, and *Proteus* spp. Gram-positive organisms that are frequently identified include *Enterococcus faecalis* and group B streptococci.

A complex and yet incompletely understood interplay between virulence factors of uropathogenic bacterial species, such as *E. coli* and *Proteus mirabilis*, and host defence mechanisms dictate the severity of urinary tract infections in women. For example, *E. coli* from a small group of O-serotypes have characteristics epidemiologically associated with acute pyelonephritis, chronic or recurrent infection, parenchymal scarring and renal failure in the normal urinary tract.[10] Although the main reservoir for *E. coli* causing urinary tract infection is the intestinal tract, only a proportion of faecal *E. coli* actually do so. Factors which enhance the adherence of *E. coli* to uroepithelial cells and thereby protect the bacteria from urinary lavage and increase their ability to multiply and invade renal tissue have been identified. These include P-fimbriae,[11-13] and haemolysin production.[14] Contributors to the uropathogenic potential of *P. mirabilis* include fimbriae and urease production.[15]

In addition to urinalysis and urine culture, laboratory evaluation often includes a complete blood cell count and serum chemistry evaluation. Evidence of haemolysis with elevated lactate dehydrogenase levels may be encountered and is attributed to endotoxin mediated haemolysis.[16] Electrolyte abnormalities are also common. Transient renal insufficiency as demonstrated by a decrease in creatinine clearance by 50% or more occurs in more than a quarter of women with acute pyelonephritis in pregnancy.[17] Spontaneous resolution of the abnormal renal function should be expected as the acute infection clears.

There is controversy regarding the long term effects of acute pyelonephritis in pregnancy as 10% of women with recurrent or persistent bacteriuria during pregnancy have been shown in some studies to have chronic pyelonephritis and chronic renal insufficiency,[18] although more recent data of patients with ASB in pregnancy revealed no residual functional impairment.[19] Renal failure rarely results from recurrent urinary tract infection in the absence of obstruction.[20]

Blood cultures are often obtained when pyelonephritis is suspected, although the utility of this practice has been questioned since the isolates of blood cultures rarely differ from those of urine cultures.[21-23] In a retrospective study of 156 patients with pyelonephritis in pregnancy, only 3% of urine and 2% of blood culture results led to a change in therapy. The vast majority of changes in therapy were made for clinical indications, including pro-

longed febrile response and continued CVAT.[21] Some authors recommend obtaining blood cultures if the patient has a high temperature, for example, 39°C or more, appears to have sepsis, or has a major co-morbidity such as respiratory distress syndrome.[24,25]

1. Complications of Acute Pyelonephritis in Pregnancy

There are both maternal and fetal complications of acute pyelonephritis in pregnancy. Approximately 15 to 20% of women with pyelonephritis will have bacteraemia,[3] and some women will develop even more serious complications such as septic shock, disseminated intravascular coagulation, respiratory insufficiency or adult respiratory distress syndrome (ARDS). The incidence of ARDS with pyelonephritis ranges from 1 to 8%.[26] It occurs as a result of endotoxin-mediated pulmonary capillary damage, and manifests with symptoms of dyspnea, tachypnea and hypoxaemia. Patients with pulmonary injury will become symptomatic within 48 hours of initiation of antibacterial therapy. Chest roentgenography reveals pulmonary oedema. This condition is usually adequately treated with supplemental oxygen therapy and diuresis. However, it can progress to ventilator dependence. In one retrospective investigation, ARDS was diagnosed more frequently in women who had been treated with β-sympathomimetic tocolytic therapy and had received excessive intravenous hydration.[27]

Septic shock occurs as a result of endotoxaemia. Capillary endothelial damage, severely diminished vascular resistance and alterations in cardiac output are characteristic. Patients with septic shock require intensive care, often with pulmonary artery catheterisation. Antimicrobial therapy and fluid resuscitation should be instituted at once. Dopamine may be required to maintain systolic blood pressure and adequate urine output.

Recurrent pyelonephritis occurs in approximately 20% of women before delivery.[3] Issues relating to costs of care and the possibility of permanent renal damage must be considered when discussing recurrent infection. The frequency of recurrences may be reduced with careful post-treatment surveillance for recurrent infection and the use of suppressive therapy.

The risk of preterm labour and delivery attributable to pyelonephritis in pregnancy is difficult to estimate.[24] Studies have a wide ranges from 6 to 50% in the incidence of premature delivery with pyelonephritis.[2] Uterine contractions are commonly encountered in patients with pyelonephritis, and because most of the cases of pyelonephritis are encountered in the second and third trimesters of pregnancy, the threat of preterm delivery is taken seriously. Despite the presence of uterine contractions, there is often little or no cervical change. The use of tocolytic therapy should be considered carefully because of the associated cardiovascular changes that predispose pregnant women to pulmonary oedema.

2. Conventional Therapy

The historical approach to pyelonephritis in both nonpregnant and pregnant women has been hospitalisation and treatment with parenteral antibacterials. The safety profile for the mother and fetus is of utmost importance when choosing an antimicrobial agent for treatment of urinary tract infection in pregnancy. Unfortunately, the human data on drug toxicity to mother and fetus are unusually limited, and animal studies of fetal toxicity are often difficult to extrapolate to humans.

As a general rule, amino- and carboxy-penicillin derivatives (either alone or in combination with clavulanic acid), ureidopenicillins and cephalosporins are considered to have good safety when used during pregnancy. Penicillin-derivatives and cephalosporins achieve good renal parenchymal and urine concentrations shortly after administration, and have effective spectrums of coverage for common uropathogens. Ampicillin monotherapy has fallen out of favour because of high frequencies of resistance in multiple organisms.[2]

Tetracyclines and quinolones are generally contraindicated. The use of aminoglycosides should be considered carefully as there is the potential for

ototoxicity with their use. To date, gentamicin has been widely used in pregnancy as first-line therapy for Gram-negative coverage with no reports of congenital complications. However, it is a category C drug in the US, meaning that studies have shown that the drug exerts teratogenic or embryocidal effects in animals, but there are neither controlled trials in women nor other studies available either in animals or women.[28] In addition, ototoxicity has been demonstrated following fetal exposure to related aminoglycoside compounds such as kanamycin and streptomycin.[29-31] Clearly, if gentamicin is chosen, monitoring of serum concentrations should be performed and adjustments made in dose administration as needed. This is partly because of concerns regarding any toxic effects such as exacerbation of renal insufficiency commonly associated with pyelonephritis, but also because maternal serum concentrations near term are more likely to be subtherapeutic because of enhanced drug clearance.[32-34]

Few studies exist comparing the efficacy of different antibacterial regimens for the treatment of pyelonephritis in pregnancy,[35-41] although many regimens are acceptable and appear to be effective (table I). The optimal antibacterial regimen for the treatment of acute pyelonephritis in pregnancy would be characterised by the following: (i) proven effectiveness in properly conducted, prospective, randomised, double-blind trials; (ii) activity against the uropathogens likely to be responsible for the symptomatic upper urinary tract infection; (iii) ability to maintain adequate tissue and serum concentrations throughout the treatment period; (iv) lack of association with the development of resistance to antibacterials; (v) inexpensive; (vi) well-tolerated; and (vii) safety for the developing fetus.

Table I. Examples of dosage administration regimens of antibacterial agents for the treatment of pyelonephritis in pregnancy

Ampicillin 1-2g IV q6h combined with gentamicin as below
Gentamicin 2 mg/kg IV to load, then 1.7 mg/kg in 3 divided doses (may be given alone)
Ampicillin/sulbactam 3g IV q6h
Cefazolin 1-2g IV q6-8h
Ceftriaxone 1-2g IV or IM q24h
Mezlocillin 3g IV q6h
Pipericillin 4g IV q8h

IV = intravenous; **q*x*h** = every *x* hours.

Intravenous antimicrobial therapy is usually continued until the patient is afebrile for 48 hours and symptoms have improved; afterward, the patient is treated with oral antibacterials. The course of oral therapy lasts 10 to 14 days. After completion of therapy, a urine culture should be obtained to verify resolution of the bacteriuria. The appropriate duration of therapy for eradication of pyelonephritis has not been subjected to scientific scrutiny, although there is growing evidence that short-course therapy (one or three days) is effective for uncomplicated lower urinary tract infections in nonpregnant women.

The incidence of recurrent pyelonephritis is decreased in patients treated with nitrofurantoin suppression for the duration of pregnancy.[42-44] Thus, patients with pyelonephritis should receive nitrofurantoin suppression 100mg every night during the pregnancy and for 4 to 6 weeks post-partum. In addition to continuous suppression, monthly urine cultures should be obtained to screen for recurrent bacteriuria.

Because most patients with pyelonephritis are dehydrated, intravenous hydration usually is given. Urinary output is monitored carefully. Patients who are treated for pyelonephritis with the appropriate antimicrobial agent usually respond within 48 hours. If the patient fails to respond clinically by 72 hours, further evaluation should ensue for bacterial resistance to the antibacterial used, urolithiasis, perinephric abscess formation or urinary tract abnormalities, and the antibacterial agent should be changed to include an aminoglycoside. Patients with recurrent pyelonephritis or those who fail to respond quickly to aminoglycoside therapy should undergo imaging evaluation for the presence of an anatomic malformation or nephrolithiasis. This may be accomplished safely in pregnancy with ultrasonography or with intravenous pyelography (IVP). To minimise the radiation exposure to the fetus, only one exposure at 20 to 30 minutes

should be obtained for the IVP. Magnetic resonance imaging also may be used if urinary tract obstruction is suspected.

3. Rationale for Hospitalisation of Pregnant Patients with Pyelonephritis

Over ten years ago, the American College of Obstetricians and Gynaecologists stated in a Technical Bulletin that hospitalisation of pregnant women with pyelonephritis is necessary[45] and this approach has been endorsed by several authors.[2,24] Theoretically, this approach will circumvent serious complications associated with pyelonephritis, including respiratory insufficiency, septic shock, preterm labour and delivery, and recurrences with the possibility of permanent renal damage. However, the recommendation to hospitalise all women with pyelonephritis was not based on evidence from clinical trials. The high cost of medical care and concerns for cost containment have provided motivation to study ambulatory methods of therapy for the pregnant patient. Because pyelonephritis is one of the most common reasons for hospitalisation during pregnancy, attention has been directed toward developing a safe and effective approach to outpatient treatment of acute pyelonephritis. Based on the evidence presented in this review, this approach in pregnancy has only limited utility.

4. Ambulatory Treatment of Acute Pyelonephritis

4.1 Non-Pregnant Patients

There is support for the ambulatory treatment of nonpregnant patients with acute pyelonephritis. Most of this evidence stems from data collected in emergency departments. From these data, a treatment regimen for the outpatient treatment of pregnant women with acute pyelonephritis can be extrapolated.

In a retrospective study of 198 women, Safrin et al.[46] compared outpatient treatment with oral antibacterials to intravenous antibacterial therapy following a period of observation in the emergency department before discharge to ensure clinical stability. Cotrimoxazole (trimethoprim/sulfamethoxazole) was the most frequently prescribed antimicrobial used in the outpatients, whereas tobramycin was the most commonly administered parenteral agent. However, most patients received more than one antibacterial agent. Approximately 90% of patients were successfully treated in both groups. No differences were seen in adverse outcomes, rate of relapse, or rates of reinfection between inpatient and outpatient therapies. The authors concluded that treatment of pyelonephritis with oral antibacterials is well-tolerated and effective in immunocompetent women without underlying illness. They observed that most emergency departments do not have sufficient resources to permit prolonged observation of women who receive ambulatory therapy for acute pyelonephritis and authors suggested the use of home-health nursing for subsequent follow-up.

Similarly, a yearlong study from the University of Mississippi of 90 patients with acute pyelonephritis[47] revealed patients with low-grade or absent fever, without nausea, and without serious underlying disease can be treated safely as outpatients with cotrimoxazole. Pregnancy, clinical sepsis or serious underlying medical disease were exclusions. Subsequent investigation reinforced the importance of careful patient selection for ambulatory therapy for pyelonephritis, and the need for an initial period of observation for hydration and subsequent triage.[48] This approach provides an opportunity not only to assess response to therapy before discharge, but also to detect evolving or occult pathology, as many of the patients initially believed to have acute pyelonephritis may be found later to have other diagnoses. A meta-analysis of the existing literature on oral therapy for pyelonephritis[49] indicates that patients who do not have diabetes mellitus or sepsis and who are not immunocompromised, can tolerate oral intake and do not have chronic illness can be treated for upper urinary tract infection with oral agents such as amoxicillin/clavulinic acid, cotrimoxazole or norfloxacin.

In order to ensure adequacy of this approach to therapy, surveillance of uropathogenic bacterial susceptibility and resistance to various antibacterial agents is imperative. Talan et. al recently published results of 225 premenopausal women with uncomplicated pyelonephritis treated with either oral ciprofloxacin 500mg twice per day for 7 days or cotrimoxazole 160/800mg twice per day for 14 days. The clinical cure rates and bacteriological cure rates for ciprofloxacin-treated women were superior to those treated with cotrimoxazole (96% *vs* 83%, and 99% *vs* 89%, respectively), largely because of increasing rates of resistance of *E. coli* to cotrimoxazole.[50]

Follow-up for ambulatory treatment of acute pyelonephritis should be scheduled within 24 to 36 hours after discharge.[51] This is because in one investigation early return visits occurred within the first day following treatment.[51] The authors speculate that this may have resulted from a tendency for the admitting physicians to hospitalise the older moderately ill patients, or from the tendency to give younger patients, regardless of their clinical presentation, a trial of ambulatory therapy. Because the majority of gravidae with pyelonephritis are young, this recommendation would seem to be applicable in ambulatory treatment of pyelonephritis in pregnancy.

Ceftriaxone, a third-generation cephalosporin, is an excellent choice of antibacterial for outpatient therapy because of its long half-life, broad-spectrum coverage against commonly encountered Gram-negative and Gram-positive uropathogens, and convenient once-a-day administration.[52,53] The use of intramuscularly administered antibacterial therapy for pyelonephritis has been evaluated. Karachalios et al.[54] reported a 93% immediate cure rate and an 85% six-week cure rate in 30 non-pregnant women with acute pyelonephritis who received a single daily dose of intramuscular ceftriaxone for seven to ten days. The pharmacokinetics of intramuscularly administered ceftriaxone are as follows: the agent is completely absorbed, reaches peak plasma concentrations within 2 to 3 hours and has an elimination half-life of 6 to 9 hours. The main route of excretion is urinary and 40% of the peak concentrations are maintained in the urine for 24 hours after administration.[55]

4.2 Pregnant Patients

There are few trials on the ambulatory management of pyelonephritis in pregnancy. Some investigators have compared antibacterial regimens that have the potential for use in an ambulatory setting, although the patients remained hospitalised. This approach permitted constant surveillance for potential complications of the acute infectious process and for adverse effects of the medications.

In 1990, Angel and colleagues[36] attempted to simulate outpatient management such that all care during the hospitalisation after initial therapy could have been accomplished at home. 90 pregnant women were treated with oral cephalexin (cefalexin) 500mg every 6 hours or intravenous cephalothin (cefalothin) 1g every 6 hours until there was a decrease in CVAT and no fever for 48 hours.[36] Over 14% of the patients had bacteraemia and received intravenous antibacterial therapy. More than 90% of the patients were treated successfully with either treatment modality. Under the conditions described, the majority of women with acute pyelonephritis in pregnancy could be treated safely as outpatients with oral antibacterials. These authors recommended that candidates for ambulatory treatment should have no signs of sepsis, no complications of pregnancy, an ability to tolerate oral intake, and if fever was present, that it be controlled with antipyretics. An initial period of observation of 24 hours is suggested by which to discern which patients might manifest severe complications.

Once-a-day intravenous ceftriaxone therapy was compared to multiple dose intravenous cefazolin therapy in a randomised, double-blind clinical trial of 178 hospitalised patients by Sanchez-Ramos and colleagues.[37] Patients were administered intravenous ceftriaxone 1g every day, or intravenous cefazolin 2g every eight hours. Approximately 5% of patients in both groups failed to respond to initial therapy, and similar numbers in

each group also demonstrated continued positive urine cultures at follow-up evaluation, approximately 10 days after initial therapy. The authors recommended that pregnant patients with acute pyelonephritis be hospitalised for a 24-hour observation period, during which time they undergo laboratory evaluation and receive an initial dose of ceftriaxone. Subsequent doses could be administered either in a clinic at the time of follow-up or by a home visiting nurse within 24 hours.

Brooks and Garite[39] reported the first study of outpatient treatment of pregnant women with pyelonephritis in pregnancy. 21 women with a mean gestational age of 26 weeks or less initially were evaluated in an obstetric emergency room. An initial two-hour period of observation was required, during which time patients underwent baseline laboratory evaluation, received intravenous hydration and received an initial intramuscular 2g dose of ceftriaxone. When stable, the patient was discharged and then seen in a clinic setting for daily intramuscular injections of ceftriaxone 2g until both fever and CVAT resolved. A 10-day course of oral antibacterials chosen on the basis of urine culture and sensitivity results followed. There was a 12% treatment failure rate. There were no adverse outcomes or preterm deliveries in the patients who received the ambulatory ceftriaxone therapy. More than 90% of women who were candidates for study inclusion were treated successfully as outpatients with no serious complications, no preterm deliveries, and one (3%) patient developing a recurrent upper urinary tract infection. The authors estimated that given their conservative inclusion criteria that more than 50% of patients reporting to an obstetric emergency room could be treated in an ambulatory fashion.

In 1995, Millar et al.[40] described their experience at Los Angeles County-University of Southern California Medical Center, Los Angeles, California, USA, in which pregnant women at 24 weeks gestational age or less with acute pyelonephritis were given intramuscular ceftriaxone 1g every 24 hours for 2 doses as outpatients or intravenous cefazolin 1g every 8 hours as inpatients. The patients were observed for up to 24 hours to ensure they were clinically stable at the time of discharge. Outpatients were seen by home health nurses 18 to 36 hours after discharge and administered the second dose of intramuscular ceftriaxone. Patients then completed a 10-day course of oral cephalexin 500mg four times a day. Home health nurses revisited the patients approximately 48 to 72 hours following initiation of treatment to assess compliance with therapy and clinical response. Inpatients were given cefazolin 1g intravenously every 8 hours until they were afebrile for 48 hours. After discharge, the inpatients were given cephalexin 500mg four times a day for 10 days. All patients were reevaluated at 5 to 14 days after completion of oral antibacterial therapy at which time repeat urine cultures were obtained.

Of 120 women, 90% were effectively treated. 10% of the outpatients eventually were hospitalised because of sepsis, abnormal laboratory tests, deviation from study protocol and recurrent pyelonephritis while on oral therapy. There was one preterm delivery at 28 weeks' in a woman who was effectively treated with intravenous cefazolin as an inpatient for *Klebsiella pneumonia* pyelonephritis. There were no pregnancy losses or other serious complications from either treatment regimen. Overall, the authors estimated that 5% of patients with pyelonephritis at less than 24 weeks gestation who are considered candidates for outpatient therapy will not be able to be discharged.

These results are sharply contrasted by a similar trial conducted by the same authors in women with pregnancies after 24 weeks' gestational age.[56] All participants meeting inclusion criteria received two 1g doses of ceftriaxone intramuscularly 24 hours apart and had continuous tocodynamometry during the initial 24 hours. All women subsequently received oral cephalexin 500mg four times a day for 10 days. Those women who were randomised to outpatient care were discharged to their homes after 24 hours of hospital observation if they were clinically stable. After receiving two doses of ceftriaxone, the inpatients received oral cephalexin until they were afebrile for 48 hours,

and then were discharged from the hospital. All patients were seen in the clinic 5 to 14 days after completion of oral therapy and repeat urinalyses and urine cultures were obtained.

During the 36-month study period, 246 subjects with acute pyelonephritis after 24 weeks' gestation were evaluated in the study centres in Los Angeles and Honolulu, but only 92 were eligible to participate and agreed to do so. Over 60%, or 154 of 246, were ineligible because of such reasons as preterm labour, obvious sepsis or respiratory compromise, recurrent pyelonephritis or other urological abnormality, previous antibacterial therapy, allergies to the medications under study, history of substance abuse or incarceration, or preexisting maternal medical condition or fetal malformation. Furthermore, nearly 30% (13/46) of outpatients remained hospitalised after 24 hours because of clinical sepsis, bacteraemia, excessive leucocytosis (>20 000/mm^3), preterm labour, and other medical complications. Six outpatients and one inpatient failed to respond to initial therapy. Although there were no differences in clinical responses or birth outcomes of inpatients or outpatients after 24 weeks' if they completed their assigned protocols, 30% of outpatients were unable to do so and most women with acute pyelonephritis after 24 weeks' gestation were not candidates for outpatient therapy. Thus, while a selective approach to outpatient management of acute pyelonephritis in the third trimester may be effective, overall, the ambulatory care of women with these infections is quite limited in the third trimester.

There are no trials describing outpatient oral therapy for acute pyelonephritis in pregnancy.

4.3 Recommendations for Ambulatory Treatment of Pyelonephritis in Pregnancy

Cumulatively, the results of the existing trials are encouraging for the ambulatory treatment of acute pyelonephritis in pregnancy only in the first and early second trimesters of pregnancy. Outpatient treatment of acute pyelonephritis in pregnancy beyond 24 weeks' appears to have limited utility, and it would appear most prudent to admit women for conventional treatment with intravenous hydration and antibacterials if their gestational ages exceed this threshold.

Clearly, careful selection of appropriate candidates for outpatient therapy of acute pyelonephritis in pregnancy is required. Patients should be less than 24 weeks' pregnant, relatively healthy and able to comply with outpatient therapy. They should not have excessive fever (more than 38°C); severe nausea and vomiting; recurrent upper urinary tract disease; signs of sepsis including tachypnea, tachycardia, rigors, or hypotension; immunocompromise; significant medical conditions such as diabetes mellitus or previous renal disease; history of substance abuse; concurrent preterm labour; and uncertain diagnosis. Liberalising the criteria for outpatient therapy, in the absence of supporting data, may lead to serious detriment.

A period of observation is required. During this time, the patient should be hydrated and antibacterial therapy with intramuscular ceftriaxone initiated. Laboratory studies (complete blood cell count, serum chemistry panel including serum blood urea nitrogen and creatinine, and urine culture) should be obtained. Although urine culture may not aid in the immediate clinical management, approximately 6 to 10% of patients will not be successfully treated in an ambulatory setting and the results of the cultures may guide subsequent therapy. Surveillance of resistance rates to empirically chosen antibacterial therapies is mandatory. The period of observation should be long enough to review laboratory results and to assess ability to tolerate oral intake, and the patient's clinical response to therapy. If women with gestational ages beyond 24 weeks' are to be managed on an ambulatory basis, even longer periods of observation with continuous fetal heart rate and uterine activity monitoring are required to ensure both maternal and fetal stability before discharge from the observation unit.

Emphasis must be placed on close outpatient follow-up evaluation until both clinical and microbiological cure are obtained. Follow-up evaluation within 24 hours may take place in an office, clinic

or emergency room. Alternatively, a home health nursing visit may be performed. At this evaluation, an additional dose of ceftriaxone should be given and an assessment made of the clinical condition. After the second dose, the antibacterial may be changed to oral cephalexin 500mg four times a day (or a similar substitute) for 10 days, or daily intramuscular administration could be continued until all symptoms have resolved. The daily intramuscular administration regimen does not exceed 5 days. If the change to oral therapy is made, another outpatient clinical evaluation should be made within the 24 hours after the change. After completion of the daily ceftriaxone, oral treatment for 7 to 10 days is continued with cephalexin or with another antibacterial to which the causative organism is susceptible.

Clinic follow-up evaluation within two weeks after acute therapy should also be required. A urine culture should also be obtained as a 'test of cure'. Throughout the remainder of the pregnancy, the patient should be followed for symptoms of recurrent infection and followed with monthly urine cultures until delivery. Nitrofurantoin suppression should be initiated in all patients and continued until 4 to 6 weeks post-partum.

5. Conclusions

The standard approach to the treatment of acute pyelonephritis in pregnancy is hospitalisation, and administration of intravenous hydration, antipyretics and parenteral antimicrobial therapy. There is insufficient data to recommend one antibacterial regimen at the current time. There is a small body of evidence by which to support the ambulatory treatment of pregnant women at less than 24 weeks' gestational age with acute pyelonephritis provided these women are relatively healthy, and do not manifest signs or symptoms of respiratory insufficiency or sepsis. Ambulatory treatment of acute pyelonephritis in pregnancy beyond 24 weeks' appears to be limited in its applicability and is therefore not recommended.

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