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Research Article

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Effective cefixime treatment in pregnant women with urinary tract infection

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ABSTRACT

Urinary tract infections (UTIs) are considered to be the most common bacterial infection during pregnancy. Early diagnosis and proper treatment have a great impact on both mother health and pregnancy outcome. The antibiotic chosen should have a good maternal and fetal safety profile. In this paper, we screened pregnant women for UTIs at different stages of their pregnancies and treated them with a third generation cephalosporin, cefixime, aiming to evaluate the efficacy of this antibiotic in treating UTIs. Our results demonstrate considerable effectiveness of cefixime in treating UTIs in pregnant women at their first, second and third trimesters with significant reduction in bacterial urine culture growth in these pregnant women. There were no changes in renal function, blood glucose, white blood cells and hemoglobin levels before and after treatment which reflect drug safety and tolerability. We conclude that cefixime is an effective therapy for pregnant women at any stage of their gestation of relatively short term treatment.

Key words: Urinary tract infection, pregnancy, cefixime.

INTRODUCTION

Urinary tract infections (UTIs) are still one of the most common bacterial infections in pregnant women [1]. Pregnancy is a unique state demonstrates multiple anatomical and physiological urinary tract changes [2]. As a result of common physiological changes in pregnancy, pregnant women develop glycosuria which encourages bacterial growth in the urine [3]. Additionally, up to 90 percent of pregnant women develop ureteral dilatation with decreased ureteral tone. Furthermore, they exhibit increased bladder volume and decreased bladder tone leading to ureterovesical reflux and increased urinary stasis [2]. Differences in urine pH and osmolality and pregnancy-induced glycosuria may facilitate bacterial growth [4]. The hormonal and immunological changes that occur over the course of pregnancy are necessary for successful pregnancy, but also dramatically affect female susceptibility to autoimmune and infectious diseases including UTI [5]. Past history of UTI, lower socioeconomic group, sexual activity and multi parity were significant risk factors for UTI [3].

On the bases of clinical presentation, UTI varies from asymptomatic bacteriuria (ABU) to acute pyelonephritis and acute cystitis. Women with ABU during pregnancy are more likely to have miscarriage during the first and second trimester and to deliver pre-mature or low-birth-weight infants during the third trimester [6]. They have a 20 to 30-fold increased risk of developing pyelonephritis during pregnancy compared with women without bacteriuria [7]. Untreated ABU can also leads to the development of cystitis in approximately 30% of cases [8,9]. In addition UTI, during pregnancy, has been associated with anemia, septicaemia, hypertension, pre-eclampsia and chronic renal disease that have significant adverse obstetric and medical outcomes [10, 11]. Iron-deficiency anemia is the most common type of anemia during pregnancy and approximately 15% to 25% of all pregnancies experience iron deficiency [12]. However, in pregnant women with UTI, hemolysis with subsequent anemia could occur due to lipopolysaccharide-induced red blood cell membrane damage [13]. The etiologic microbial agents associated with bacteriuria are similar in pregnant and non-pregnant women [14, 15, 16]. Appropriate investigation and proper treatment are needed to avoid serious life threatening condition and morbidity due to UTI that can occur in pregnant

women. Cefixime is a third generation cephalosporin which is administered as a single oral dose with a marked activity against the most important pathogens responsible for UTIs and has few mild side effects with no reported teratogenic effects [17].

This study was performed with the objective to evaluate the effectiveness of a single daily dose of cefixime on the UTIs in pregnant Iraqi women in different trimesters with clinical diagnostic framework.

EXPERIMENTAL SECTION

2.1 Thirty pregnant women with established urinary tract infection were enrolled in the study. They attended the outpatient clinic of the maternity teaching hospital in AL-Qadisiyah city/Iraq and they were allocated into three main groups according to their gestational age (first, second and third trimester with ten patients in each group).

2.2 Urinalysis Procedure includes general urine examination and culture. Collection of urine sample was done in a specimen cup with midstream urine in order to avoid contamination. Alcohol wipes were avoided as these may irritate the area and samples analyzed soon after collection. Microscopic urinalysis involves quantitative examination of urine pus cells (contain dead epithelial, bacteria and white blood cells) per high power field (HPF). Up to 10 cells /HPF was considered to be normal findings in pregnant women without urinary tract infection. A urine culture was performed along with general urine examination for all patients and a culture that is reported as no growth in 48 hours indicated as negative while those numbers between 1,000 to 100,000 colony forming units (CFU)/mL indicated low infection and heavy infection was considered when numbers were more than 100,000 CFU/mL [18].

2.3 Blood urea and serum creatinine. Blood urea was quantitatively measured through determination the concentration of blood urea nitrogen in blood by means of the enzymatic conductivity rate method. A precise volume of sample is injected into the urease reagent in a reaction cup containing an electrode that responds to changes in solution conductivity. Electronic circuits determine the rate of increase in conductivity, which is directly proportional to the concentration of urea in the sample. To determine the concentration of creatinine in serum, a precise volume of sample is introduced into a reaction cup containing an alkaline picrate solution. Light absorbance readings are taken at both 520 nm and 560 nm. Creatinine from the sample combines with the reagent to produce a red color complex. The observed rate measurement at 25 seconds after sample introduction has been shown to be a direct measure of the concentration of the creatinine in the sample [19].

2.4 Random blood sugar (R.B.S): A blood sample was obtained from a vein at a random time regardless of when patient last ate. Enzymatic determination of glucose level was done by colorimetric procedure at wave length 553 nm [20].

2.5 Total white blood cell count was done using conventional method including analysis of collected blood samples place them on a glass slide for visual review under a microscope [21].

2.6 Hemoglobin is measured in a blood sample that is chemically treated to release hemoglobin from red blood cells where the released hemoglobin is bound chemically to cyanide forming a compound that absorbs light. The amount of absorbed light was measured, and this value was directly related to how much hemoglobin is present in the blood [22].

2.7 Cefixime was given to these patients as a single daily dose (400 mg orally) for 7 days.

2.8 Statistical analysis: Data were analyzed using the unpaired student t test.

RESULTS AND DISCUSSION

Our findings demonstrated significant improvement in GUE results and urine culture results after treatment, as shown in (Table 1). Cefixime significantly reduced the number of puss cells in urine of pregnant women enrolled in the study.

Table 1: Results of GUE (Puss cells /HPF) in all women enrolled in the present study

Puss cells/HPF	Women in 1st trimester		Women in 2nd trimester		Women in 3rd trimester	
	Before	After	Before	After	Before	After
0	0	4	0	4	0	2
2-3	0	3	0	2	0	4
4-10	1	3	1	4	1	4
25-50	5	0	3	0	5	0
75-100	4	0	6	0	4	0
Total	10	10	10	10	10	10
P-value	<0.05		<0.05		<0.05	

This improvement was observed in all three trimesters with similar effectiveness. Furthermore, cefixime treatment results in a significant reduction in bacterial urine culture growth for those pregnant women at all trimesters (Table 2).

Table 2: Results of urine culture in all women enrolled in the present study

Culture	Women in 1st trimester		Women in 2nd trimester		Women in 3rd trimester	
	Before	After	Before	After	Before	After
Negative	0	6	0	7	0	6
Low	6	4	5	3	6	4
Heavy	4	0	5	0	4	0
Total	10	10	10	10	10	10
P-value	<0.05		<0.05		<0.05	

Table 3: Biochemical and hematologic parameters of pregnant women, in their first, before and after treatment

Parameter	Before	After	P-value
Blood urea mg/100mL	29.60±5.80	38.30±3.77	>0.05
Serum creatinine mg/100mL	0.70±0.08	0.83±0.08	>0.05
RBS mg/100mL	100.50±8.28	106.50±6.33	>0.05
WBC Cells/HPF	8150.00±1028.75	8600.00±575.42	>0.05
Hb mg/100mL	11.99±0.33	11.92±0.49	>0.05

Such renal infection could affect kidney functions and, additionally, physiological changes during pregnancy may alter the pharmacokinetic properties of cefixime in a way that produces harmful effects on the kidneys. So that, next step was to examine the consequences of this infection on renal functions before starting the treatment and as well as the effect of cefixime on renal functions in these pregnant women at the end of the treatment. Mean blood urea and serum creatinine levels showed normal values before staring the treatment with no significant changes among pregnant ladies in their first, second and third trimester following cefixime treatment as shown in (Tables 3 through 5).

High blood glucose level produces glycosuria which may create favorable environment for renal bacterial growth. Therefore, it is necessary to assess the blood glucose levels in those pregnant women with renal infection before cefixime treatment and when they are cured. We found that those women in their first, second and third trimester have normal blood glucose levels before starting the treatment and did not have significant changes in their blood glucose levels following treatment as shown in (Tables 3 through 5).

Table 4: Biochemical and hematologic parameters of pregnant women, in their second trimester, before and after treatment

Parameter	Before	After	P-value
Blood urea mg/100mL	31.50±4.17	36.90±3.57	>0.05
Serum creatinine mg/100mL	0.70±0.11	0.74±0.11	>0.05
RBS mg/100mL	106.60±8.87	105.70±6.13	>0.05
WBC Cells/HPF	8400.00±1591.64	8450.00±776.39	>0.05
Hb mg/100mL	11.98±0.42	11.79±0.41	>0.05

Table 5: Biochemical and hematologic parameters of pregnant women, in their third trimester, before and after treatment

Parameter	Before	After	P-value
Blood urea mg/100mL	29.00±4.50	35.40±5.95	>0.05
Serum creatinine mg/100mL	0.75±0.07	0.80±0.07	>0.05
RBS mg/100mL	104.20±8.48	127.90±15.58	>0.05
WBC Cells/HPF	7630.00±715.00	7940.00±787.68	>0.05
Hb mg/100mL	12.08±0.54	11.59±0.79	>0.05

Urinary tract infections, if untreated, can lead to bacteremia which can be manifested as increased blood white cell count. In order to evaluate the extent of infection in those pregnant women, we did white blood cell count test and found normal values in all three trimesters. Administration of cefixime did not affect white blood cells in pregnant women in their first, second and third trimester as shown in (Tables 3 through 5).

Finally, we measured the hemoglobin levels in these pregnant women before starting the treatment because anemia could be leading factor in developing UTIs. We found that those women have normal hemoglobin levels and cefixime treatment didn't affect it (Tables 3 through 5).

The prevalence of urinary tract infection in pregnant women varies among gestational stages with different clinical consequences [23]. Early and adequate treatment decrease the risk of obstetric complications related to UTIs. Our results demonstrate that cefixime effectively treated UTIs in pregnant women in their first, second and third trimester.

The successful treatment resulted in reduction in the number of high pus cells in the urine of pregnant women to nil in all three trimesters. A possible explanation for that would be the sensitive causative pathological microorganism that causes the UTIs. Cefixime is a broad spectrum antibiotic with effective bactericidal activity against wide range of gram positive and gram negative bacteria. Unfortunately our lab facilities were inefficient to do antibiotic culture sensitivity tests which could show the causative microorganism and their antibiotic susceptibility nature. However, urine growth culture showed a significant reduction in bacterial growth upon antibiotic treatment which further strength the assumption of susceptibility of causative microorganism to cefixime treatment.

The sample size in our study is comparable for a clinical based research. Nevertheless, it will be highly useful to have a large sample size with inclusion of pregnancies complicated by medical conditions like hypertension, heart diseases and renal diseases to extend future study. Those pregnant women may have more diverse microorganisms and their UTIs response to cefixime treatment could yield different results.

Our observations presented treatment effectiveness with a similar pattern in the all three trimesters which possibly indicate that pregnancy's physiological stages have no impact on successful antibiotic therapy. It would be interesting to test whether there is any congenital side effect of cefixime, but due to time limit, we were unable to follow those pregnant women until delivery. However, there weren't any previous publications concerning fetal adverse effect of cefixime treatment at any pregnancy stage, collectively this indicate the safety and effectiveness of cefixime in pregnant women.

In addition to that, we didn't find any differences in renal function, blood glucose, hemoglobin and white blood cell count during the course of the cefixime treatment. This could partly due to short term treatment but also propose that this drug is safe to be used in pregnant women suffering from impaired renal function, hyperglycemia or anemia.

CONCLUSION

The simplicity of treatment, by single oral daily dose, added another beneficial point to our work so that patients are not submitted to annoying frequent doses or painful parenteral routes of drug administrations.

In this study, we have made a clear demonstration that cefixime treatment of UTIs in pregnant women can be considered a s one of the best option and recommended it for all the pregnancy trimesters.

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