Volume 13 Issue 10
Originally issued as E2

Global Journal of Medical research
Gynecology and Obstetrics
Volume 13 Issue 2 Version 1.0 Year 2013
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN : 0975-5888

The Effect of Oral Metronidazole in the Prevention of Preterm Labour among Pregnant Women With Bacterial Vaginosis

By Yossra salihkhudur, Huda salihkhude & Sarab salihjassim
University of Tikrit, Iraq

Abstract - *Aim of the study:* To evaluatethe effectiveness of oral metronidazole in prevention of preterm labouramong pregnant women with bacterial vaginosis.

Settings and study design: An experimental (longitudinal-prospective) study done in Tikrit city between April 2011 and April 2012.

Methods: A total number of 50 pregnant women in their midtrimester were included in the study, they received oral metronidazole 200 mg orally in two divided doses for 7 days,selection criteria include pregnant women with singleton viable pregnancy in midtrimester with intact membranes. Demographic profile and prolongation of pregnancy and neonatal outcome were recorded is special forms.

Results: Oral metronidazole was not effective in prolongation of pregnancy despite its efficacy in eradicating bacterial vaginosis.

Conclusion: Our findings suggest that second trimester screening and treatment of bacterial vaginosis during pregnancy with oral metronidazole is not effective regarding prolongation of pregnancy and preventing adverse neonatal outcome.

Keywords: *metronidazole, preterm labour, bacterial vaginosis.*

GJMR-E Classification : *NLMC Code: WJ 190, WC 240*



Strictly as per the compliance and regulations of:

© 2013. Yossrasalihkhudur, Huda salihkhude & Sarabsalihjassim. This is a research/review paper, distributed under the terms of the Creative Commons Attribution-Noncommercial 3.0 Unported License http://creativecommons.org/licenses/by-nc/3.0/), permitting all non-commercial use, distribution, and reproduction inany medium, provided the original work is properly cited.

The Effect of Oral Metronidazole in the Prevention of Preterm Labour among Pregnant Women With Bacterial Vaginosis

Yossra salihkhudur [α], Huda salihkhude [σ] & Sarab salihjassim [ρ]

Abstract- Aim of the study: To evaluatethe effectiveness of oral metronidazole in prevention of preterm labouramong pregnant women with bacterial vaginosis.

Settings and study design: An experimental (longitudinal-prospective) study done in Tikrit city between April 2011 and April 2012.

Methods: A total number of 50 pregnant women in their midtrimester were included in the study, they received oral metronidazole 200 mg orally in two divided doses for 7 days,selection criteria include pregnant women with singleton viable pregnancy in midtrimester with intact membranes. Demographic profile and prolongation of pregnancy and neonatal outcome were recorded is special forms.

Results: Oral metronidazole was not effective in prolongation of pregnancy despite its efficacy in eradicating bacterial vaginosis.

Conclusion: Our findings suggest that second trimester screening and treatment of bacterial vaginosis during pregnancy with oral metronidazole is not effective regarding prolongation of pregnancy and preventing adverse neonatal outcome.

Keywords: metronidazole, preterm labour, bacterial vaginosis.

I. Introduction

Preterm labour is defind as birth before 37 completed weeks of gestation (up to 36 + 6 weeks) and is one of the most significant causes of perinatal morbidity and mortality. Incidence is between (5 – 10 %) in most developed countries, preterm labour is diagnosed by regular painful uterine contractions and evidence of cervical change. It may be associated with rupture of membr- anes or positive fetal fibronectin[1] To date, no effective means of preventing spontaneous preterm delivery has been identified At least in some cases, however, microbial colonization of the fetal membranes or the amniotic fluid, or alteration in the vaginal flora such as are seen in patients with bacterial vaginosis , have been associated with spontaneous labour and preterm delivery An extensive body of evidence indicates that infection is associated with preterm delivery and with low birth weight of the infant[2] Chorioamnionitis is strongly correlated with preterm delivery, and the failure of tocolytic drug therapy Evidence of infection, manifested by the presence of organisms or inflammatory cytokines in the amniotic fluid or chorioamniotic membranes, commonly accompanies preterm labour and preterm premature rupture of membranes, particularly as the earliest gestational ages[3] Most microorganisms found in the amniotic fluid and placenta are thought to come from the vagina, especially among women with bacterial vaginosis.Bacterial vaginosis is an imbalance of vaginal flora caused by a reduction of the normal lactobacillary bacteria and a heavy overgrowth of mixed anaerobic flora including Gardenellavaginalis, Mycoplasma hominis and Mobiluncus species[4].Bacterial vaginosis is present in up to 20% of women during pregnancy. The majority of these cases will be asymptomatic, the natural history of bacterial vaginosis is such that it may rsolve without treatment although most women identified as having bacterial vaginosis in early pregnancy are likely to have persistent infection later in pregnancy[5].There is now a substantial body of evidence associating bacterial vaginosis in pregnancy with poor perinatal outcome, in particular an increased risk of preterm birth with potential neonatal sequelae due to prematurity[6] There is also evidence associating intermediate flora with adverse pregnancy outcome, whilst a number of other genital microorganisms such as Escherichia coli, Listeria monocytogenes and viridians streptococci may be involved in chorioamnionitis, carriage of these organisms during early to mid pregnancy has not associated with an increased risk of preterm labour [7]. Although maternal carriage of group B streptococcus increases the risk of neonatal sepsis due to this organism, there is conflicting evidence about whether carriage during pregnancy increases the risk of preterm birth[8].Infctions during pregnancy for which there is good evidence of an increased risk of prterm birth and preterm labourprelabour rupture of membranes, include asymptomatic bacteriuria, Neisseria gonorrhoae, Chlamydia trachomatis, Trichomonasvaginalis and bacterial vaginosis the apportunity therefore exists to reduce the preterm birth rate by treatment of these

Author α: Department of Obstetrics and Gynecology, College of Medicine, University of Tikrit.
Author σ: Department of Pharmaceutics, College of Pharmacy, University of Tikrit.
Author ρ: Departmentof Obstetrics & Gynecology, College of Medicine, University of Tikrit.

© 2013 Global Journals Inc. (US)

infections during pregnancy [9].Bacterial vaginosis is relatively common even in populations of women at low risk of adverse events and as it is amenable to treatment, identification during pregnancy and treatment may present a rare apportunity to rduce the preterm birth rate and resulting risk of of prematurity to the newborn [10]. There are several factors for the acquisition of bacterial vaginosis, it has been associated with racial origin, smoking, sexual activity, and vaginal douching Bacterial vaginosis is more common in black women, women who smoke, women who are sexually active compared with virginal women, and those who use vaginal douches. Bacterialvaginosis is a syndrome that can be diagnosed both clinically and microbiologically[11]. Diagnostic criteria are the same for pregnant and non-pregnant women. Amselet al [12]. published clinicl diagnostic criteria in 1983, and these still in use today. The clinical diagnosis of bacterial vaginosis is made if three of the four following signs are present: An adherent and homogenous vaginal discharge, vaginalpH greater than 4.5, detection of clue cells(vaginal epithelial cells with such a heavy coating of bacteria that the peripheral borders are obscured) on a saline wet mount, an amine odour after the addition of potassium hydroxide (positive whiff test).Gram stain of vaginal fluid is the most widely used and evaluated microbiological diagnostic method for bacterial vaginosis. To perform a Gram stain, vaginal discharge is collected on a glass slide, allowed to air dry, stained in the laboratory, and examined under oil immersion for the presence of bacteria. Most laboratories use an objective diagnostic scheme that quantifies the number of Lactobacillus morphotypes and pathogenic bacteria, resulting in ascore that used to determine whether the infection is present. The most commonly used system is the Nugent score (table1) [13], the criterion for bacterial vaginosis is a score of 7 or higher. A score of 4 to 6 is considered intermediate, and a sore of 0 to 3 is considered normal. Metronidazole is an antimicrobial drug with high activity against anaerobic bacteria and protozoa ,it is usually given orally and is rapidly and completely absorbed, achieving pak plasma concentration in 1 to 3 hours, with a half –life of about 7 hours. It is distributed rapidly throughout the tissues, reaching high concentration in body fluids, som is metabolized, but most is excreted in urine [14].

Table 1 : Scoring system (0-10) for gram stained vaginal smears

SCORE	LACTOBACILLUS MORPHOTYPES	GARDNELL AND BACTEROIDS SPP.MORPHOTYPES	CURVED GRAM-VARIABLE RODS
0	4+	0	0
1	3+	1+	1+ OR 2+
2	2+	2+	3+ OR 4+
3	1+	3+	
4	0	4+	

II. Subjects and Methods

This study is an experimental (longitudinal – prospective) study. It was conducted in Tikrit city between April 2011 and April 2012 where about 50 pregnant women who were at the second trimester of pregnancy were enrolled in this study after taking a verbal consent during attending a private clinic in Tikritcity. Demographic and obstetric data were recorded in a special forms for each participant. Gestational age determination was based on precisely recalled menstrual dates as they were having regular menstrual cycles, and further confirmed by their first or early second trimester ultrasound. We identified for inclusion in the study otherwise healthy women with uncomplicated singleton pregnancy between 22 and 24 weeks of gestation who had previously had a spontaneous preterm labour. Women were excluded from the study if they were having known allergies to metronidazole, an uncertain length of gestation, a multiple gestation, prior vaginal bleeding, or a medical complication of pregnancy, such as diabetes mellitus or hypertension. Only women who had not received antimicrobial therapy for at least four weeks were enrolled.

One Dacron swab, taken from the junction of the upper third and lower two thirds of the lateral vaginal wall was rolled on a glass slide and then touched to a pH stick (ColorPHast PH stick, Curtin Matheson, Grand Prairie, Tex.). The slides from women whose vaginal pH was higher than 4.4 were sent to the laboratory, were they underwent Grams staining with the results interpreted according to the criteria of Nugent et al [13]. we defined bacterial vaginosis as a Gram,s staining score of 7 or higher in conjunction with a vginalpH higher than 4.4. After these specimens were obtained, the women were received metronidazole 200 mg orally twice daily for 7 days.One follow –up visit was scheduled between 24 weeks, 0 days weeks of gestation and 27 weeks, 6 days of gestation, at least 14 days after the initial visit. All women were treated again with the same (two dose regimen) received initially, regardless of the results of the follow- up Gram, s staining. Data were analyzed using the statistical

© 2013 Global Journals Inc. (US)

packages for social sciences (SPSS version 11). The data were presented as numbers, percentages, frequencytables, graphs, Chi square test was used to measure statistical significance.P-value of <0.05 indicated the level of significance.

III. Results

All the 50 women were enrolled in this study.As shown in table (2), bout 5(17.2%) of primiparous women who used oral metronidazole delivered at term, whileabout 16(31.4%)had preterm delivery.Metronidzole had higher effective rates among multiparous women,12(23.5%).The study revealed that metronidazole had higher effectiveness rate ,8(25%),among women at age group (25-30) years old while showed low effectiveness rate at maternal age (30-35)years old which was 5(26.3%),table(3).Table (4) showed that about 15(13%) of pregnant women with bacterial vaginosis who used oral metroniazole were delivered before 37 weeks of gestation ,also it revealed that about 31(22%) of pregnant women with bacterial vaginosis and history of previous preterm labour who used oral metronidazole were delivered before 37 completed weeks of gestation.

Table 2 : The relation between parity and drug effect

PARITY	METRONIDAZOLE EFFECT			
	YES		NO	
	NUMBER	%	NUMBER	%
PRIMIPAROUS WOMEN	5	17.2	16	31.4
1-4	12	23.5	7	24.1
5 AND MORE	2	10	8	40

Table 3 : The relation between maternal age and drug effect

MATERNAL AGE	METRONIDAZOLE EFFECT			
	YES		NO	
	NUMBER	%	NUMBER	%
15-	2	33.3	0	0
20-	7	31.8	3	13.7
25-	8	25	4	12.5
30-	7	28.6	5	26.3
35-	2	28.5	3	42.9
40-	4	33.3	3	25
45-50	1	8.3	1	50
TOTAL	31	31	19	19

Table 4 : Rates of delivery before 37 weeks of gestation among study group.

GROUP OF WOMEN	NUMBER	%	P-VALUE
ALL STUDIED	50	100%	0.01
WITHOUT BACTERIAL VAGINOSIS	4	1	0.02
WITH BACTERIAL VGINOSIS	15	13	0.006
WITH BACTERIAL VAGINOSIS AND PREVIOUS PRETERM LABOUR	31	22	0.55

IV. Discussion

Recently, it has bcome apparent from many studies that bacterial vaginosis approximately doubles the risk of spontaneous preterm labour. There is now a substantial body of evidence that associates bacterial vaginosis in pregnancy with poor perinatal outcome, in particular an increased risk of preterm labour. This strong association between bacterial vaginosis and preterm labour has led many researchers and clinitians to believe that bacterial vaginosis may be the cause of preterm labour in these women.Regarding demographic and obstetric data in our study, metronidazole had a higher effect, 8 (25%), among pregnant women at age group (25-30) years old, while lower effect was found at maternal age (30-35) years old which was 5 (26.3%). Metronidazole was more effective among multiparous women, 12(23.5%), while it has less effect in primiparous women 16 (31.4%), table (2). In our study, we evaluate the efficacy of oral metronidazole for prevention and treatment of preterm labour in pregnant women with bacterial vaginosis. Our data indicate that

© 2013 Global Journals Inc. (US)

oral metronidazole is not effective in regards to the prolongation of pregnancy and pregnancy outcome, table(4). Our resultsagree with those of McDonald et al [15], who also reported no reduction in the risk of preterm delivery among pregnant women with bacterial vaginosis who were treated with metronidazole. The administration of therapy earlier or later in pregnancy might have produced different results, because the intrauterine infection associated with bacterial vaginosis may antedate the pregnancy. We chose to treat early in the second trimester to avoid fetal exposure to metronidazole in the first trimester and to repeat the regimen late in the second trimester or early in the third trimester so as to spread treatment over as wide as a period as practical. Our results show that screening pregnant women for asymptomatic bacterial vaginosis and treating the condition with a short course of orally administered metronidazole did not reduce the risk of preterm birth despite its effectiveness in eradicating bacterial vaginosis. Our results are similar to the results of a study done by Carey et al [16], in which asymptomatic women were screened at 16 – 24 weeks of gestation and treated with metronidazole. A repeat vginal smear and pH were done at 24 – 30 weeks of gestation and treatment repeated if indicated. There was no difference in low or very low birth weight babies before 32, 35, or 37 weeks. In contrast, the study of Ugwunduet al [17], demonstrated a reduction in the rate of miscarriage or spontaneous preterm delivery, (95%, CI 5.0-15.8) in asymtomatic women with bacterial vaginosis at 12-22 weeks of gestation who received metronidazole. In another study, by Lamont and colleagues [18], women with bacterial vaginosis were randomised to receive metronidazole or placebo, the placebo group had a lower gestational age at delivery and a higher rate of neonatal intensive care unit admission. These two studies in contrast to that of Carey et al, therefore, support the identification and treatment of bacterial vaginosis in pregnant women during their early pregnancy.

References Références Referencias

1. Klebanoff M, HauthJ, Heine R, et al. Asymptomatic bacterial vaginosis in pregnancy with and without treatment. Amer J Obstet Gynecol 2004; 190: 363-70.
2. LeitichH, BodnerB,HussleinP. Bacterialvaginosiss a risk factor for preterm delivery: a meta-analysis. Amer J Obstet Gynecol 2003; 189(1):139-47.
3. Paternoster D,MagginoT,AmbrosiniA.Efficasy of an acidic vaginal gel on vaginal PH and interleukin-6 levels in low risk pregnant women. Maternal-fetal J 2004; 15(3): 198-201.
4. Rosnes J, NICHD MFMU Network. Does vaginal PH or gram stain score alter the likelihood of successful metronidazole treatment of bacterial vaginosis during pregnancy.Amer J ObstetGynecol 2002; 187(6 Pt2): S228.
5. Shennan A, CrawshawS, JonesG, et al. A randomized controlled trial of metronidazole for the prevention of preterm labour in women positive for cervicovaginal fetal fibronectin. BJOG 2006; 113(1): 65-74.
6. Steyn PS, Odendaal HJ, Grove D. A randomisd, double-blind placebo –controlled trial of ascorbic acid supplementation for the prevention of preterm labour. J of Obstet and Gynecol 2003; 23(2): 150-50
7. Yudin MH, Landers DV, Meyn L .Clinical and cervical cytokine response to treatment with oral or vaginal metronidazole for bacterial vaginosis during pregnancy. Obstet and Gynecol 2003;102 (3): 527-34.
8. DarwishA, HamadehSM, MakaremMH. Treatment options for bacterial vaginosis in patients at high risk of preterm labour and premature rupture of membranes. J of Obstet and GynecolRsearch 2007; 33(6):781-7.
9. Giuffrida G, Mangiacasale A. Bacterial vaginosis in pregnancy.J of Obstet and Gynecol 2006; 28(12): 539-43.
10. Kurtzman J, Chandiramane M, Briley A .Quantitative fetal fibronectin screening at 24 weeks substantially discriminates the risk of recurrent preterm delivery in asymptomatic patients with prior preterm labour.Amer J of Obstet and Gynecol2008; 199(6 Suppl 1): S10.
11. Larsson PG, Fhraeus L, ForsumU. Late miscarriage and preterm labour after treatment with metronidazole. BJOG2006; 113 (6): 629-37
12. Amsel R, Totten PA, Spiegel CA. Non specificvaginitis. Diagnostic criteria and microbial and epidemiological associations. Amer J of Med 1983; 74: 14-22.
13. Nugent RP, Krohn MA, Hillier SL.Reliability of diagnosing bacterial vaginosis is improved by a standardized method of Gram stain interpretation. J of Clin Micro 1991; 29: 297-301.
14. Rang H P, Dale M M.Drugs used in treatment of infections and cancer.Pharmacology.6thed, Churchill Livingstone & Elsevier.2007:700.
15. McDonald HM, Jolley PT, Pharm et al. Metronidazole treatment of bacterial vaginosis in pregnancy, and preterm birth. Inf Dis in Obstet and Gyncol 1996; 4: 49.
16. Carey J, KlebanoffM, HauthJ, Heine R, et al. Time course of the regression of asymptomatic bacterial vaginosis in pregnancy with and without treatment. Amer J ObstetGynecol 2004; 190: 363-70
17. Ugwumadu A, Reid F, Hay P. Oral metronidazole and histologic chorioamnionitis in women with abnormal vaginal flora.Obstet and Gyncol 2006; 107(4): 863-8.

© 2013 Global Journals Inc. (US)

18. Lamont RF, Fisk NM, The role of infection in the pathogenesis of preterm labour.In: Studd JWW editor (s).Progress in obstetrics and gynecology.Vol.10, London: Churchill Livingstone, 1993: 135-58.

© 2013 Global Journals Inc. (US)

This page is intentionally left blank

© 2013 Global Journals Inc. (US)