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Does the Method of Treating Bacterial Vaginosis in Early Pregnancy Affect the Re-occurrence Rate Near Term?

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DOES THE METHOD OF TREATING BACTERIAL VAGINOSIS IN EARLY PREGNANCY AFFECT THE REOCCURRENCE RATE NEAR TERM?

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ABSTRACT

DOES THE METHOD OF TREATING BACTERIAL VAGINOSIS IN EARLY PREGNANCY AFFECT THE REOCCURRENCE RATE NEAR TERM?

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There is no significant difference in the relationship between oral or vaginal metronidazole and oral clindamycin in the treatment of bacterial vaginosis (BV) in early pregnancy and the reoccurrence rate of BV at 35 to 37 weeks gestation. Treatment of BV in pregnancy has been shown to decrease the preterm delivery rate saving millions of dollars and improving the health of infants. This was a descriptive, correlational study using a retrospective chart review. A constructed checklist was used for collecting data from 186 charts.

Age, parity, and insurance were comparable in each of the three drug groups. The reoccurrence rate of BV when tested in the third trimester showed no significant differences in comparison of the three drug treatment groups (Chi-square = .55; df = 2; p = .76). All three drugs were equally effective in the treatment of BV.

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Chapter One

INTRODUCTION

Preterm births continue to be the most significant pregnancy related problem in the United States. Prematurity is responsible for almost 75% of neonatal mortality and as much as 50% of long term neurological damage in children (Hauth, Goldenberg, Andrews, DuBard, & Copper 1995). Reports have shown one-fifth of children weighing less than 1000g at birth have moderate to severe neurosensory handicaps at 2 years of age (Novy, McGregor, & Iams 1995). Handicaps can include blindness, deafness, mental retardation, epilepsy, and cerebral palsy. In 1990 the costs for special education for 85,000 preterm children in the United States was $370 million (Novy et al.). As of 1994, the United States ranked 22 out of 186 in world infant mortality rates. Many feel the poor ranking is due to the high number of premature births and low birth weight infants born here. Preterm birth rates remained relatively constant for 40 years until the 1980s. There has been a slow rise in rates especially in certain groups of women.

Nurse practitioners frequently make decisions on desired drug treatment given to obstetrical patients; therefore, they have the ability to have a positive influence on the preterm delivery rate. Prevention of

preterm deliveries is of utmost importance worldwide, because it not only will improve the health of many children but also will also save billions of dollars spent on their healthcare. Early identification and optimal treatment of bacterial vaginosis has the potential to decrease the incidence of preterm labor (Hack & Merkatz, 1995).

Why do preterm birth rates continue to rise despite hundreds of preventative interventions throughout the world? Programs such as early prenatal care, better nutrition, easier access to health care, increased social support, home uterine monitoring, increased education of patients and about tocolytic drugs have been shown to be unsuccessful in affecting the overall rate of preterm births (Goldenberg & Andrews, 1996). Therefore, researchers are focusing more on the reasons why preterm labor happens versus how to stop labor once it occurs. Numerous studies have shown that bacterial vaginosis (BV) has been a common link to labor before 37 weeks (Hillier et al. 1995). BV is one of the most common genital tract infections found in women. Up to 22% of pregnant women have this infection present at their initial examination (Hillier et al.). Chorioamnionitis is commonly caused by BV and is found in up to 80% of deliveries prior to 30

weeks gestation (Goldenberg & Andrews).

Bacterial vaginosis is an overgrowth of normal vaginal organisms. It begins in the lower genital tract and often ascends through the cervix to the uterus affecting the pregnancy. Even after adjustment for variables such as previous preterm delivery or maternal weight below 110 lbs, women with BV are 40% more likely to give birth before term (Hillier et al, 1995). One study in Indonesia showed the rates of preterm delivery were almost doubled for those diagnosed with BV in the early second trimester (20.5%) as compared with those diagnosed in late pregnancy (10.7%) (Riduan et al. 1993).

Antimicrobial therapy given to pregnant women positive for BV in the second trimester decreases the risk of preterm delivery (Hauth et al. 1995). Currently there are four primary antibiotic treatments used. Metronidazole has always been the drug of choice for treatment of BV in the non-pregnant woman. Many practitioners are reluctant to use metronidazole in the pregnant patient because of the possible mutagenic and/or carcinogenic effects in the infant, especially in the first trimester. A recent meta-analysis does not show teratogenicity in humans (Centers for Disease Control and Prevention, 1998). Centers for Disease Control (CDC) treatment guidelines for 1998

continue to recommend oral metronidazole as the drug of choice in the treatment of BV. Other drug choices include oral clindamycin, metronidazole vaginal gel 0.75%, and clindamycin 2% vaginal cream. CDC guidelines no longer recommend clindamycin vaginal cream during pregnancy due to recent studies indicating an increase in the rate of preterm births with its use.

Much discussion has taken place on which drug treatment is the most effective in eradicating the infection. Once the microorganisms ascend the upper reproductive tract, intravaginal medications may not be helpful to prevent preterm deliveries. Thus, the CDC (1998) no longer recommends intravaginal treatments for pregnant women who have previously delivered a premature infant. Studies vary slightly on the effectiveness rates of the above mentioned antibiotics. Joesoef and Schmid (1995) found no significant difference in efficacy between oral metronidazole and oral clindamycin (96% vs 94%). Ferris, Litaker, Woodward, Mathis, and Hendrich (1995) reported similar findings. Some clinicians are hesitant to use clindamycin due to possible gastrointestinal problems including pseudomembranous colitis (occurrence rate 2% to 10%) (Reynolds, 1991). Recommended doses for the treatment of BV in pregnancy are well within dosage guidelines. Due

to the fact that many clinical practices may not reevaluate the patient unless symptomatic, the most effective drug should be used if possible in order to increase the patient cure rate. Many times nurse practitioners are the primary providers for identification and treatment of bacterial vaginosis. Nurse practitioners may not only save lives of infants born too early, but also save millions of dollars through decreased hospitalizations and long term care.

The purpose of this study was to examine differences in the relationship between oral metronidazole, vaginal metronidazole or oral clindamycin treatment of BV in early pregnancy (before 16 weeks) and the recurrence rate of BV at 35 to 37 weeks gestation.

Chapter Two

CONCEPTUAL FRAMEWORK

The conceptual framework for examining the relationship between treatment method for BV in early pregnancy and the recurrence rate near term will be based on the Betty Neuman Health Care Systems Model (Neuman, 1989). Neuman began developing her theory in the late 1960s in response to requests from graduate students (Beckman, 1994). Her completed conceptual model was presented in 1970 and has been further developed several times since then (Beckman). The model is a product of her philosophy and observations made in teaching mental health nursing and in counseling (Neuman).

Neuman labels her systems theory as a general theory involving an open system approach. Neuman's systems model incorporates stress as the deciding factor for all interventions for the self or environment. Neuman (1993) believes a person's health centers around stressors and coping. Inability to cope results in illness and sometimes death. The self is in constant interaction with the environment. The goal of the intervention is to strengthen the basic structure (the self) so that the effect of the stressor is minimized (Bullock, 1993).

Neuman's model contains several circles or rings

around the self(See Figure 1). The rings differ for each person because they include information from physiologic, psychologic, sociocultural, developmental, and spiritual attributes (Bullock, 1993). The outermost ring is the flexible line of defense. It expands to provide increased protection and contracts for less protection of the self or core. The flexible line of defense represents the immediate responses an individual makes to actual or potential stressors. Distance of the stressors from the core varies according to the needs and abilities of the client. Stressors vary with age, health status, educability and resources. The next inner ring is the normal line of defense. This represents a stability state, baseline or standard, which develops over time.

The innermost circles are called the lines of resistance and are the body's attempt to stabilize against the disequilibrium caused by the stressor (Bullock, 1993). The lines of resistance include those things an individual does at a conscious or subconscious level to restore equilibrium or achieve an even higher level of stability. The lines of resistance include prevention at primary, secondary, and tertiary levels. Educating a woman on how to reduce her risk factors for BV (e.g. frequent partners, smoking, and douching) is an example of primary

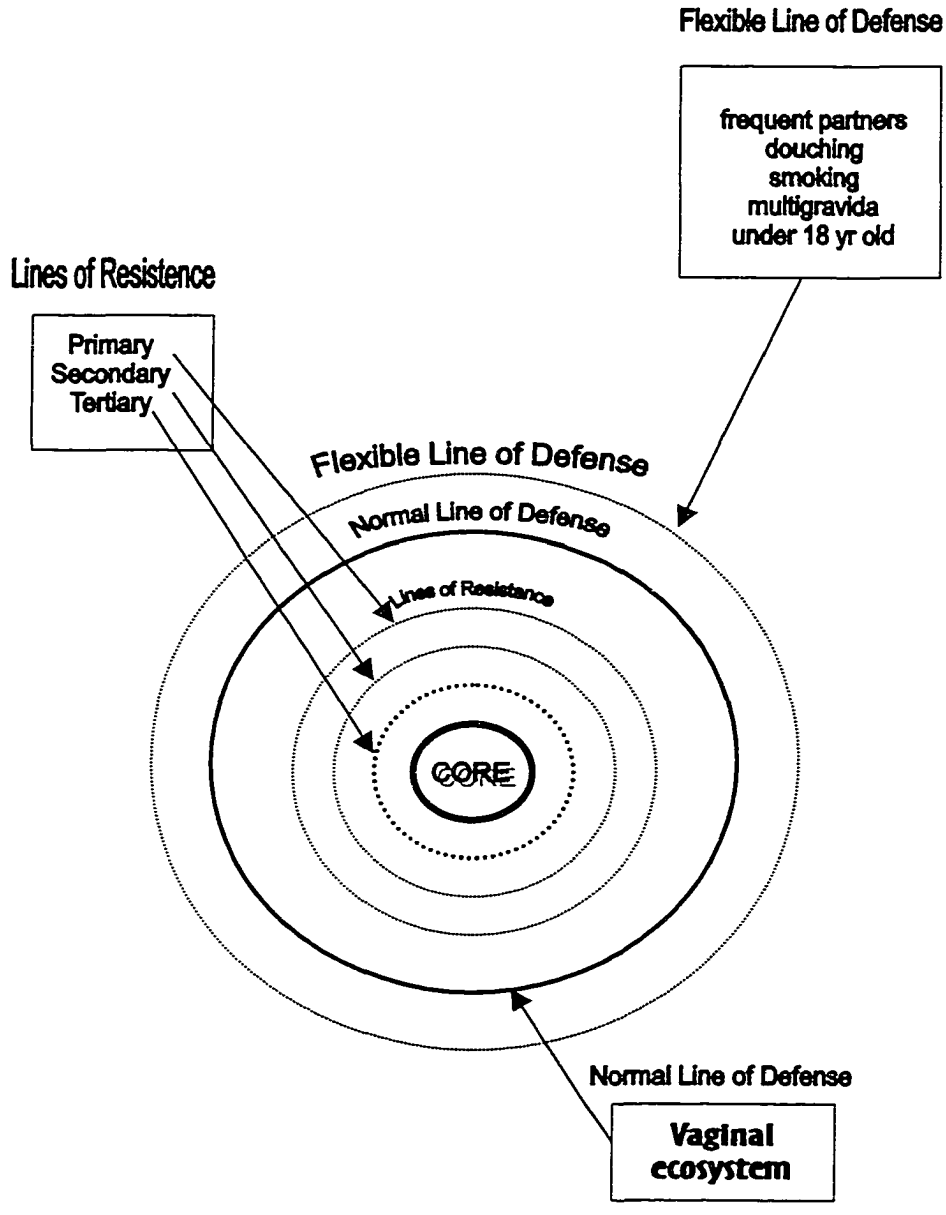

Figure 1. Neuman's Systems Model

Neuman (1989)

prevention. Secondary prevention involves interventions or treatments initiated after symptoms have occurred. This would include antibiotic treatment of BV. Tertiary intervention occurs after actual treatment. The goal of tertiary intervention is reconstitution of the woman to an optimal level of health (Bullock, 1993). Exploring ways to decrease the recurrence of BV would be an example of tertiary intervention. It focuses on readjustment toward optimal stability.

The inner most ring is the core. The core is represented by a solid line to indicate its stability. The core consists of those things necessary for survival such as temperature and organ function. The person's individual genetic makeup, such as weaknesses and strengths of different body parts, ego, and response patterns also affect the core. The core may also represent a family, group or community. Penetration of the core could lead to death or destruction. Strengthening the lines of defense and the lines of resistance helps to protect the core.

In summary, Neumans Systems Model (1989) is a holistic model which addresses the social, developmental, psychological, physical, and spiritual aspects of the pregnant woman and how they are impacted by stressors. The rings of resistance protect the inner core of the woman and

her pregnancy. Bacterial vaginosis may weaken the flexible line of defense leading to pelvic infections, premature rupture of membranes or preterm labor. Treating the pregnant patient with the most effective antibiotic will help her to strengthen her lines of resistance and reestablish her normal line of defense.

Review of Literature

The vaginal ecosystem is the normal line of defense. Lactobacilli, a Gram positive bacilli, dominate other vaginal microorganisms to maintain a healthy genital tract through maintenance of pH and generation of antimicrobial hydrogen peroxide (Overman, 1993). Eschenbach and Mead (1992) reported that 96% of normal women were found to have peroxide-producing lactobacilli. Vaginosis is an imbalance of this ecosystem associated with decreased numbers of lactobacilli and increased Gram-negative organisms. The normal vaginal ecosystem may be influenced by the menstrual cycle, pregnancy, menopause, contraceptive methods, douching, use of antibiotics, disease, stress, frequent intercourse, and trauma.

Lactobacilli control the lower genital tract by two mechanisms, primarily by producing a by-product called lactic acid. It is thought that conversion of glycogen from vaginal epithelial cells creates lactic acid (Overman,

1993). Lactic acid produces an optimal acidic environment that limits the growth of microorganisms requiring an alkaline environment to survive. The second feature is the production of hydrogen peroxide by the lactobacilli. Peroxidases are found in white blood cells, mucus, and vaginal secretions, and halides are found in cervical mucus (Overman, 1993). Hydrogen peroxide, peroxidase, and halide are normally present in the healthy female genital tract. Together they create a environment toxic to many potential pathogens.

According to Reynolds (1991), Gardner and Dukes were first to identify bacterial vaginosis in 1955. Initially it was called *Haemophilus vaginalis* due to its appearance like the *Haemophilus* genus. Until this time, clinicians called the infection "nonspecific vaginitis". Over the years, it has assumed several other names as more information unfolded as to the particulars of the infection and criteria for diagnosis. When the organism resembled the genus *Corynebacterium* rather than *Haemophilus*, the name changed to *Corynebacterium* vaginalis (Reynolds). Anaerobic vaginitis was another descriptive name given due to the high levels of Gram-negative anaerobes (Ament & Whalen, 1996). Probably the most recognized name is *Gardnerella vaginalis* (named for its discoverer, Gardner). The current

term is bacterial vaginosis or BV.

All the organisms associated with bacterial vaginosis are found normally in the vagina. In women with BV, the normal vaginal ecosystem is altered from one with high concentrations of hydrogen peroxide producing lactobacilli to one with high concentrations of Gram-negative anaerobes and other bacteria (Freeman, 1995). These bacteria can increase 100 to 1000 fold over what they would be normally (Hillier, 1995). Bacteria can include *Bacteroides* species, *Mobiluncus species*, *Gardnerella vaginalis*, and *Mycoplasma hominis*. Anaerobes produce amines such as putrescine and cadaverine which raise the pH to an alkaline level, promoting overgrowth and causing an unpleasant odor (Handsfield, 1992).

Bacterial vaginosis is a noninflammatory response to the change in the vaginal ecosystem. Women will quite frequently have no symptoms of infection. Reported symptoms can include frothy, watery, milky gray or yellow homogenous discharge. Often, a characteristic foul fishy odor is present also (Moore & Freda, 1998).

Diagnosis of BV can usually be made with microscopic examination of vaginal secretions during a clinical visit. The test is easy, inexpensive, and accurate. Two slides are prepared with one drop of vaginal discharge on each.

Each slide is examined at 10X and 40X. The first sample is mixed with normal saline. In BV, clue cells, coccobacilli adhering to squamous epithelial cells, give them a "peppered" appearance. Lactobacillus, normally visible in abundant numbers, are greatly reduced or absent. A drop of 10% potassium hydroxide (KOH) is added to the second slide. Potassium hydroxide volatilizes the amines, putrescine, and cadaverine giving off a fishy, ammonia-like odor. These same amines are found in rotting fish. This odor is present in 90% of BV infections (Eschenbach & Mead, 1992).

Due to the likelihood of an alkaline environment with BV, pH should also be done to confirm the diagnosis. Bacterial vaginosis generally has a pH greater than 4.5. Normal vaginal pH is between 3.0 and 4.0. Gram staining is another option if the diagnosis is inconclusive. Vaginal secretions are rolled onto a glass slide and heat fixed or air dried. The smear is then stained with Gram stain by the usual Gram stain procedure. Bacteria that remain purple are Gram positive and those which stain red are Gram negative. Vaginal cultures, although more expensive, can also be done.

The origins of bacterial vaginosis are not well understood. Although there is an increased incidence in women with multiple sex partners, it is not considered to

be sexually transmitted. Young girls and virginal women have been diagnosed with BV. Other risk factors may include low socioeconomic status, frequent douching, increased parity, smoking, young age, Black race, frequent intercourse, and condom use (Morales et al, 1994). A study in Milwaukee reported 33% of pregnant adolescents tested positive for BV (Ament & Whalen, 1996). Hauth and coworkers (1995) reported that Black women had nearly three times as much BV as white women. The use of intrauterine devices also increases the risk of infection.

"How does *Gardernella vaginalis* get into the uterus during pregnancy?" Two theories are suggested. The first explanation is that the bacteria are already present in the uterus prior to pregnancy. This colonization often causes an asymptomatic endometritis. The infection remains low key until the membranes adhere to the decidual lining of the uterus at about 20 weeks gestation, sealing the uterus closed (Goldenberg & Andrews, 1996). The second theory is that lower genital tract bacteria ascend through the cervical canal to the uterus. Novy et al.(1995) stated that organisms associated with BV have been recovered from the amniotic fluid in 5-20% of women in preterm labor with intact membranes.

Elevated by-products of BV such as vaginal or cervical

endotoxin, mucinase, sialidase, and interleukin-A1 are thought to produce inflammatory cytokines (Hillier et al. 1995). Arachidonic acid metabolites called eicosanoids are also produced (Novy et al. 1995). Eicosanoids are involved in the biosynthesis of prostaglandins and leukotrienes. Women with cervical dilation and amnionic infection have higher levels of cytokines and prostaglandins (Novy et al.). The role of prostaglandins in cervical dilatation and effacement has been well documented (Reynolds, 1991). It has been suggested that inflammatory cells produce proteases which may overpower mucous membranes and weaken the connective tissue strength of the chorioamnion and cervix (Novy et al.). The connective tissue is an example of the flexible line of defense. The weakened state can lead to premature rupture of placental membranes or cervical dilatation.

Metronidazole has been the drug of choice for the treatment of BV since the 1980s. It is a member of the imidazole class of antibacterial drugs. Metronidazole is believed to reduce its nitro group under anaerobic conditions which leads to cytotoxic products that interfere with the DNA and kill the bacteria (Murphy & Jones, 1994). More than half of the drug is broken down in the liver. This breakdown produces metabolites that also kill

bacteria. Lactobacilli are not affected by the drug, which allows the vaginal ecosystem to return to normal. Peak serum levels of 20-25 ug/ml are achieved in one to three hours unless taken with a meal (Peppercorn, Shelley, & Sobel, 1993). Serum half-life varies from 6 to 12 hours. Metronidazole passes through the placenta and can be found in fetal tissue and amniotic fluid (Murphy & Jones). It is also found in breast milk in concentrations equal to serum levels (Murphy & Jones). Side effects may include gastrointestinal upset, nausea, metallic taste, vaginal burning, sleeplessness, headache and ataxia. Metronidazole should not be used concomitantly with disulfiram (Antabuse) which can cause respiratory depression, cardiovascular collapse, arrhythmias, myocardial infarction, acute heart failure, seizures, unconsciousness, or death.

Many clinicians are reluctant to use metronidazole during pregnancy due to questions regarding possible carcinogenic and teratogenic effects. Metronidazole was shown to be nonteratogenic in rats, mice, and guinea pigs and carcinogenicity has never been reported in humans (Burtin, Taddio, Ariburnu, Einarson, & Gideon, 1995). A meta-analysis performed by Burtin et al. (1995) reported that the use of metronidazole in pregnant women does not

appear to increase teratogenicity. Burtin et al. reviewed all medical literature published on metronidazole use during pregnancy since its release in 1959. Thirty-two articles were found that reported original data. Oral metronidazole or a combination of oral and vaginal metronidazole was used for treatment courses lasting 7 to 10 days. Comparisons were made between treatment in the first trimester and treatment during the third trimester when dysmorphologic development cannot occur (Burtin et al.) Three criteria were developed to be included in the meta-analysis: (1) at least 10 women exposed to metronidazole during the first trimester of pregnancy; (2) at least 10 women not exposed to metronidazole or only during the third trimester; (3) all malformations observed in live-born infants reported in each group (Burtin et al.). Seven out of the 32 studies met all three criteria for meta-analysis. Studies ranged from 13 to over 1000 exposed women. None of the odds ratios detected a significantly increased risk of birth defects among infants with exposure to metronidazole in the first trimester. The overall odds ratio of exposure versus no exposure during the first trimester was 0.93. There was no increased teratogenic risk found (Burtin et al.) The Centers for Disease Control (CDC) and Prevention agrees with these

meta-analysis findings (1998). Metronidazole is the preferred drug of choice in the treatment of BV in pregnancy according to the CDC. Metronidazole eradicates anaerobes through the activity of its hydroxy metabolite.

McDonald, O'Loughlin, Vigneswaran, Jolley, and McDonald (1994) conducted a randomized, double-blind, placebo controlled study of metronidazole treatment in pregnant women with BV. Diagnosis was made with the use of direct smears and low vaginal vault cultures. The antenatal clinic screened 2606 women for BV at 16-24 weeks gestation. Twenty-eight percent (739) tested positive for BV. Due to exclusions such as refused consent, age less than 17, antibiotic therapy for vaginal discharge in the preceding 2 weeks, allergy to metronidazole, placenta previa with bleeding, premature rupture of membranes, multiple gestation, and diabetes, the final sample size was 135 women. Sixty-six with BV were treated with medication and 69 were in the control (placebo) group.

Chi-square with Yates correction was used to test the differences between the metronidazole group (n=66) and the control placebo group (n=69). McDonald et al. (1994) also calculated the odds ratio and 95% confidence intervals. Sequential allocation from a list of random numbers, in blocks of 16 was used for randomization to the control the

and experimental group. Metronidazole effectively suppressed BV in 43% of pregnant women compared with 25% in the placebo group ($p<.05$). The odds ratio was 0.12 and the confidence interval was 0.03-0.4 (McDonald et al.)

Hauth et al. (1995) found similar results in their research. Over 5000 pregnant women were screened to participate and a total of 624 were enrolled. Both groups of women had similar characteristics such as weight, parity, compliance, age, weeks of gestation, and Black race. Of the 624 participants, 433 received metronidazole and 191 received the placebo. A blocked randomization schedule in a ratio of 2:1 was used (two women treated with metronidazole for every one woman assigned to a placebo). Similar diagnostic tests used by McDonald et al. (1994) were performed to confirm BV. The same tests were repeated two to four weeks after treatment was completed. T-test, chi-square, and Fisher's exact tests were used to analyze the data. Follow-up cultures on the group treated with metronidazole showed a 25.6% decreased incidence of BV. Initially, 40.7% had BV whereas 15.1% had BV post treatment ($p <.001$). The placebo group only had a 2% decrease. Initially, 45.6% had BV and 43.6% tested positive after treatment (p .71).

Morales, Schorr, and Albritton's (1994) research

supports the previous study. Research methods and diagnosis of BV were similar. Eighty pregnant women were enrolled in a double-blind study. Forty-four women were treated with 250 mg of metronidazole orally, three times daily, for seven days; and 36 women were given a placebo. Demographic variables were comparable between the treatment and the control group. This study did not re-culture the pregnant women. It compared the number of hospital admissions for preterm labor, gestational age at delivery, birth weight, and premature rupture of membranes.

Data were analyzed with t tests and Chi-square tests. Hospital admissions, low birth weight, and premature rupture of membranes were shown to be statistically significant with a $p<.05$. Admissions for the metronidazole group were 27% vs 78% for the placebo group. Birth weight less than 2500 g was 14% for the metronidazole-treated group vs 33% for the placebo group. Premature rupture of membranes occurred in 5% of the metronidazole group vs 33% in the placebo group.

Clindamycin is also effective against anaerobic bacteria associated with BV and is not contraindicated in the first trimester. Clindamycin is a semisynthetic antibiotic produced by a 7(S)-chloro-substitution of the 7®-hydroxyl group of the parent compound lincomycin. It is

excreted by the liver and kidneys.

McGregor et al. (1995) conducted a prospective, controlled trial on the use of oral clindamycin in pregnant women. The study included 1138 pregnant women who were divided into two groups. The first group (559) was enrolled at the initial prenatal visit before 22 weeks gestation. The second group (579) was followed beginning between 22 and 29 weeks. BV was diagnosed in 30.9% of the women in group 1 and 33.6% in group 2 (p=.4) McGregor et al. Variables such as maternal age, ethnic background, marital status, parity, diabetes, and antenatal bleeding were similar for both groups. Diagnosis was made through microscopic examination and vaginal cultures. Oral clindamycin, 300 mg, twice daily was given to women testing positive for infection. Test of cure cultures were done between 22 and 29 weeks gestation.

Descriptive statistics and logistic regression were used to examine the effects of the risk factors. Women in both groups treated with oral clindamycin showed a cure rate of 92.5% at the 2 to 4 week follow-up visit (McGregor et al. 1995). Treating BV in the second trimester reduced the risk of premature labor to 25%. A woman with BV and a prior preterm delivery has a risk of premature delivery of 46.2%; p=.1, relative risk 0.54, 95% confidence interval

0.2 to 1.3).

The Centers for Disease Control released treatment guidelines for bacterial vaginosis in January, 1998. Recommendations include screening and treating high risk pregnant women early in the second trimester. High risk women are those who have delivered premature infants. Low risk women do not need to be screened unless they are symptomatic. Centers for Disease Control (1998) treatment guidelines for high risk pregnant women are as follows:

Recommended: Metronidazole 250 mg orally, three times a day for 7 days

Alternative: (1) Metronidazole 2 grams orally, in a single dose or (2) Clindamycin 300 mg orally, twice daily for 7 days

Treatment guidelines for low risk pregnant women are as follows: *Recommended:* Metronidazole 250 mg orally, three times a day for 7 days

Alternative: (1) Metronidazole 2 grams orally, in a single dose or 2) Clindamycin 300 mg orally, twice a day for 7 days or (3) Metronidazole gel, 0.75%, one full applicator (5g) intravaginally twice a day for 5 days (pp. 70-74)

Metronidazole doses have been lowered from the previous 500 mg dose to limit drug exposure to the fetus. Also, the

use of clindamycin vaginal cream in pregnancy is no longer recommended due to the possible link with increased preterm deliveries.

Summary and Implications for Study

Numerous research studies have shown that BV increases the incidence of premature rupture of membranes and preterm labor. Treatment of BV with oral metronidazole, vaginal metronidazole, or oral clindamycin greatly reduces the percentage of ruptured membranes and/or preterm labor. Limitations of the previous studies include no comparison of metronidazole vs clindamycin nor comparison of oral vs vaginal route in the pregnant patient; therefore, it is not known which drug and method of administration is most beneficial to the pregnant woman.

Research Question

The purpose of this study was to examine the relationship between the type of drug treatment of bacterial vaginosis (oral metronidazole, vaginal metronidazole, or oral clindamycin) in pregnancy in females ages 12 to 43 years old before 16 weeks gestation and the recurrence rate between 35 and 37 weeks, using a retrospective chart review. The goal was to discover if there were a difference in recurrence rates as reported in the charts at 35 to 37 weeks gestation among pregnant women

treated with either of the three treatment regimens. Vaginal clindamycin will not be included in the study because the Centers for Disease Control recommended discontinuing its use in pregnancy (Mead & Eschenbach, 1998). Variables in the study will be the three types of medication (oral metronidazole, vaginal metronidazole, and oral clindamycin) and recurrence rates.

The answer would not only be helpful for health care providers treating BV in pregnancy but would also benefit the patient and fetus. Using the most successful drug could possibly eliminate years of health problems for a neonate born prematurely.

Chapter Three

METHODS

Research Design

This was a descriptive, correlational study using a chart review to examine the relationship between metronidazole (oral or vaginal) or oral clindamycin treatment of BV in early pregnancy (before 16 weeks) and the recurrence rate of BV at 35 to 37 weeks gestation.

A checklist developed by the investigator was used for collecting data from the patient's chart. Problems of response biases are greatly reduced when obtaining data from existing records (Polit & Hungler, 1993). One limitation of this type of data collection is that of assuming all information was assessed and entered correctly into the chart.

A retrospective chart review was used to obtain needed data. Retrospective studies look at events that have already occurred and try to determine what variables contributed to the effect (Talbot, 1995). An advantage is that existing data in the patients chart may be used.

Sample and Setting

Information and data were collected from completed patient charts in an obstetric and gynecology office. Prior written approval to review all charts was obtained

from the office manager (Appendix A). The office is located in a mid western state and currently employs two physicians and five certified nurse midwives. All providers care for pregnant women. The population consists mostly of Caucasians; however, Black, Hispanic, and Indian women are also in this setting. Payer mix is about 50% private insurance and 50% public assistance.

Data collection was done after office hours and on weekends. This provided easier access to patient information and did not interfere with patient flow. No charts were removed from the office. Patient names or identification were not collected to maintain confidentially. Approval for this study was obtained from the Human Research Review Committee of Grand Valley State University (Appendix B).

All patient charts in the office were audited to identify the pregnant patients. Charts from 1532 patients pregnant in 1996, 1997 and 1998 were reviewed for the appropriate information. It was estimated that approximately 4-6 charts could have been omitted if locked in a providers private office although this was against office policy. Patients included in this study were those testing positive for bacterial vaginosis on a routine culture before 16 weeks gestation who then had a routine

culture between 35 and 37 weeks gestation (N=186). Exclusion criteria included diagnosis of vaginal group B beta strepcocci(GBS) infection prior to current pregnancy(not re-cultured routinely at 35 to 37 weeks), delivery before 37 weeks, and identification and treatment of BV between 16 weeks and 35 weeks with current pregnancy. Patients excluded for the above reasons do not have the routine vaginal culture performed between 35 and 37 weeks. Treatment with oral metronidazole, vaginal metronidazole, or oral clindamycin was also a requirement for inclusion. All providers use all drugs listed. All providers used the same laboratory facilities and diagnostic standards.

Instruments

A check list developed by the researcher was used (Appendix C). Checklist categories included: patient number, gestation at first culture, gestation at second culture, culture results before 16 weeks, culture results between 35 and 37 weeks, oral metronidazole use, vaginal metronidazole use, oral clindamycin use, BV recurrence before 35 weeks, and delivery before 37 weeks. Demographic patient information available in the chart such as parity, age, and insurance status were also collected. Each chart was identified with an assigned number.

Chapter 4

RESULTS

This descriptive, correlational study used a chart review to examine the relationship between metronidazole (oral or vaginal) or oral clindamycin treatment of BV in early pregnancy. Statistical analyses were done using SAS statistical software to provide statistics. Statistical analysis was performed through chi-square which is used to assess differences between two or more nominal-level variables (Polit & Hungler, 1993). Differences were considered significant at $p<.05$. Of the 1532 charts reviewed, 271 pregnant women tested positive for BV. Eight-five women were eliminated for the following reasons: initial culture performed after 16 weeks gestation, no drug treatment given with initial diagnosis, different drug treatment used, positive diagnosis of GBS with previous or current pregnancy, preterm delivery, and recurrence of BV before 35 to 37 weeks gestation. After review of the criteria, 186 women were included in the study: 70 (37.6%) treated with oral metronidazole, 56 (30.1%) treated with vaginal metronidazole, and 60 (32.3%) treated with oral clindamycin. The three drug treatment groups did not differ significantly with regard to age, parity, and insurance, as summarized in Table 1. The mean age of women

was 23.9 (standard deviation [SD]=5.48) years with a range of 12 to 43 years. Mean parity was 2.2 (SD=1.17) with a range of 1 to 6. Seventy percent of the study group received medicaid public assistance.

Table 1. Comparison by drug group of women

Drug	*Metronidazole oral (n=70)*	*Metronidazole vaginal* (n=56)	*Clindamycin oral (n=60)*	*Significance*
Age (yrs)	Mean 23.8 SD 6.3	Mean 24 SD 5.4	Mean 23.9 SD 4.3	NS
Parity	Mean 2.2 SD 1	Mean 2.3 SD 1.3	Mean 2.1 SD 1.7	NS
Medicaid	51	41	39	NS
Private Insurance	19	15	21	NS

Table two compares age, parity, and insurance in women who had recurrence of BV between 35 and 37 weeks gestation. Findings were similar to those reported in table one and were not significant.

Table 2. Women with positive BV cultures

	Initial Group	Final Group	Significance
Age (yrs)	Mean 23.9 SD 5.48	Mean 22.3 SD 5.24	NS
Parity	Mean 2.2 SD 1.17	Mean 1.8 SD .71	NS
Medicaid	70	73	NS
PI	30	27	NS

NS = not significant; SD = Standard deviation; PI = private insurance

The recurrence rates for bacterial vaginosis between 35 and 37 weeks gestation were 20% for oral metronidazole, 18% for vaginal metronidazole, and 15% for oral clindamycin. As shown in Table 3, there was no statistically significant difference in recurrence rates of BV at 35 to 37 weeks gestation among pregnant women in the three treatment groups.

Table 3. Culture results at 35 to 37 weeks gestation

	Positive	*Negative*
Metronidazole	14 (20%)	56 (80%)
Vaginal Metronidazole	10 (18%)	46 (82%)
Oral Clindamycin	9 (15%)	51 (85%)

Chi-square = .55; df = 2; p = .76

Chapter 5

DISCUSSION AND IMPLICATIONS

Discussion

This was a study done to examine the relationship between oral metronidazole, vaginal metronidazole, or oral clindamycin treatment of BV in early pregnancy and the recurrence rate near term. Age, parity, and insurance type were comparable in each of the three drug groups. All women in the three test groups were cultured vaginally before 16 weeks gestation and between 35 and 37 weeks gestation. There were 186 women who met the review criteria to be included in this study.

The recurrence rate of BV when tested between 35 and 37 weeks gestation showed no differences when comparing the three drug treatment groups. Twenty percent of the oral metronidazole group tested positive for BV while the vaginal metronidazole group had 18% and oral clindamycin had 15%. Therefore, there was no relationship between the use of oral metronidazole, vaginal metronidazole, and oral clindamycin in the treatment of BV in early pregnancy (before 16 weeks) and the recurrence rate of BV at 35 to 37 weeks gestation. There were no studies found that compared the three drugs used but the findings were comparable to the research studies done by McDonald et al. (1994), Morales, Schorr, and Albritton (1994), and McGregor et al. (1995) as mentioned in chapter two. This study was built

on the previous author's research comparing any two of the drugs mentioned.

Limitations

Retrospective chart reviews help to control bias and increase validity due to the fact that information collection occurs afterward. One limitation to this type of study is the assumption that all information was entered correctly into the medical record. Making the assumption that the patient completed the drug treatment as directed is another limitation. The time frame between vaginal cultures was approximately 20 to 25 weeks. Due to this extended period of time, it would be difficult to determine if the positive BV results at 35 to 37 weeks were due to continuance of the same infection or an acquired new infection of BV. Comparison to findings in other research studies was difficult due to the inability to find studies with similar interests and variables. And, because of the small sample size, this study may not have sufficient power to detect different recurrence rates among the three treatment regimens. Data stating what drug was used in the treatment of BV in patient's who delivered before 35 weeks gestation would have been helpful.

Efforts to control internal validity were as follows: the same two laboratories were used; all patients were cultured at first visit (before 16 weeks); charts were reviewed by one person; the same criteria were used to

determine diagnosis of BV; and, all three groups were evaluated by the same personnel in the same office setting. Bias was decreased because all pregnant women meeting the criteria were included in the study. A limitation to external validity was that there was no control over high-risk behaviors such as frequent intercourse, multiple partners, condom use, douching, and smoking.

Implications

Prevention of preterm deliveries is of utmost importance throughout the world because it will help to save the lives of preterm neonates, improve the health of many children, and save millions of dollars. Numerous studies have shown that BV increases the incidence of premature rupture of membranes, preterm labor, chorioamnionitis, and postpartum endometritis. Early identification and optimal treatment of BV in pregnancy will certainly contribute to the worldwide goals listed above.

Nurse practitioners are frequently the ones providing care to obstetrical patients. Since they often make decisions on whether to treat BV and which medication to use if drug treatment is selected. They have the ability to have a positive influence on the preterm delivery rate. Most practitioners would elect to prescribe the optimal drug in the treatment of BV in pregnancy. Results of this study show little difference in recurrence rates of the

three drugs used. Therefore, decisions about which drug to use in the treatment of BV in pregnancy must be individualized. A patient who appears hesitant to use oral medications might only accept treatment via vaginal route to reduce perceived drug exposure to the fetus. Vaginal metronidazole would be the choice for her. Cost of the medication is also a factor. Generic oral metronidazole averages $12.09 in the local area whereas vaginal metronidazole costs $35.97 and oral clindamycin costs $28.49. A woman's inability to pay for a more expensive prescription could lead to lack of treatment and increased risk of preterm labor, premature rupture of membranes, chorioamnionitis, and endometritis. Many of the reported side effects are similar for all three drugs such as gastrointestinal upset, nausea, vomiting, and abdominal cramps. The use of oral or vaginal metronidazole can also cause a metallic taste and vaginal candidiasis. And, clindamycin has been associated with pseudomembranous colitis (2% to 10%).

Recommendations

Because BV has been associated with increased risk of preterm labor and premature rupture of membranes, further studies on a larger scale are needed to evaluate the effectiveness of drug treatments used in pregnancy. Additional research is needed on BV risk factors such as low income, unmarried, and Black race. Research should

continue to evaluate the risks and benefits of medications to the mother and fetus. More focus needs to be placed on prevention of preterm labor and premature rupture of membranes rather than treatment of preterm labor once it occurs. We need to increase our understanding of BV and its relationship to pregnancy, preterm labor, and premature rupture of membranes.

Finally, we, as nurse practitioners, must remember our training on health promotion and wellness. Educate the woman on risk factors for BV such as frequent change of partners, frequent intercourse, condoms, smoking, and douching. Help her to keep the "rings" of her Neuman System's Model strong to maintain optimal health and wellness. The following are case reviews showing how to maintain a strong Neuman Model.

Patient A is a 28 year old Black female who is 15 weeks pregnant at the time of her initial physical. The NP has diagnosed BV through the routine vaginal culture. Upon interviewing the patient, it was discovered she douched once or twice a week with plain water or a mixture of vinegar and water. Frequent douching is a culturally encouraged practice among Black women in this area. After treatment with oral metronidazole and education on perineal hygiene the infection resolved for the remainder of her pregnancy. This case involved primary, secondary, and tertiary interventions which strengthened Patient A's line

of defense.

Patient B is a 16 year old White female who is 16 weeks pregnant. She also had a diagnosis of BV at her first office visit. Upon interviewing the patient, she reveals a recent change of partners with the occasional use of an unknown type of condom. Due to questionable compliance, a one dose oral metronidazole treatment was given. Education included increasing her awareness of increased BV with partner change and possibly the use of a new type of condom. Counseling on sexually transmitted diseases was also discussed. Treatment and education strengthened the primary, secondary, and tertiary lines of resistence. The return to a normal vaginal ecosystem strengthened the normal line of defense. Decreasing the patients risk factors (frequent partners and change in type of condom) strengthened the flexible line of defense. Patient B had no further episodes of BV during her pregnancy and delivered at 39 weeks gestation.

The selection of which researched drug to use makes little difference in the efficacy rate in treating BV. Education and health promotion consistent with Neuman's beliefs would serve a more valuable service. Helping the pregnant woman to understand her risk factors and the importance of taking her medications as directed by her health care provider, when appropriate, will help to keep her lines of defense and lines of resistence strong to

protect her inner core.

APPENDICES

Appendix A

Grand Valley State University

STANDARD RELEASE FORM

I, [redacted], hereby give permission to the Grand Valley State University, Kirkhof School of Nursing,

_____ 1. To utilize photographs, films, video or audio taped segments of self for educational purposes.

__X__ 2. To copy or reproduce the following material(s) for educational purposes by faculty and/or students within said institution:

age, parity, race, economic status, gestation at 1st culture, culture results, meds used, recurrance of BV, delivery before 32 wks

_____ 3. _____

Date: 9-21-98 Signature: [redacted]

Name Printed: Diane Niederstadt

Institution/Agency: Bay Health Care

Address: 3175 W Professional

City: Bay City

State: MI Zip: 48706

Witness: [redacted] Witness: [redacted]

Date: 9-21-98 Date: 9/21/98

Appendix B

Human Research Committee Approval

GRAND VALLEY
STATE UNIVERSITY

1 CAMPUS DRIVE • ALLENDALE, MICHIGAN 49401-9403 • 616/895-6611

January 19, 1999

Karen Taylor
16661 SE 102 CT Rd.
Summerfield, FL 32691

Dear Karen:

Your proposed project entitled "***Does the Method of Treating Bacterial Vaginosis in Early Pregnancy Affect the Reoccurrence Rate Near Term?***" has been reviewed. It has been approved as a study which is exempt from the regulations by section 46.101 of the Federal Register 46(16):8336, January 26, 1981.

Sincerely,

[redacted]

Paul Huizenga, Chair
Human Research Review Committee

Appendix C

BV Log Sheet

Patient #														
Age														
Parity														
Insurance														
Gest/1st culture														
Culture results														
PO Metronidazole														
Vag. Metronidazole														
PO Clindamycin														
Recurrence <35wks														
Delivery < 37wk														
Culture 35-37wks														

LIST OF REFERENCES

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