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Rationale of Cross-Sectional Descriptive Study on Clinical Effectiveness of Oral Combination Therapy Based on Secnidazole, Azithromycin and Fluconazole in Syndromic Treatment of Abnormal Vaginal Discharge in Kinshasa/DR Congo

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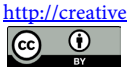
Abstract

Background: Vaginal discharge is one of the most common troubles faced by childbearing age women. About 20% - 25% of women who visit service of gynecology complain of vaginal discharge and leucorrhoea. Management of vaginal discharge in low-income countries generally depends on syndromic approach, which limits the understanding of specific responsible agents. Thus targeted management is based on the identification of causal organism and targeting of therapy against it, while syndromic management is based on presence of high risk factors. Thus the oral combination kit (Azimyn FS Kit®) offers convenience of a one-day treatment compared to other multidose treatments, which will also ensure high patient adherence to treatment, thus increasing chances of desired results. Due to its widespread use, it is proposed to evaluate the effectiveness of this oral association kit therapy in management of vaginal discharge in the population of our milieu in the Democratic Republic of Congo (DRC) particularly those received in outpatient consultation in some medical facilities in city of Kinshasa. Expensive laboratory tests and the associated waiting period for result mean that patient remains without treatment while waiting for test results. Therefore, by adopting a syndromic management approach, patient's eligibility for treatment will be de-



cided based on abnormal vaginal discharge, their characteristics, severity and other presentations symptomatic. This approach will also avoid losing sight of patients during follow-up and will help to reduce financial burden for patients. **Objectives:** To determine the efficacy and safety of oral combination kit therapy containing secnidazole, azithromycin and fluconazole (Azimyn FS Kit®) in syndromic treatment of abnormal vaginal discharge in patients received in outpatient consultation in some medical facilities in the city of Kinshasa; to measure rate of recurrence of abnormal vaginal discharge in these patients. And to identify the adverse effects observed in these patients who received treatment with the combined oral kit containing secnidazole, azithromycin and fluconazole (Azimyn FS Kit®) in outpatient consultation in some medical facilities in the city of Kinshasa. **Methods:** It will be a cross-sectional descriptive study. Sample size will be 319 women of childbearing age who consult the gynecology department with complaint of abnormal vaginal discharge and suspicion of vaginal infection, who agree to abstain from sex during treatment and who have given their written consent to use their personal and/or health data in the study. **Conclusion:** A study on clinical efficacy of oral combination therapy based on secnidazole, azithromycin and fluconazole is beneficial.

Keywords

Combination Therapy, Syndromic Treatment, Abnormal Vaginal Discharge

1. Introduction

Vaginal discharge is one of most common and nagging problems facing women of childbearing age. About 20% - 25% of women who visit gynecology department complain of vaginal discharge and leukorrhea. Although, in some cases, discharge may be a physiological increase in normal vaginal secretion, in more than 60% of cases it is due to infection of the vagina and/or cervix [1].

This is second most common problem after abnormal uterine bleeding. It is a neglected health problem, most often caused by vulvovaginal candidiasis, trichomonas and bacterial vaginosis [2].

Thus, infectious vaginal discharge can be classified as vaginitis or mucopurulent cervicitis. Vaginitis is mainly caused by bacterial vaginosis, vaginal candidiasis, vaginal trichomonas, etc. Mucopurulent cervicitis is due to chlamydia or gonococcal infection. Targeted management is based on identifying causal organism and targeting therapy against it, while syndromic management is based on presence of high risk factors [3].

It is important to report that abnormal vaginal discharge is a frequent manifestation of reproductive tract infections, including sexually transmitted infections (STIs) and vulvovaginal candidiasis. It is also a manifestation of bacterial vaginosis, prevalence of which can reach 50% in women of childbearing age. Reproductive infections are associated with a range of reproductive health problems

and increase risk of contracting HIV [4].

WHO has introduced syndromic management to help control STIs in resource-poor countries. This needs to be adapted to local contexts taking into account prevalence of various agents responsible for STIs. This led to a need to validate the algorithm. Study aimed to correlate syndromic vaginal discharge management algorithm with the etiological diagnosis based on laboratory investigations. Specifically, sensitivity, specificity and positive predictive values of syndromic management compared to a baseline diagnosis were evaluated [5].

Trichomoniasis, a disease caused by *Trichomonas vaginalis*, is most common non-viral sexually transmitted infection in world. The importance of its diagnosis lies in its ease of transmission and the absence of symptoms in most cases, as happens in men, who have an important role as asymptomatic carriers. The most commonly used diagnostic methods are fresh examination of vaginaTl or urethral secretions and molecular techniques. However, as they have some disadvantages and, at times, low sensitivity, new diagnostic methods for trichomonas are needed [6].

And vulvovaginitis is a common problem in practice of general practitioner. The causes are bacterial vaginosis (BV), Candida infection and sexually transmitted infections (STIs). It is only in case of failure of empirical treatment that a vaginal sample is sent for culture and detection of BV. However, without an essential culture, bacterial pathogens can escape diagnosis. Many molecular tests of VB have recently appeared on the market [7].

Bacterial vaginosis (BV) affects about one-third of women in the United States. Although often asymptomatic, BV infection can have serious health consequences, such as premature birth and pelvic inflammatory disease, and can facilitate the acquisition of sexually transmitted infections [8].

Indeed, *Trichomonas vaginalis*, vulvovaginal candidiasis, bacterial vaginosis are most common causes of pathological vaginal discharge. Thus, all women with vaginal discharge should receive treatment for these infections [9].

Vaginal discharge is often polymicrobial and treatment of a single cause or the most apparent cause can lead to a flare-up and clinical manifestations of the other cause. Thus, it is important to treat vaginal discharge as a syndrome rather than as most clinically apparent cause or disease [10].

In syndromic management, diagnosis and treatment are not based on a specific disease based on tests, but rather on syndromes, that is, a group of clinical outcomes in the patient. Treatment is usually given for most diseases that could cause this syndrome [11].

The oral combination kit (Azimyn FS Kit) offers convenience of a one-day treatment compared to other multidose treatments, which will also ensure high patient adherence to treatment, hence increasing chances of desired results.

Due to its widespread use, it is proposed to evaluate the effectiveness of this oral association kit therapy in management of vaginal discharge in population of our setting in Democratic Republic of Congo (DRC) particularly those received

in outpatient consultation in some medical facilities in the city of Kinshasa.

2. Objectives

- Study the clinical effectiveness of the oral combination kit containing secnidazole, azithromycin and fluconazole (Azimyn FS Kit®) in syndromic treatment of abnormal vaginal discharge in patients received in outpatient consultation in some medical facilities in the city of Kinshasa.
- To comprehensively determine the efficacy and safety of oral combination kit therapy containing secnidazole, azithromycin and fluconazole (Azimyn FS Kit®) in the syndromic treatment of abnormal vaginal discharge in patients received in outpatient consultation in some medical facilities in the city of Kinshasa.
- Measure rate of recurrence of abnormal vaginal discharge in these patients.
- To identify the adverse effects observed in these patients who received treatment with combined oral kit containing secnidazole, azithromycin and fluconazole (Azimyn FS Kit®) in outpatient consultation in some medical facilities in city of Kinshasa.

2.1. Rationale for Study

The goal is to evaluate the effectiveness and safety of treatment of abnormal vaginal discharge in repeated use of the oral kit in population of DR Congo in general and more particularly those who consult ambulatory in some structures of city province of Kinshasa also because of the expensive laboratory tests and waiting period associates for results patient remains without treatment pending the results of the tests therefore by adopting a syndromic management approach we can easily tell the eligibility of patient for treatment will depend on abnormal vaginal discharge of their features of their gravites and other symptomatic presentations so a syndromic approach allows reduction of financial burden for patient and avoids loss of patients during follow-up.

2.2. Study Methods

Study Type: cross-sectional descriptive.

Sample size: calculated according to the formula below:

$$n \geq \frac{Z^2 \cdot p \cdot q}{d^2}$$

Z: confidence coefficient for a 95% confidence threshold.

p: expected proportion 29.4% [12].

q: 1 − p.

n: minimum size.

d: degree of accuracy (=0.05).

n: great than or equal to 319.

After incorporating these elements into the formula, minimum size of our sample (n), taking into account those lost to follow-up, abandoned or unsatis-

factory data, will be 319 women, which will be included in the study.

2.3. Inclusion Criteria

- Women of childbearing age who consult gynecology department with complaint of abnormal vaginal discharge and suspicion of vaginal infection.
- Patients who agree to abstain from sex during treatment.
- Patients who have given their written consent to use their personal and/or health data in the study.

2.4. Exclusion Criteria

- Patients with contraindications or allergy to any of the active ingredients of combined kit.
- Pregnant and breastfeeding women.
- Women with a history of STIs in the previous month.
- Patients living with HIV.
- Women with intrauterine contraception devices.
- Patients who have received any type of vaginal discharge medication in past two weeks.

2.5. Variables of Interest

1) Socio-demographic and anthropometric variables: age, marital status, parity, weight, height, number and type of abortion, education level, economic status, body mass index (BMI) calculated from weight and height.

Information on sociodemographic and anthropometric variables, and medical-surgical and gynecological history were obtained during the anamnesis of women in consultation.

2) History: menstruation, parity, pregnancy, abortion, ATCD STI patient and partner.

3) Clinical parameters: type of vaginal discharge, severity of vaginal discharge.

4) Treatment parameter: clinical improvement; tolerance to treatment, adverse reaction, recurrence,

5) Other symptoms: pruritus, dyspareunia, hypogastralgia, urinary symptoms.

2.6. Procedure

Study is to be conducted for two months (October 2023-November 2023) in some medical facilities in city of Kinshasa, in particular: University clinics of Kinshasa; Kinshasa Reference General Hospital, Saint Joseph Hospital; King Baudouin Hospital, Barumbu Mother and Child Center, Ngaba Mother and Child Center, Bumbu Mother and Child Center, Elvic St andré Clinic.

After written consent, for each patient admitted to study, collection of information (sociodemographic data, history and clinical data) will be done by interview during the outpatient consultation (visit 1). After diagnosis of presumption based on the appearance and abundance of abnormal vaginal discharge and as-

sociated symptoms, patient will be put on one-day treatment with Azimyn FS kit containing fluconazole 150 mg 1 tablet, azithromycin 1 g 1 tablet and secnidazole 1 g 2 tablets. A first appointment after treatment will be given after one week for a clinical evaluation to note if clinical improvement as well as tolerance of treatment. A second appointment after two weeks will note if recurrence.

2.7. Expected Results of the Study

In this study we aim to determine the efficacy and safety of combination oral kit treatment, measurement of the recurrence rate of abnormal vaginal discharge in patients who have benefited from treatment and thus identify the adverse effects observed

2.8. Statistical Considerations

Data will be entered using Microsoft Excel 2013 software and exported to an SPSS 22.0 database for analysis.

Descriptive statistics such as calculation of proportions, mean and standard deviation will be used.

For normally distributed parametric data, comparison of averages will be made using Student t test or the ANOVA test as appropriate. And comparison of proportions will be made using Pearson's Khi-square test or Fisher's Exact test.

2.9. Ethical Considerations

This project was submitted for consideration to the Ethics Committee of School of Public Health of the University of Kinshasa. Already, we note that drug used hasalready been subjected to clinical trials and obtained marketing authorization Congolese, it is not about the to do it again, but rather to obtain evidence of its effectiveness in our environment, the majority of which have limited resources, in the absence of means for paraclinical exploration.

For all patients included in study, prior written and informed consent will be obtained and signed by the patient herself. This consent will be translated into lingala (local language) to facilitate comprehension. Patient will be informed of voluntary nature of study. She will receive a copy of consent form and the investigator will receive another.

For treatment purposes, patient names and phone numbers will be required in order to retrieve them if necessary. To ensure confidentiality, this information will be filled in on a coupon that will bear same number as rest of gestant's research documents. After being filled out, this coupon will be immediately separated and kept under seal by lead investigator alone. No other reference will be made to this coupon outside of processing purposes.

3. Discussion

Vaginal discharge is a major problem faced by women of reproductive age [1]. Their management in low-income countries generally depends on syndromic

approach, which limits the understanding of specific causative agents. Targeted management is based on identifying causative organism and targeting therapy against it, while syndromic management is based on presence of high-risk factors [2] [3]. The valuable laboratory tests and the associated waiting period for result cause patient to remain without treatment while awaiting test results [4]. Thus the oral combination kit (Azimyn FS Kit) offers convenience of one-day treatment compared to other multi-dose treatments, which will also ensure high patient compliance to treatment, thus increasing chances desired results [13]. Our study aims to evaluate the effectiveness of this oral combination kit therapy in the management of vaginal discharge in population of our environment in the DRC.

Several studies have recognized the effectiveness of a single dose treatment in management of abnormal vaginal discharge [14]. All of these studies demonstrated the effectiveness of a single dose treatment compared to multidose treatments. Furthermore, all of these studies only used a single molecule, effective only for certain types of germs. We therefore judge that a therapeutic combination may be more effective because abnormal vaginal discharge is often polymicrobial and treatment of a single cause or most apparent cause can lead to a flare-up and clinical manifestations of the other cause.

There is an abundant literature which concludes that *Trichomonas vaginalis*, vulvovaginal candidiasis, bacterial vaginosis are most common causes of pathological vaginal discharge. This leads to evidence that all women with vaginal discharge should receive treatment for these infections. On the other hand, expensive laboratory tests and the extended waiting period remain an obstacle to initiating targeted treatment, hence the importance of a therapeutic combination that is effective on all these germs. We believe that combined kit including Azythromycin, Fluconazole and Secnidazole could fulfill this role [15] [16].

All these points will be addressed during our study.

Strengths of the Study

1) Although it seems obvious treatment of abnormal vaginal discharge with the oral combination kit is effective no wide-ranging study has ever been conducted in our environment.

2) This study is therefore first to want to determine the efficacy and safety of this combined oral kit on such a large sample.

3) Prospective nature of study makes it possible to record all data and to follow up in real time.

4. Conclusion

A study on clinical efficacy of oral combination therapy based on secnidazole, azithromycin and fluconazol in syndromic treatment of abnormal vaginal discharge in Kinshasa is beneficial in determining management of this major problem of women and to make up for lack of study in our middle.

Authors' Contributions

MAM and MFM are the main investigators. MAM generated and designed study. MFM participated in study design and will be actively involved in data collection. DMNRW, LAJ, NFM, MEPL, NBK, NNL, BJL, OCN and MRM contributed to drafting and improvement of manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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