Compliance and Treatment Outcomes of Various Regimens for Trichomoniasis in Trinidad & Tobago

Aruna Kumari Divakaruni [1,*], Bisram Mahabir [1], F.A.Orrett [2], Sneha Rao Adidam [3], Srikanth Venkata Adidam [3], Chalapathi Rao Adidam [3] and Srinivas Divakaruni [4].

[1] Consultant, Queens Park Counseling Center and Clinic, Ministry of Health, Port of Spain, Trinidad and Tobago
[2] Consultant, South West Regional Health Authority, Trinidad and Tobago
[3]Faculty of Medical Sciences, The University of the West Indies, St. Augustine, Trinidad & Tobago.
[4] Epidemiologist, MBBS, DCH, MPH, (PhD Epidemiology)

Corresponding Author: Dr. Srinivas Divakaruni, sdivakaruni@umass.edu

Abstract:

Background: Trichomoniasis is the most common non-viral STI globally and yet is not a reportable disease. Trichomonas Vaginalis is an important source of reproductive morbidity and may increase risk of acquisition and transmission of HIV. WHO and CDC recommend various regimens of Nitro-Imidazoles for treatment. The common Nitro-Imidazoles used for Trichomoniasis are Metronidazole and Tinidazole, which vary in their cost, efficacy and side effect profile and it is relevant to study these factors, for better management of the patients.

Objectives: This study aims to compare and study the efficacy, compliance of various treatment regimens, their outcomes and side-effects for Trichomoniasis, among STI clinic attendees in Trinidad.

Methods: A clinical trial study was designed and after obtaining the informed consent a routine clinical examination was conducted and the swabs for Trichomoniasis tests were collected for diagnosis from the 692 participants. Out of 692 participants, Eighty two (82) patients with established diagnosis of Trichomonas infection were quasi-randomly treated using different regimens. Compliance to treatment, side effects and outcome were evaluated.

Results: The prevalence of the Trichomoniasis in population attending our STI clinic is 11.9% and prevalence of HIV is 9%. Of the total 82 participants for the treatment, 80% were females; nearly 90% of the patients belonged to age group 15-45 years and over 60% were below 30 yrs. Among those diagnosed for Trichomonas vaginalis, 13.3% had associated HIV infection. The compliance with respect to single dose treatment was significantly better than the long duration oral regimen and has significant relation with side effects of the treatment. The outcome is generally better and comparable and shows no significant difference between different treatment regimens used in the study.

Conclusions: Metronidazole and Tinidazole are commonly used drugs in various regimens. compliance is better with those treated with Tinidazole and Metronidazole stat, than with other groups. Outcome is comparable between these regimens, especially when combined with other important factors like abstinence and treatment of the partners. The treatment regimens mainly differ in the compliance and side effects profile, which suggests that to improve the compliance the drugs with less side effects, short course regimen would be a preferred choice.

Keywords: Trichomonas Vaginalis; Compliance; Treatment; STIs; HIV; Cost-effectiveness

1. Introduction

Trichomoniasis is a highly prevalent, treatable, non-viral STI of worldwide importance and is the most common curable STI. According to the World Health organization's fact sheet, it is estimated that more than 143 million cases of Trichomoniasis occur annually worldwide[i] almost half of all curable sexually transmitted diseases worldwide might be attributable to T vaginalis[ii]. The estimated incidence in normal population is approximately 10%. Trichomoniasis has been considered one of the most common sexually transmitted diseases due to prevalence rates of 15% or higher among women in many developing countries[iii]. Despite being a readily diagnosed and treated STD, trichomoniasis is not a reportable infection and control of the infection has received

relatively little emphasis from public health STD control programs. *T. vaginalis* infection is associated with two- to threefold increased risk for HIV acquisition, preterm birth, and other adverse pregnancy outcomes among pregnant women[iv] [v] [vi]

Trichomoniasis is commonly treated with Metronidazole and Tinidazole drugs. These drugs belong to the 5-Nitro-Imidazoles drug family with 95% cure rate for TV. The guidelines as per The WHO and US CDC include:

1) MNZ or TNZ 2 gm single dose
2) MNZ 400-500 mg BID 7 days dose

Furthermore, if a patient fails a single dose of MNZ therapy, 7 day dose of MNZ or even single dose TNZ can be administered[vii].

Nitro-Imidazoles are inexpensive and short treatment regimens are as effective as longer treatment regimens which makes treatment of individual cases or even large-scale interventions quite feasible in under-resourced areas[3], but medication resistance for above drugs is a worldwide concern. Also, failure to treat partners shows a lack of therapeutic success.

In one study, Tinidazole was found to be more effective than metronidazole although the study quality of this comparison was not optimal(ref).

The incidence and prevalence rates have not been clearly and reliably established in Trinidad and Tobago especially in the high-risk population. There are no published reports about prevalence of this disease in the Caribbean Islands. Trichomoniasis causes significant morbidity, psychological stress and economic burden on the community and its association with transmission of HIV has cost implications in terms of time and money to the individual or the government. In this study our aim is to compare the drug efficacy, the compliance and outcomes of various treatment regimens, for Trichomoniasis in the high risk populations of Trinidad & Tobago.

Aim of the study: To study and describe the drug efficacy, drug compliance, treatment outcomes and side effects of various regimens for Trichomoniasis in high risk populations of Trinidad & Tobago.

2. Materials and Methods

Study design: The study is a quasi-experimental clinical trial design combined with cross sectional survey method which is more appropriate to estimate the prevalence of an STI through laboratory conformation. Patients were recruited at the public STI disease clinic, Queens's Park Counseling Center and Clinic (QPCC&C), Ministry of Health, Trinidad and Tobago. A convenience sample with consecutive sampling is used to recruit all males and females who were eligible, if they are over 15 years of age or had sexual exposure and consented for routine genital examination. Informed consent was obtained from all the patients recruited in the study. In the case of minors (persons below the age of eighteen), informed consent was obtained from the parent or guardian. At the time of obtaining consent, the participant was given the required information regarding the purpose of the study, treatment options, confidentiality and rights and responsibilities.

Sample size: Sample size was calculated based on precision and estimated prevalence. Considering the estimated prevalence of Trichomonas among high risk population is 20% and precision of 3% (for disease prevalence >10%), then the largest sample size needed for Trichomonas would be 683. The current study included a sample 692 participants in total which is slightly more than the estimated value of 683[viii].

Data collection: A questionnaire that was prepared, tested, revised and approved by Medical Ethics Committee was administered to collect the clinical data. Following a routine clinical examination, the samples were collected for laboratory testing. Vaginal/Urethral swabs were collected– one for wet mount preparation of T.V; and one for In Pouch culture; and other two (2) for OSOM Rapid test/and Fluorescent antibody testing and HIV testing. When laboratory test results were positive for Trichomonas Vaginalis, the patients were treated according the treatment guidelines. After discussing treatment options with the patients, they were categorized into four (4) groups based on their most acceptable treatment regimen by quasi-random method.

- Group I Metronidazole 2g stat PO,
- Group II - Metronidazole 400mg bid for 7 days,
- Group III with Tinidazole 2g stat PO,
- Group IV Topical Vaginal Metronidazole gel/cream bid for 7-10 days.

Metronidazole is relatively cheap and is widely available in public health institutions in Trinidad. Tinidazole is comparatively more expensive and is less widely available. The patients who received treatment were re-evaluated clinically upon follow up with emphasis on drug compliance, side effects, abstinence, treatment of the partner(s) and efficacy by testing for organisms. Patients were asked to return seven and 14 days after the start of therapy; and all those returned for follow up were tested for TV organisms with repeated tests as above. Compliance to treatment, side effects and outcome were evaluated. The patients who did not return for follow up and test of cure were interviewed over telephone about the clinical response and side effects.

Treatment failure was considered when reappearance of Trichomonas within 14 days of the start of treatment in a patient who denied sexual contact.

Reinfection was defined as reappearance of Trichomonas in a patient who admitted further sexual contact. *Recurrence* was treatment failure plus reinfection.

Those who failed to return for follow up were contacted for assessment of response. Contact tracing was done on a few patients and partners of T.V positive patients also were treated.

Results were documented and statistical analysis was done with the help of SAS software version 9.4. Simple frequencies and descriptive statistics were applied. The different treatment regimens used were compared using Chi Square test and correlation studies, further confirmed by linear regression. The p-value was considered significant at < 0.05.

3. Results

The results of the study of treatment regimens in patients with trichomoniasis are given below: 82 patients with established diagnosis of Trichomonas infection were treated using different regimens. Among these 82 patients, who were treated for Trichomonas, the majority of 80% were females. It was also observed that nearly 90% of the patients belonged to age group 15-45 years and over 60% were below 30 years of age. Among those diagnosed for Trichomonas vaginalis, 14.6% had associated HIV infection.

Table 1. below compares the demographic variables like sex, age and HIV positivity in the participants of the study.

variable	Sub-category	Trichomoniasis positive (N=82)		Trichomoniasis negative (N=610)	
		Frequency	Percent	Frequency	Percent
Sex	Male	17	20.7	249	40.8
	Female	65	79.3	361	59.2
Age (in Years)	5-14	0	0	9	1.5
	15-24	33	40.2	243	39.8
	25-34	27	32.9	197	32.3
	35-44	18	22	83	13.6
	45-54	3	3.6	59	9.7
	55-64	1	1.2	15	2.4
	>65	0	0	4	0.7
HIV	Positive	12	14.6	51	8.3
	Negative	70	85.4	559	91.7

Table 2. Comparison of different treatment options for trichomoniasis who were treated.

Variable	Metronidazole 2g stat PO;	Metronidazole 400mg bid for 7 days;	Tinidazole 2g stat PO;	Metronidazole Vaginal gel/cream gel/Twice daily/1 week.
No. of cases (N=82)	18	36	22	6
Drug compliance	100%	61.1%	100%	33.3%
Abstinence	33.3%	36.1%	27.27%	16.67%

Cure rate	94.4%	97.2%	90.9%	100%
Side effects	55.6%	50%	31.8%	0%
Nausea	38.9%	27.8%	13.7%	0%
Vomiting	22.2%	30.6%	4.6%	0%
Anorexia	16.7%	13.9%	9.1%	0%
Metallic Taste	44.4%	25%	2%	0%
Abdominal cramps	5.6%	13.9%	0%	0%
Loose stools	0%	3%	0%	0%
Headaches	5.6%	13.9%	0%	0%
Rash	0%	5.6%	0%	0%

Table 2 compares different groups who received treatment upon diagnosis of Trichomoniasis. Various parameters evaluated are listed in the first column. Drug compliance was poor for Group 2 and Group 4 and metallic taste was prominent with Group 1 (Metronidazole 2g stat). There was no statistically significant difference for other side effects like nausea, vomiting, anorexia, headache, rash, and treatment outcome. Overall results were better with those treated with Tinidazole and Metronidazole stat for drug compliance than with other groups as expected.

Table 3.

Statistics	Correlations (Probability)		
	Treatment vs side effects	Treatment vs compliance	Compliance vs side effects
Chi-square	0.0566	0.0867	<0.0001
Mantel-Haenszel Chi-Square	0.0114	0.0699	<0.0001
Fishers exact test	0.0004	<0.0001	<0.0001
Mante-carlo estimate for the exact test	0.0519	0.0721	<0.0001

Table 3 shows correlations between Treatment, side effects and drug compliance. The correlation between drug compliance and side effects of the treatment were more significant, although Fisher's exact test shows all the 3 correlations were significant in the study.

The above correlations were further confirmed with Linear regression, where drug compliance was considered as the dependent variable on side effects and treatment modality. The model as shown in table 4a and 4b shows the relation between side effects and drug compliance in the study is statistically significant.

Table 4a:.

Analysis of Variance					
Source	DF	Sum of squares	Mean square	F Value	Pr > F
Model	4	32.26141	8.06535	5.97	0.0003
Error	77	103.9825	1.35042		
Corrected Total	81	136.2439			

Table 4b. Simple linear regression.

Parameter Estimates						
Parameter		**DF**	**Estimate**	**Standard error**	**t Value**	**Pr > |t|**
Intercept		1	2.666667	0.474416	5.62	<.0001
treat	1	1	-0.50545	0.568307	-0.89	0.3766
treat	2	1	-0.23824	0.530202	-0.45	0.6544
treat	3	1	-0.33343	0.542179	-0.61	0.5404
treat	4	0	0	.	.	.
seffect	1	1	-1.19019	0.272267	-4.37	<.0001
seffect	2	0	0	.	.	.

Table 5 below shows the drug efficacy as (absolute risk= negative events/total events or Trichomoniasis negativity/Total patients) negative tests percentage and frequency in treated patients. The negative tests are based on combined results of Trichomoniasis rapid test, wet mount test, culture (in pouch). Even if one test is positive the combined results were considered as positive and when all the 3 tests were negative the tests were considered as negative.

Table 5.

Absolute Risk (AR)	**Metronidazole 2g stat PO;**	**Metronidazole 400mg bid for 7 days;**	**Tinidazole 2g stat PO;**	**Metronidazole Vaginal gel/cream gel/Twice daily/1 week.**
Drug efficacy percentage (AR)	94.4	97.2	90.9	100
Drug efficacy frequency	17/18	35/36	20/22	6/6

4. Discussion

Nitro-Imidazoles are the mainstay in the treatment of trichomoniasis. Metronidazole is the most commonly used drug worldwide and is widely available. Presently different options are available for the treatment of Trichomoniasis. It may be noted that over the years there has been gradual reduction in the duration of treatment with a single dose of metronidazole or Tinidazole giving satisfactory results.

The current study compares various treatment regimens used in Trichomoniasis. It compares the efficacy of various strategies for the treatment of Trichomoniasis particularly, short versus long oral treatment regimens, compliance and side effects. The overall efficacy of treatment options for oral Nitro-Imidazoles were satisfactory and compares well with other studies. The cure rates ranged from 90-100% and similar cure rates were observed by Csonka (1971), Woodcock (1972) and Morton, Sawyer et al (1976) [ix] [x] [xi] [xii] [xiii]. There was no significant difference between the oral Nitro-Imidazoles treatment options[xiv]. Although fewer numbers of cases were studied, the efficacy of vaginal application of metronidazole was comparatively high. The results of few previous studies have reported that vaginal application and its effectiveness is unsatisfactory and undefined[13].

We observed that the compliance with respect to single dose treatment was significantly better than the long duration oral regimen and vaginal application. Advantage of this would be that patient receives the drug under supervision or has less risk of missing the dose that may occur with long duration regimen. The single dose administration is an advantage in the treatment of outpatients and also convenient for patients and their partners[xv] [xvi].

Side effects of oral Nitro-Imidazoles are previously well documented. They include a bitter metallic taste, nausea, and vomiting, a disulfiram-like reaction with ingestion of alcohol and

dizziness. Despite the low doses required for treatment of trichomoniasis, side effects occur in more than half of patients, especially with the metronidazole 2 g dose. This research study reports that 40-55% of patients receiving oral Nitro-Imidazoles had side effects. The common side effects were of gastrointestinal origin and comprised of metallic taste, nausea, vomiting and anorexia. Metallic taste was more significant with single oral dose of metronidazole than long duration oral Metronidazole or Tinidazole. Overall, other side effects were more prominent with Metronidazole than Tinidazole and compares well with reports and reviews. Some of the studies state that Tinidazole is curative at lower doses than metronidazole. The therapeutic doses of Tinidazole result in fewer and milder side effects[xvii xviii xix]. In our study the final tests showed comparative response with Metronidazole and Tinidazole. The main difference between different treatment regimens is observed in drug compliance and side effect profile.

It is estimated that perhaps as few as 20% of partners receive treatment[xx]. Majority of the Trichomonas positive patient partners were treated in our study through contact tracing protocol. Failure to treat partners may lead to apparent lack of therapeutic success and, because trichomoniasis is a sexually transmitted infection (STI), treatment of sex partners must be part of the treatment regimen of infected participants. Contact tracing should be undertaken and all resulting sexual contacts attending should be treated for *Trichomonas vaginalis* regardless of the results of their investigations.

Treatment Failure: Only two cases were found to be non-responsive to treatment. They were confirmed to be drug compliant and followed abstinence for the required period. This problem was seen with long duration treatment by Metronidazole. Treatment failure in some patients prescribed the five-day course may have been due to failure to take the treatment as directed. Some cases classed as re-infections may have been due to treatment failure[xxi xxii]. Metronidazole resistance is an emerging problem, but its clinical importance is not yet clear[xxiii xxiv].

There is conflicting data on the use of metronidazole during pregnancy. Some studies claim possible teratogenicity and other adverse effects like prematurity, however others deny the association[xxv xxvi]. Vaginal application of Metronidazole can be used in those who were pregnant or possibly pregnant and in those who preferred the method.

Cost effectiveness of various regimens: Nitro-Imidazoles are inexpensive (the mean cost of generic Tinidazole is $0.04/500 mg tablet, or, $0.16 for a typical 2 gm dose)[xxvii]. This feature, combined with the fact that short treatment regimens (typically single dose) are highly effective, make treatment of individual cases or even large-scale interventions quite feasible in under-resourced areas[xxviii xxix xxx]. Tinidazole stat is more cost effective compared to other treatment regimens for the sponsor but outcome is not greater than other regimens. Cost effectiveness is not an important factor for the patients in this trial because the medicines were sponsored by government.

Strengths and weaknesses: Convenient sampling method was used in recruiting the TV patients because it is a practical and cheaper way of recruiting study participants and uses an existing infrastructure such as clinic facilities and staff. This is further supported by the fact that this study establishes TV prevalence in high risk population coming to STI clinic and did not try to attempt TV prevalence in the general population. The power of the study calculated is good for high prevalence in the STI clinic participants. The study chose a quasi-experimental method in placing the participants according to their choice in treatment groups because we considered strict experimental method is unethical, especially when there were previous evidence showing the difference in side effects of treatment options and followed patients' choice. This resulted in unequal number of participants in treatment groups, but did not affect the quality and power of the study as shown in the statistics.

Conclusion: Trichomoniasis is the most common non-viral STI globally and it is not a reportable disease. Trichomonas Vaginalis is an important source of reproductive morbidity and may increase risk of acquisition and transmission of HIV. The Nitro-Imidazoles are the only class of antimicrobial medications known to be effective against *T. vaginalis* infections. Of these drugs, metronidazole and tinidazole are commonly used in various regimens. In this study, overall results were comparable in those treated with Tinidazole and in other groups. Side effects of medication

were more prominent with Metronidazole than Tinidazole. Tinidazole is more expensive than Metronidazole and it is not widely available. Only two cases were found to be non-responsive to treatment. The association between drug compliance and side effects of the various medication were confirmed in our study. To make the patient more compliant with treatment, it is always better to use the drug with less side effects and of shorter regimen.

Funding: We sincerely thank National AIDS Coordination Committee (NACC), Trinidad and Tobago for supporting and funding this research project.

Competing interests: None declared

Ethical approval: The study was approved by Medical Ethics Committee, Ministry of Health, Port of Spain. Informed consent was obtained from all the patients recruited in the study. In the case of minors (persons below the age of eighteen), informed consent was obtained from the parent or guardian. At the time of obtaining consent the participant was given the required information regarding the purpose of the study, confidentiality and rights and responsibilities.

Acknowledgments: We are grateful for the participation of patients, clinicians, and laboratory staff of Queens Park Counseling Center and Clinic, Ministry of Health, Port of Spain, Trinidad. We thank Mr. Steve Lalman, The University of the West Indies, St. Augustine for providing laboratory support and Ms. Alesha Howe Phillip for the assistance in data management and preparation of the document.

References

[i] WHO. Fact sheet on Sexually Transmitted Infections (STIs), August 2016. Available at http://www.who.int/mediacentre/factsheets/fs110/en/ (accessed on 10 January 2018)

[ii] Bickley LS, Krisher KK,Punsalang A Jr, Trupei MA, Reichman RC,Menegus MA. Comparison of direct fluorescent antibody, acridine orange, wet mount, and culture for detection of Trichomonas vaginalis in women attending a public sexually transmitted diseases clinic. Sex Transm Dis. 1989 Jul-Sep; 16(3):127-31

[iii] Schmid G. Trichomoniasis treatment in women: RHL commentary (last revised: 28 July 2003). The WHO Reproductive Health Library; Geneva: World Health Organization.

[iv] McClelland RS, Sangare L, Hassan WM, et al. Infection with Trichomonas vaginalis increases the risk of HIV-1 acquisition. J Infect Dis 2007;195:698–702.

[v] Van Der Pol B, Kwok C, Pierre-Louis B, et al. Trichomonas vaginalis infection and human immunodeficiency virus acquisition in African women. J Infect Dis 2008;197: 548–54.

[vi] 2015 STD Treatment Guidelines https://www.cdc.gov/std/tg2015/trichomoniasis.htm

[vii] Kissinger BMC Infectious Diseases (2015) 15:307:

[viii] Daniel WW, editor. 7th ed. New York: John Wiley & Sons; 1999. Biostatistics: a foundation for analysis in the health sciences.

[ix] Csonka, G. W. Trichomonal vaginitis treated with one dose of metronidazole. British Journal of Venereal Diseases. 1971; 47: 456-458.

[x] Woodcock, K. R. Treatment of trichomonal vaginitis with a single oral dose of metronidazole. British Journal of Venereal Diseases 1972; 48: 65-68

[xi] Morton, R. R. Metronidazole in the single-dose treatment of trichomoniasis in men and women. British Journal of Venereal Diseases.1972; 48: 525-527

[xii] Sawyer, P. R., Brogden, R. N., Pinder, R. M., Speight, T. M., and Avery, G. S. Tinidazole; A review of its anti-protozoal activity and therapeutic efficacy. Drugs. 1976; 11: 423-440

[xiii] Nancy Malla, Indu Gupta, Mahajan RC. Human Trichomoniasis. Indian Journal of Medical Microbiology.2001; 19 (1): 6-13

[xiv] Krieger JN and Alderete JF. Trichomonas vaginalis and trichomoniasis. In: K. Holmes, P. Markh, P. Sparling et al (eds). Sexually Transmitted Diseases, 3rd Edition. New York: McGraw-Hill, 1999; 587-604

[xv] Garber GE. The laboratory diagnosis of Trichomonas vaginalis. Can J Infect Dis Med Microbiol. 2005 Jan–Feb; 16(1): 35–38.

[xvi] Ann Kurth, William L. H. Whittington, Matthew R. Golden, Katherine K. Thomas, King K. Holmes, and Jane R. Schwebke. Performance of a New, Rapid Assay for Detection of Trichomonas vaginalis. J Clin Microbiol. 2004 July; 42(7): 2940–2943

[xvii] H Swygard, A C Seña, M M Hobbs, M S Cohen. Trichomoniasis: clinical manifestations, diagnosis and management. Sex Transm Infect 2004; 80:91-95

[xviii] Nobuo Kawamura. Metronidazole and tinidazole in a single large dose for treating urogenital infections with Trichomonas vaginalis in men. British Journal of Venereal Diseases.1978; 54: 81-83

[xix] Sarah L. Cudmore, Kiera L. Delgaty, Shannon F. Hayward-McClelland, Dino P. Petrin, and Gary E. Garber. Treatment of Infections Caused by Metronidazole-Resistant Trichomonas vaginalis. Clinical Microbiology Reviews.2004, October; Vol. 17, No. 4: 783-793

[xx] H Swygard, A C Seña, M M Hobbs, M S Cohen. Trichomoniasis: clinical manifestations, diagnosis and management. Sex Transm Infect 2004; 80:91-95

[xxi] Ann Kurth, William L. H. Whittington, Matthew R. Golden, Katherine K. Thomas, King K. Holmes, and Jane R. Schwebke. Performance of a New, Rapid Assay for Detection of Trichomonas vaginalis. J Clin Microbiol. 2004 July; 42(7): 2940–2943

[xxii] OSOM® Trichomonas Rapid Test [package insert]. Cambridge, MA: Genzyme Corp; 2004

[xxiii] Schwebke JR. Trichomoniasis care today: A clinician's guide to timely diagnosis and successful treatment. Genzyme Monograph, 2004 Available at www.screenmed.pl/pdf%20files/Trichomonas_Monograph.pdf.

[xxiv] Ann Kurth, William L. H. Whittington, Matthew R. Golden, Katherine K. Thomas, King K. Holmes, and Jane R. Schwebke. Performance of a New, Rapid Assay for Detection of Trichomonas vaginalis. J Clin Microbiol. 2004 July; 42(7): 2940–2943

[xxv] Schmid G. Trichomoniasis treatment in women: RHL commentary (last revised: 28 July 2003). The WHO Reproductive Health Library; Geneva: World Health Organization.

[xxvi] Spence MR, Hollander DH,Smith J,McCaig L, Sewell D, Brockman M. The clinical and laboratory diagnosis of Trichomonas vaginalis infection. Sex Transm Dis. 1980; Oct-Dec 7(4): 168-71

[xxvii] Bickley LS, Krisher KK,Punsalang A Jr, Trupei MA, Reichman RC,Menegus MA. Comparison of direct fluorescent antibody, acridine orange, wet mount, and culture for detection of Trichomonas vaginalis in women attending a public sexually transmitted diseases clinic. Sex Transm Dis. 1989 Jul-Sep; 16(3):127-31

[xxviii] OSOM® Trichomonas Rapid Test [package insert]. Cambridge, MA: Genzyme Corp; 2004

[xxix] Schmid G. Trichomoniasis treatment in women: RHL commentary (last revised: 28 July 2003). The WHO Reproductive Health Library; Geneva: World Health Organization.

[xxx] W. David Hager, MD; Stuart T. Brown, MD; Stephen J. Kraus, MD; George S. Kleris, MD; Goldie J. Perkins, MS; Musetta Henderson, RN. Metronidazole for Vaginal Trichomoniasis Seven-Day vs Single-Dose Regimens. JAMA 1980; 244(11):1219-1220.