

# "VALUE OF FLAGYL IN THE TREATMENT OF TRICHOMONIASIS"

( Final Evaluation Report )

By

S. S. NARANG<sup>1</sup>, N. C. BHARGAVA<sup>2</sup>, B. K. CHOHAN<sup>3</sup>, M. SESHAGIRI RAO<sup>4</sup>.

The efficacy of Flagyl, a derivative of Nitroimidazole in the treatment of human Trichomoniasis was recently reported by various authors in other countries. In India, only two studies appear to have been conducted and published.<sup>5,9</sup> Before adopting Flagyl (May & Baker) as a routine method of treatment for Trichomoniasis, the V. D. Training Centre, Safdarjang Hospital, New Delhi started a research scheme to evaluate the efficacy of the above drug under local conditions. The objectives of this study were as follows :

1. To establish the value of oral treatment of Trichomoniasis with Flagyl (May & Baker) derivative of Nitro-imidazole, both in the male and female patients.
2. To study the various methods used for the diagnosis of trichomoniasis, viz. culture, smears examination etc.

## MATERIAL AND METHODS

180 cases of trichomonal infection (155 females and 25 males) established by examination of vaginal, urethral or prostatic discharge for T. V. during the year have been included in the present study. In 18 cases, T. V. was negative in Smears but was detected by culture.

Before starting the research study all the procedures have been standardised by designing various forms and work schedules for guidance in clinical, laboratory and epidemiological aspects including follow-up of TV cases. Details of clinical conditions at the time of first attendance have been entered on cards and proformas specially designed for the purpose.

All patients were given a routine blood test ( STS ) and Smear examination for Gonococci.

In males the condition of the urethral adnexa was noted which also included the prostatic examination. In all cases, Urine sediment and prostatic fluid was examined for TV.

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" From Venereal Diseases Training and Demonstration Centre, Safdarjang Hospital, New Delhi-16.

1. Pathologist & Incharge.
2. Junior Medical Officer.
3. Assistant Research Officer,
4. Statistician.

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A total and differential blood count was also done before starting the treatment and after the course of Flagyl.

The dosage of Flagyl employed was 200 mgm by mouth three times daily for 7 days both in male and female cases. Only one day's tablets (3) were given to patients except during the intervening holidays and no local treatment was given during the course. In all cases emphasis was made on examination of marital and extra-marital partners and sexual relationship was prohibited during the therapy and for 3 months. During treatment all cases were examined for discharge by dark-field on alternate days and after treatment once a week for a month, and once a month for another 2 months. In the latter part of the study, culture for trichomonas vaginalis was also done as a test of cure.

### RESULTS

The data are included in the following tables :-

TABLE I.

Showing sex distribution of 180 patients of T. V. Infection, who attended the V. D. Training Centre, Safdarjang Hospital, New Delhi during 1962-63.

Sex	No.	Percent
Male	25	14.0
Female	155	86.0
Total	180	100.0

It can be seen from table I that out of 180 total cases 25 (or 14%) were males and 155 (or 86%) were females. The proportion of trichomonal infections in males and females was 1:6 in the group of patients included in this study.

TABLE 2.

Showing the Age Sex distribution of 180 patients of T. V. infection who attended the V. D. Training Centre, Safdarjang Hospital, New Delhi during 1962-63.

Age Group	Sex				Total	
	Males		Females		No.	%
	No.	%	No.	%		
12-17	—	—	4	2.6	4	2.2
18-22	1	4.0	49	31.6	50	27.7
24-29	7	28.0	45	29.0	52	28.9
30-35	7	28.0	39	25.1	46	25.5
36-41	4	16.0	12	7.7	16	8.9
42-47	2	8.0	1	0.6	3	1.7
48 & above	4	16.0	5	3.2	9	5.0
Total	25	100.0	155	100.0	180	100.0

Table 2 shows the age and sex distribution of the patients included in the study. 60% of the males were in the age group 18-35. The corresponding percentage for females was 86%. 84% of the total patients were between age 18-35 which is sexually more active period.

TABLE 3.

*Showing sex and Marital Status of 180 Patients With TV Infection Who Attended V. D. Training Centre Safdarjang Hospital, New Delhi During 1962-63.*

Marital status	Male		SEX Female		Total	
	No.	%	No.	%	No.	%
Single			2	1.3	2	1.1
Married	23	92.0	149	96.1	172	95.6
Widowed	2	8.0	4	2.6	6	3.3
Total	25	100.0	155	100.0	180	100.0

From Table 3 showing the sex and marital status of patients included in the study, it can be seen that all the male patients were married. Of the 155 female patients, 149 females (or 96.1%) were married and living with husbands. 4 patients (or 2.6%) were widows and 2 patients (or 1.3%) were single patients.

TABLE 4.

*Showing the Duration and Complaints of 25 Male Patients of Trichomonas Urethritis.*

Complaints	Duration				No.	Total %
	1 Week	1-3 Month	3-6 Month	1 Year		
Discharge	2	2	—	5	9	36
Burning Micturitions	2	1	1	6	10	40
Ulcer with STS + Ve	7	—	—	—	7	28
Ulcer with STS-Ve	2	—	—	—	2	8
Asymptomatic	1	6	—	—	1	4

Table 4 shows the duration and complaints of 25 male patients. It can be seen that burning micturition of one year's duration was the commonest symptom and was present in 40% of the patients. 36% of the patients gave history of discharge. 28% of the patients has ulcers with positive serological test for syphilis. 4% of the cases were asymptomatic.

TABLE 5,  
Showing Duration and Complaints of TV Patients (Females)

Complaint	Months			Years			Total	
	1 Week	1-3	3-6	1st	2nd	3rd & more	No.	%
1. Discharge	10	19	13	22	17	24	105	67.7
2. Burning Micturition	3	6	5	7	7	5	33	21.3
3. Itching	3	6	9	11	9	7	45	29.0
4. Dysparunia	-	-	2	-	-	-	2	1.3
5. Ulcer with STS+ Ve	4	-	-	-	-	-	4	2.6
6. Ulcer with STS-Ve	2	-	-	-	-	-	2	1.3
7. Back-ache	-	-	3	-	-	1	4	2.6
8. Asymptomatic	-	-	-	-	-	2	21	13.6

Table 5 shows the duration and complaints of 155 females patients with TV infection. It can be seen that in 67.7% of females, discharge of different duration, was the commonest symptom. Burning micturition and itching were stated by 21.3% and 29% of the female patients respectively. A few cases gave a history of dysparunia, backache, ulcer with and without positive STS. 13.6% of the cases were asymptomatic.

TABLE 6,  
Showing the Appearance of Vagina in 155 Cases of TV

Appearance	No.	Percent
Diffuse redness of vagina	72	46.4
Strawberry appearance	8	5.1
Cx. Erosion	19	12.3
Cx. Congestion	37	23.9
Normal Vagina & Cx	24	15.5

Table 6 shows the appearance of vagina in 155 female cases. In 72 cases (or 46.4%) diffuse redness of vagina was observed. Strawberry appearance was seen in 5.1% of the patients. The Cervix was congested in 37 cases (or 23.9%) of the patients. Erosion of the cervix was noted in 12.3% of the patients. Vagina and Cervix were normal in 24 cases (15.5%) of the patients.

TABLE 7,  
Showing type of Discharge in 114 Patients with TV.

Type of discharge	No.	Percent
White and thick	39	34.7
Yellow frothy	54	46.7
Creamy yellow	21	18.6
Foul Smelling	46	40.4

Table 7 shows the type of discharge in 144 patients in the study. The discharge was white and thick in 34.7% of the patients. It was yellow and frothy in 46.7% of the patients. Creamy yellow discharge was noticed in 18.6% of patients. The discharge was foul smelling in 40.4% of the patients.

The amount of discharge in 124 patients is shown in table 8.

TABLE 8.

*Showing the Amount of Discharge in 124 TV Cases.*

Amount of discharge	No.	Percent
Slight (+)	25	21.9
Moderate (++)	44	38.6
Profuse (+++)	45	39.5

TABLE 9.

*Showing the Associated Diseases in 155 Cases of TV.*

Associated diseases	Males No.	(25) Percent	Females No.	(155) Percent	Total No.	(180) Percent
STS Positive	4	16.0	32	20.6	36	20.0
Gonorrhoea	2	8.0	5	3.2	7	3.9
Moniliasis			2	1.2	2	1.1
Chancroid	4	16.0	1	0.6	5	2.8
Impetigo			1	0.6	5	0.6

The associated diseases in male and female patients are given in Table 9.

STS was found reactive in 16.0% of the males and 20.6% of the female patients. Gonorrhoea was found in 8% of the males and 3.2% of the female patients. Moniliasis was noticed in 1.2% of the patients. Chancroid was diagnosed in 16% of the male patients and in females only one case out of 155 patients was seen.

14 wives of the 25 males have been brought for examination and all were found to be TV positive. 5 were STS positive.

TABLE 10.

*Showing defaulters During the Treatment.*

Time of default	Males 25	Females 155	Total 180
After one day	—	1	1
After 2 days	—	3	3
After 3 days	1	1	2
After 4 days	—	5	5
After 5 days	1	3	4
After 6 days	—	—	—
Total	2	13	15
Percent	8.0%	8.4%	8.3%

The defaulters during the period of treatment are included in table 10. 8.3 percent of the cases defaulted during the seven days period of treatment. There is no appreciable difference between the two sexes for defaulting.

TABLE 11  
*Showing the Duration & Surveillance of 25 Male Patients.*

Duration	No. followed	Successful TV-VE	Failure TV positive
1 Week	23	21	2
2 Week	23	23	—
3 Week	22	21	1
4 Week	18	14	4
2 Months	17	16	1
3 Months & over	17	17	—
Total	25		8

The period of surveillance and the result of treatment in male cases is shown in table 11 and it can be seen that the treatment was successful in 21 cases giving a primary cure rate of 91.3%. Treatment was termed as primary cure when TV were not seen in the smear or culture immediately upto one month after the completion of 7 days treatment. 18 cases have been followed up and in 4 cases, TV were seen in the smears. After 3 months, out of 17 cases that have been followed up, no case was seen with TV by darkfield. Upto 2 months, 8 cases can be considered as treatment failures probably due to either relapse or reinfection. In spite of the fact, that the patients have been advised to avoid sexual exposure, we cannot emphatically say whether the above 4 cases were due to relapse or reinfection.

TABLE 12  
*Showing Results of Treatment and Duration of Surveillance of 142 female TV Cases.*

Duration	No. followed	Successful (TV Negative)		Failure (TV-Ve)	
		No.	%	No.	%
1 Week	142	139	97.9	3	2.1 (Retreated after 3 months)
2 Week	123	123	100.0	—	—
3 Week	115	115	100.0	—	—
4th Week	103	99	96.1	4	4.9
2 Months	74	68	91.9	6	8.1
3 Months	63	56	88.9	7	11.1

Table 12 shows the results of Treatment and duration of surveillance of 142 female cases.

After one week, the treatment was found to be successful in 139 out of 142 cases, giving an immediate cure rate of 97.9%. After one month, out of 103 cases

that were followed up 4 showed T. V. in Smears and might be considered as treatment failures (3.9%). After 2 months, out of 74 cases that were followed up, 6 cases showed TV in Smears. 7 cases (or 11.1%) were observed as failures out of 63 cases followed for 3 months. As expressed earlier, it is difficult to say whether these cases are due to relapse of reinfection.

TABLE 13

*Showing Side Reaction of 17 Patients of TV Infection Treated With Flagyl*

S. No.	Reactions	No.	Per cent
1.	General Weakness	2	11.7
2.	Loss of appetite and	6	35.1
3.	Giddiness	6	35.1
4.	Palpitation	2	11.7
5.	Dyspepsia	1	5.8
6.	Vomiting	3	17.4
7.	Itching all over body	1	5.8

The side reactions have been shown in table 13. Most of the symptoms were vague and even these were present in 17 patients or 9.4% of the total patients. It is possible that all reactions might not be due to Flagyl therapy.

Out of the 155 female patients included in the study 13 females gave a history of repeated abortion, 16 were pregnant (ranging from 3 to 8 months) and 56 cases were sterile.

A long term follow up of the above 85 cases will enable us to know whether Flagyl is effective in the above condition, in addition to its efficacy for Trichomonal infection. No congenital deformity was noted in the infants born of the mothers who received the drug during pregnancy. 2 patients who were reported as sterile before the therapy, became pregnant.

#### DISCUSSION

An analysis of 831 V. D. Cases diagnosed during 1962 revealed the following. Of the total 178 urethritis cases, 11% of the cases were due to TV and rest were due to Nonspecific infections. The proportion of TV cases among the total VD cases was 13 percent. Out of the 155 females included in the study 96.1% were married, a finding which is in conformity with Menon & Willmott, who reported that 108 cases of 116 total cases were married. This shows that sex life is a major contributory factor in acquiring the trichomonal infection. Trussell<sup>11</sup> also found the

parasitism is uncommon among children and virgins and is most commonly found between the age of 16 to 35, the period of greatest sexual activity.

The most common symptoms observed in the present group of patients were discharge, burning during micturition and itching. 4 percent of the male patients and 13.6 of the female patients were asymptomatic which shows that the persons were carrying infection but at the same time not aware of it.

Menon and Willmott<sup>5</sup> also reported that 10% of the cases were asymptomatic and that 88% of the cases had discharge. In our study 67.7% of the females patients complained of discharge.

Diffuse redness of vagina and cervical congestion have been noticed in 46.4% and 23.9% of the patients. Yellow frothy discharge appears to be common and was observed in 46.7% of the patients. The discharge was white and thick in 34.7% of the patients.

In 16 per cent of the males and 20.6 per cent of the female patients, Blood STS was found to be reactive, thereby indicating syphilitic infection of one stage or the other. 8 per cent of the male and 3.2% of the female patients were found to be suffering from Gonorrhoea. Chancroid was diagnosed in 16 per cent of the males and 0.6 of the females. The patients were treated simultaneously for the associated diseases and in some cases the patients were diagnosed as Trichomonal infection after getting the treatment for Gonorrhoea. Menon and Willmott<sup>5</sup> reported 10% positive serological tests for syphilis and 2% Gonorrhoea in their series.

The routine treatment previously given in the centre for Trichomoniasis was stovarsol Co. Tab. (Intra-vaginal) preceded by alkaline douche daily for 10 days. The above requires the attendance of the patients at the Centre daily for 10 days and also often resulted in many relapses.

By Flagyl therapy, primary failure rate was very low and the patients could be treated on ambulatory basis as the tablets may be taken at home easily without the patients' attending the clinic daily. Trussell<sup>11</sup> in her monograph, discussed the utility of nearly 160 drugs in the treatment of Trichomoniasis and found that with acetarsone, a cure rate of 95% was obtained by local therapy which requires daily attendance or admission of patients.

After one month the percentage of failure was about 6.6% and at the end of two months the failure rate was 7.7%, 17 males and 56 females were followed for 3 months and a failure rate of 8.7% was observed.

The following table shows the percentage of success and failure rates observed by different authors.



TABLE 14.

*Showing Comparative Results of Treatment by Various Authors.*

Author	No. of Cases	No of cases followed up to 3 months	Success No.	Percent	No.	Failures %
Rodin <sup>7</sup>	52	52	43	83	9	17
Walt & Jennison <sup>10</sup>	44	31	25	56.8	6	12
King A. J. <sup>2</sup>	82	52	43	83	9	17
Willcox <sup>11</sup>	34	34	29	85.9	5	14.7
Nicol etal <sup>6</sup>	122	57	40	70.1	17	29.9
Cw. C. Sonke	37	37	34	91.9	3	8.1
Menon & Willmot <sup>5</sup>	100	71	40	56.3	31	43.7
Narang etal	142	63	56	88.9	7	11.1

It can be seen from the above table that our results are in conformity with that of C. W. Sonka.

This low percentage of failure rate can be due to the following factors.

1. The patients were given one day's tablets except for the intervening holidays thereby ensuring the regular intake of the drug.

2. Efforts made to bring contacts of 155 female patients resulted in 140 males attending the clinic. They were given a thorough check up which included examination of urethral smear, urine sediment and prostatic smear for TV and also culture for TV in some cases. 13 cases were found to be positive and they were given a full course of Flagyl therapy simultaneously.

3. All the contacts were also asked to avoid sexual inter-course during the period of surveillance. Out of the 25 males who were infected, 19 contacts have been examined and 14 were found to be TV positive.

This drug showed low toxicity as can be seen from table 13. Some of the symptoms showed therein were vague and may not be attributed as toxic effects of drug.

The importance of performing TV culture can be known by the fact that out of 155 patients, 18 cases were detected by culture but missed by smears. This means that 12% of the cases would have been missed had culture not been done.

17 cases showed moniliasis after treatment whereas before the therapy there were only 7 patients.

18 patients were given more than one course of treatment with Flagyl due to relapse. 10 patients showed a relapse after 4 to 8 weeks. 2 patients relapsed after 14-16 weeks and 3 patients showed a relapse after 5 months to one year.

One patient was treated 5 times with Flagyl in 2 years. She was reinfected at a period of 2 months, 4 months, 7 months and 8 months interval. The husband was treated simultaneously with the 4th course of treatment.

2 patients were given 3 courses. The husband of one case was treated simultaneously with wife at 3rd course. She was followed up for 14 weeks and she showed negative results in the smears. The husband of second case was treated simultaneously at 2nd and 3rd courses. She was followed up for 6 months and showed negative results for TV.

The rest of the cases (12) were given 2 courses and at the 2nd course of the wife, the husbands also were treated simultaneously. Out of these 11 cases were followed up for 3 months and all showed negative TV results in smears. One case did not come for check up.

The above findings show that most of the recurrences were actually due to reinfections by the contacts. Simultaneous examinations of the contact is therefore essential. In Gynaec O. P. D. here most of these cases are treated, such facilities are not available. It is, therefore, essential that in such circumstances the husbands should also be given a course of Flagyl simultaneously to prevent recurrence of symptoms.

#### SUMMARY & CONCLUSIONS

1. 180 patients consisting of 25 males and 155 females all of Trichomonal infections were administered Flagyl 200 mgm orally three times a day for seven days. All cases were thoroughly investigated and established for TV infections. 3.3% of the patients showed immediate failure of treatment. Of 80 patients that were followed up for 3 months, Flagyl was effective in 91.3% of cases. No toxic effect of the drug was observed and this study proved the high efficacy of the drug.

2. T. V. was not seen in smear in 18 cases but was detected by culture. Thus in 12% of cases the diagnosis would have been missed had culture not been done. Only one case was seen where T. V. was negative in culture but present in the routine smear. This might be pure chance. Culture is thus a superior method and should be done as a routine in all clinics dealing with such cases.

3. This study also proved the importance of examining and treating sexual contacts. The high percentage of successful results might have also been due to the above.

4. Majority of the patients were married and in the age group 18 to 35 years.

5. Positive serology was present in 16 percent of male patients and 20.6 percent of females patients. Gonorrhoea was diagnosed in 8 percent of the male patients and 3.2 percent of the female patients.

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