BROXYQUINOLINE AND BROBENZOXALDINE IN THE TREATMENT OF TRICHOMONAL AND MONILIAL VAGINITIS

by

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Introduction

After Donne (1836) discovered T. vaginalis in vaginal discharge, there are about more than 300 preparations tried for its treatment. The incidence of specific vaginitis as quoted by Meigs *et al* (1957) is 15 to 54 per cent in general population survey. DeSa Souza *et al* (1963), Menon *et al* (1962) quote the incidence of T. vaginalis as 17 to 36 per cent in hospital cases. The major advance in the management of T. vaginalis infection was noted when Durel *et al* (1961) introduced oral use of metronidazole (Flagyl) for the first time. This preparation with the exception of other antibiotics is the first oral chemotherapeutic agent used systemically. Its efficacy as reported by Naval Kishore (1965) is 90 per cent in the initial stages and 75 per cent after 3 months, following cessation of the treatment. Menon quotes (1962) cure rate with Flagyl as 56.3 per ce after 3 months and failure rate 43.7 per cent. With such variatic of results of treatment, this combi tion of broxyquinoline and brob zoxaldine was undertaken for clinical efficacy in trichomonal well as monilial vaginitis. This paration has been widely used general medicine in the treatment o mixed intestinal infections, part cularly protozoal infections, li amoebae and giardia lambliae. It action is entirely local and no absorp tion of the drug occurs systemically Therefore, the following study wa undertaken to evaluate the efficacy of this drug.

Material and Methods

From the gynaecological (C Unit outpatient department of S. S. Hospital, Baroda, 75 cases of spe vaginal infections were selected this clinical trial during 1st Sep ber 1965 to 31st August 1966, f period of one year. The tablets topical use were specially prepa Each tablet consisted of 400 m Broxyquinoline and 80 mg. of benzoxaldine with a suitable

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making a total weight of the tablet as 0.5 gm. These compounds are dibromo derivatives of 8-hydroxyquinoline and 8-hydroxyquinaldine respectively.

These cases were clinically examined and diagnosis was established by wet smear study (with saline and potassium hydroxide 10% and 20% preparations). During the treatment the patients were advised to avoid sexual intercourse. Male partners were investigated in cases which failed to respond, by prepuceal swab and prostatic fluid for culture. Use of condom during the follow-up period was advised to three males but only one followed its use.

A pilot study to note the disintegration time of the tablet in vagina was made in 16 cases. These cases had other gynaecological complaints and six of them were pregnant and admitted in antenatal ward for the treatment of anaemia with pregnancy. In 13 cases, the disintegration was 6-24 hours, in 2 cases it was 36-48 hours, and in the remaining one case half tablet was seen in the vagina 15 days following insertion.

On the basis of clinical findings and disintegration time, the schedules of therapy in this study were planned as below:

Initially two schedules were planned. Schedule A consisted of one tablet at bed time daily per vaginam for 7 days in 41 cases. Schedule B consisted of one daily for 7 days as above and one alternate day for 7 days, the total period being 14 days in 34 cases. Schedule C was selected in failure cases of schedules A and B. This schedule consisted of either two or three successive courses of schedules A and B.

These cases were followed up for a period of 4 to 8 months following the completion of the treatment. In the follow-up study, criteria for cure were symptomatic relief, absence of previous physical signs, repetition of wet smear study for 2-3 occasions with weekly intervals. The cases were considered resistant when there was no symptomatic relief, persistence of physical signs and positive wet smear. When wet smear was negative, culture for trichomonas and monilia was done in 3 cases. It was also negative.

The follow-up was done in 47 cases (62.66%). The fall-out rate after initial treatment for unknown reasons was 37.33%.

Analysis of the cases

Age incidence: Sixty-four cases were below 35 years of age, the youngest case being 15 years, and oldest 5 years. Thus, 15-35 years was the frequent age period for these specific infections in this series. There were 54 cases of T. vaginalis, 18 of monilial and 3 were having both.

Symptomatology: Leucorrhoea was the main presenting symptom in 69 cases. The additional symptoms like burning micturition (14 cases), backache (7 cases) and pruritus vulvae (9 cases) were seen less frequently. Association of pruritus vulvae appeared more common with monilial infection than trichomonal, but burning micturition was more often met with trichomonal infection than monilial. The duration of leucorrhoea was 0-6 months in 53 cases,

TABLE 1

Summary of Treatment

Schedule	Total cases	Cured cases	%	Trichomonal Infection			Monilial Infection			Mixed Infection		
				Incomplete treatment	Failure cases	%	Cured cases	%	Incomplete treatment	Failure cases	%	Cured cases	%	Incomplete treatment	Cured cases	%
A.	41	7	22.6	17	7	22.6	3	30	5	2	20	—	—	—	—	—
B.	34	14	60.86	4	5	21.74	5	62.5	2	1	12.5	1	33.33	—	2	66.66

7-12 months in 6 cases and 1-4 years in 10 cases. It was of recent origin in 53 cases. Six cases of specific vaginitis had no complaint of leucorrhoea. In 54 cases of T. vaginalis, 2 were virgins, 37 were non-pregnant, 13 were pregnant and 2 were postmenopausal. In 18 cases of moniliasis, 9 were non-pregnant and the other 9 were pregnant. Three cases of mixed infections occurred in non-pregnant state.

Treatment

The treatment of these cases was planned with schedules A and B as indicated earlier. The results of the treatment with these schedules are seen in Table 1. In trichomonal infection, 31 cases were treated with schedule A of which 17 cases were untraceable. Of the followed up 14 cases, 7 cases were relieved of their symptoms and in the remaining 7 cases symptoms were unaffected. The other 23 cases had schedule B of which 4 cases could not be traced at the time of follow-up. Of the followed up 19 cases, 14 were relieved of symptoms and 5 remained unrelieved.

In monilial infection 10 cases were administered schedule A, and 5 of them could not be traced. Of the followed up 5 cases, 3 were relieved and 2 were unaffected. Remaining 8 cases had schedule B. Two cases were untraceable. In 6 of the followed cases, 5 were relieved of symptoms and 1 failed to do so.

In 3 cases of mixed infection, only B schedule was given. Out of these 3 cases, only one was relieved of symptoms.

Those cases showing unfavourable response to above schedules were given schedule C as mentioned earlier. There were 17 cases treated with schedule C. The results of this treatment are shown in Table 2. There were 12 cases of T. vaginalis, 3 of monilial infection and 2 of mixed infection. Of the 12 cases of T. vaginitis, 5 were cured, 2 cases could not be traced and the remaining 5 remained unaffected. In 3 cases of monilial infection, one was cured, one discontinued treatment and the remaining one failed to respond. Thus, these 8 cases of trichomonal, monilial and mixed infection, showing persistence of these infections following these three schedules, are termed as resistant to this drug. T. vaginalis is more frequent in the resistant group.

TABLE 2

Effect of Schedule C following failure of A & B Schedules.

Type of Infection	Total cases	Cure cases	Cure %	Incomplete treatment	Failure cases	Failure %
chomonal nfection	12	5	29.41	2	5	29.41
nilial nfection	3	—	—	1	2	11.76
ed fection	2	1	5.88	—	1	5.88

TABLE 3

Duration of follow up after completion of the treatment

Duration of follow up	No. of cases	Percentage
0-3 months	32	68.08
4-6 months	11	23.40
7-8 months	4	8.52
Total cases followed up	47	62.66
Fallout cases during schedule 'C'	3	—
Resistant cases	8	17.0
Total cases cured	36	48.0

Follow-up

In Table 3 follow-up results after completion of treatment with all schedules are presented. Out of 47 cases, 43 cases were followed for 3-6 months and 4 cases were followed upto 8 months. Eight cases were resistant to this therapy, out of which 5 were trichomonal, 2 monilial and 1 of mixed infection. Three cases of schedule C could not be traced. Thus, totally cured cases, including all infections were 36. During the earlier follow-up (2-3 weeks) of these cured cases, 7 cases showed positive wet smear. But further follow-up revealed both clinical relief as well as negative wet smear.

Discussion

The incidence of trichomonal, monilial and mixed infection was 24.31 per cent, 12.15 per cent and 1.17 per cent respectively in O.P.D. cases of gynaecological department of S.S.G. Hospital (C Unit), Baroda. It appears that the incidence has wide variations. This may be also due to methods of diagnosis employed in different series. The age distribution of this series is in conformity with those of other reported series. The preponderance of T. vaginalis cases during the child-bearing period substantiates venereal aetiology as proposed by Perl *et al* (1956), Watt and Jennison (1961) and Caterall and Nicol (1960). We have not carried out routine examination of all the male partners whose wives had T. vaginalis. The examination of male partners was carried out in 3 of the 8 resistant cases, and the results failed to detect T. vaginalis in them.

The symptomatology encountered in these cases reveals that in T. vaginalis the accompanying symptoms, like burning micturition, pruritus vulvae and coital discomfort, are less frequently seen. Riba (1957) has described these symptoms as commonly seen. Though there were no asymptomatic cases in this series, 8 per cent of these cases had many vague symptoms but no leucorrhoea. Meigs (1957) believes that these asymptomatic cases may be the carriers of clinical T. vaginitis in future. Moore *et al* (1954) have suggested emotional stress as a precipitating factor responsible to convert asymptomatic carriers into full fledged clinical T. vaginalis infection.

The pregnant patients form 29.33 per cent in this series. But the non-pregnant cases during the child-bearing period form the largest group of the series (65.33 per cent). Incidence of monilial infection in pregnant and non-pregnant cases is equal whereas in T. vaginalis infection pregnant cases comprise one fourth of the cases. This may be due to vaginal acidity which is increased during pregnancy. It is likely that the cases of T. vaginalis occurring during pregnancy are due to different

strains which thrive in increased acidity.

The treatment of T. vaginalis underwent a major evolutionary phase following the systemic use of metronidazole (Durel *et al* 1961). The variable results of therapy with this drug by various authors justify a continued research for newer anti-trichomonal agents. Metronidazole has a number of side-effects like bad taste, nausea, vomiting and abnormal blood pictures as quoted by Hesseltine *et al* (1963). The cost of this therapy is also not within the reach of many hospital patients. Therefore, its widespread use in hospital practice will have limitations. It is also claimed that metronidazole need not be considered totally safe for pregnant cases. This drug passes freely the placental barrier and is excreted in the breast milk (Scott-Graves, 1964). Therefore, its effects on foetus and new-born need further study.

The various drug schedules (Tables 1 and 2) indicate that schedule B gave most satisfactory results. The efficacy of the drug with reference to individual infections is difficult to conclude, the number of cases of each infection being unequal and less. A further study in greater number of these cases (particularly monilial and mixed) is indicated for a thorough evaluation. The institution of different schedules indicates that the response can be obtained in more number of cases. Thus in schedule C the response can be raised by 29.4 per cent in T. vaginalis and 5.8 per cent in mixed infection, though in monilial infection, no change is seen. These cases were studied in detail for any derangement in their carbohydrate metabolism. There was no abnormality of carbohydrate metabolism detected in them.

The percentage of cure with reference to total cases (75) treated (Table 3) is 48.0 and with reference to cases followed (47) is 76.59 per cent. The cure rate thus obtained is almost identical with the reported ones with other drugs. This preparation in addition affords an advantage in mixed infections and monilial vaginitis.

During this study we did not encounter any side-effects of this preparation particularly locally. As the drug is unabsorbed there were no systemic ill-effects observed.

Conclusions

(1) Seventy-five cases of specific vaginal infections were studied with a topical use of combination of broxyquinoline 400 mgs. + brobenzoxaldine 80 mgs. in the form of a vaginal tablet.

(2) Eighty-five per cent (64 cases) of the cases were in the age groups of 15-35 years.

(3) The commonest presenting symptom was leucorrhoea (69 cases).

(4) The therapy was given as in schedules A and B.

(5) The failure cases of A & B schedules were treated by schedule C, thus increasing the cure rate.

(6) B schedule gave most satisfactory results. As regards trichomonal and monilial infections, the cure rates were 60.85 and 62.5 per cent respectively. Since cases of monilial infection were less in comparison with T. vaginalis, the efficacy

of this drug in moniliasis requires further study.

(7) The resistant cases of this series were 17 per cent.

(8) No side-effects of the drug noted.

(9) Further clinical trials with uniform disintegration time of the tablet may help in getting more satisfactory response.

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