Clinical Experimental Obst. & Gynecology
Vol. III, 1-4, 1976 pp. 92-95

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Monotherapy with mepartricin versus combined amphotericin b plus tetracycline in mycotic and protozoal vaginitis

by

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INTRODUCTION

In the last years the etiologic pattern of infectious vaginitis has undergone deep transformations ([6]). In fact mycetes of the Candida genus (*C. albicans*) and protozoa such as *T. vaginalis*, are among the principal pathogenic agents encountered nowadays ([1]).

This evolution depends on several factors, previously unknown or scarcely represented, which favour infectious colonization of the vagina such as the use of hormonal contraceptives ([5, 15]), of anti-inflammatory steroids ([14]) and broad spectrum chemobiotics ([4, 12, 13, 14, 16]).

Other well known factors are chronic endocrinopathies such as diabetes and also pregnancy ([7]). At vaginal level this problem is further complicated by some mechanisms of pathogenic interconversion recently identified. It appears that mycotic infection can coexist with protozoal infection or arise secondarily ([2]), especially if the latter was not adequately treated. In this regard we must point

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out that vaginitis cannot be regarded as « cured » only on the basis of microbiological findings at the end of antibiotic treatment; cure must be confirmed by persisting negativity for 20-30 days afterwards.

We believe that this criterion is even more applicable if we consider that often patients do not closely follow the clinician's directions as to duration of treatment; they in fact discontinue it as soon as the subjective symptoms subside, attending follow-up with a therapeutic gap of some days. In these cases only a delayed culture examination and an accurate anamnesis can differentiate apparently unfavourable results from incorrect application of therapy.

Bearing in mind these points, the problem of whether a « single drug » chemobiotic therapy should be preferred to the use of pharmacologic combinations is of great interest.

Mepartricin, a recently identified polyene antibiotic, is endowed with both antimycotic and antiprotozoal activity ([3,9,10,11]). The drug is more efficacious than amphotericin B against *C. albicans* and only slightly less active than metronidazole against *T. vaginalis*. In vitro findings were confirmed by a wide series of clinical researches also of a controlled type ([8]).

We thought that it would be interesting to carry out a controlled trial of mepartricin in mycotic and protozoal vaginitis as compared to that of a commonly used chemobiotic combination.

MATERIAL AND METHODS

The research was carried out on 68 patients affected with either mycotic or protozoal vaginitis. 8 patients were excluded from overall evaluation as they failed to attend the established follow-up controls.

The patients' mean age was 33.5 ± 2.3 years. Diagnosis of infectious vaginitis was based on anamnestic and clinical objective findings (gynecological and colpocytologic examination in all cases). Etiological diagnosis was established by observation of fresh secretion from the posterior fornix and the vaginal walls, using Trichomonas diluent and Gram staining. Nickerson's medium was used for the identification of mycetes.

Thus 2 homogeneous groups were formed: Group I comprised 31 patients with *T. vaginalis* vaginitis and Group II comprised 29 cases with *C. albicans* vaginitis.

Cases presenting uteroadnexal degenerative or neoplastic processes were excluded from the study. Pregnancy in 16 subjects was not considered a reason for exclusion.

Mepartricin (supplied by SPA, Milan) was administered in the form of one vaginal tablet containing 25,000 Units, to be placed deep in the vagina just before retiring to bed every evening for 15 days. The reference drug, also in the form of vaginal tablets containing amphotericin B and tetracycline, was administered in the same way.

Both treatment were carried out also during the menstrual period.

Each group was divided into 2 sub-groups according to the type of vaginitis and treated as described in table I.

Obviously, group II patients' partners were also treated with metronidazole, by oral route at the usual doses.

In the course of the trial administration of other topical or systemic substances capable of interfering with the treatment was avoided.

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Table 1. *Experimental design.*

Group	Total no. of cases	Subgroups	No. of cases admitted	Dropouts	No. of cases evaluated	Treatment
I *T. vaginalis* vaginitis	34	I_A	17	1	16	Mepartricin
		I_B	17	2	15	Amphotericin B + Tetracycline
II *C. albicans* vaginitis	34	II_A	17	2	15	Mepartricin
		II_B	17	3	14	Amphotericin B + Tetracycline

The results obtained were classified according to the evolution of the microbiological findings as:

« cured » : microbiological negativity at the end of treatment and 30 days afterwards

« not cured » : presence of the infecting agent at the end of treatment

« relapsed » : negativity at the end of treatment and microbiological positivity at follow-up, 30 days afterwards.

Treatment with other chemobiotics was then given to the « not cured ».

Tolerance of the treatments was thoroughly assessed as regards local side effects. Moreover, at the beginning and end of treatment a complete blood test (SGOT, SGPT, RBC/WBC and differential count) and urinalysis were carried out.

RESULTS

The results obtained with each treatment are shown in table 2. In the *T. vaginalis vaginits* group comparison by χ^2 test corrected according to Yates, demonstrated a significant difference in favour of mepartricin ($\chi^2c=4.66$; $P<0,05$). A high incidence of relapses (33.3%) was found with amphotericin B plus tetracycline treatment.

Table 2. *Synthesis of the results.*

Group	Subgroups	Treated and evaluated	Cured	Not cured	Relapsed
I	I_A	16	15	1	–
	I_B	15	8	2	5
II	II_A	15	11	2	2
	II_B	14	10	1	3

In the subjects affected with *C. albicans* vaginitis, statistical analysis showed no significant difference in the results of the two drugs compared; the incidence of relapses was low (13% with mepartricin and 21.4% with the reference drug).

Local and general tolerance was satisfactory for both products also in pregnant women.

CONCLUSIONS

Some interesting considerations can be drawn from this trial.

Mepartricin efficacy in protozoal vaginitis was further confirmed even in vaginal tablet form.

The amphotericin B plus tetracycline combination appeared nearly as active with regard to the microbiological negativity rate at the end of treatment.

However the high incidence of relapses in the group treated with the combination was, in our opinion, the most significant finding. This implies in fact an incomplete disappearance of the agent since it is known that *T. vaginalis* can lie quiescent in the extravaginal structures.

Mepartricin showed to be endowed with an intense and long lasting trichomonacidal action. The results obtained in *C. albicans* vaginitis agree with what already reported in literature on amphotericin B and mepartricin activities. Both these antibiotics are capable of efficaciously counteracting mycotic infection.

However preferential opinion for mepartricin is supported by the possibility to obtain, in monotherapy, more stable results particularly in *T. vaginalis* infections. Its outpatient use is justified by the difficulty to make an etiological diagnosis by microbiological test. In this case a « single drug » broad-range treatment seems, more suitable. Mepartricin fulfils these requirements and obviates the need to choose chemobiotic combinations sometimes not well balanced.

SUMMARY

Mepartricin efficacy was compared to that of an amphotericin B plus tetracycline combination in a controlled trial concerning 68 patients affected with mycotic or protozoal vaginitis.

The two drugs were administered at the dose of 1 vaginal tablet daily for 15 days.

In the patients with T. vaginalis vaginitis mepartricin induced a « cure » rate significantly higher ($P < 0.05$).

In the two groups of subjects with vaginal moniliasis the results obtained were alike.

Tolerance was always excellent.

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