THERAPEUTIC EFFECTS OF TOPICAL BENZYDAMINE IN GYNECOLOGY

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SUMMARY

The study was performed on 124 patients divided into 4 groups on the basis of vaginal smears:

1) 60 patients with mild non-specific bacterial vaginitis;

2) 40 patients with moderate or severe non-specific bacterial vaginitis;

3) 10 patients with moderate or severe monilial vaginitis;

4) 14 patients with moderate or severe trichomonal vaginitis.

Each group was subsequently divided at random into two subgroups, comprising the same number of patients, who were treated under double blind conditions with vaginal douches of 1‰ benzydamine or placebo (1 douching per day for 10 days).

Specific standard therapy with antibiotics, antimycotic and antitrichomonal agents was used concomitantly in groups 2, 3 and 4 respectively.

Vaginal smears, performed a few days after the end of the treatment period, and the improvement in symptoms and signs, demonstrated the curative action of benzydamine in mild non-specific vaginitis as well as its symptomatic effect and potentiation of specific therapy in moderate and severe bacterial, monilial and trichomonal vaginitis.

Many factors (local and general, internal and external) may cause an imbalance in the vaginal flora, favouring the onset of inflammation of the vulva and vagina. Examples of this are endocrine changes, debility states, the indiscriminate use of antibiotics and corticosteroids, mechanical and chemical stimuli (pessaries, contraceptives, spermicides, hypersensitivity to underwear, etc.) ([1, 2, 3, 4]).

In view of this, we decided to study the therapeutic effects of benzydamine, a compound with an anti-inflammatory, analgesic and protective action on the tissues and a mild antimicrobial effect on various bacteria and fungi.

Extensive pharmacological and toxicological investigations have already been conducted on benzydamine (N'N-dimethyl-3-[[1-(phenylmethyl)-1H-indazol-3-yl]oxy]-1-propanamine) which has been shown to have an anti-inflammatory activity and an analgesic action on inflammatory pain ([5,6]). Its anti-inflammatory effect has been attributed to its protective action on vessels, its stabilization of the cell membrane and its selective inhibition of some prostaglandins ([7, 8, 9]). Hence the drug's ability to control the passive or negative component of inflammation, i.e. cell damage, without inhibiting the active or positive component ([10, 11]).

The topical use of benzydamine is justified by its capacity to penetrate the epithelial lining, reaching high concentrations in the underlying inflamed tissues ([6, 14]).

At the concentrations used topically, benzydamine has been shown to possess a local anaesthetic effect and an aspecific antibacterial and antifungal action ([12, 13]).

Clinical studies on the mouthwash (benzydamine 0.15%) have shown it to be effective in different oropharyngeal conditions (gingivitis, periodontitis, pharyngitis, etc.) relieving pain and improving both edema and hyperemia ([15, 16, 17, 18]).

On this basis, we decided to study the efficacy of 1‰ benzydamine vaginal dou-

che as an adjunct to specific antimicrobial therapy in moderate-severe vulvovaginal inflammations and as the sole therapeutic agent in mild inflammations.

MATERIAL AND METHODS

A double-blind randomized placebo controlled clinical trial was carried out on 124 patients divided into four groups, on the basis of vaginal smears.

Patients and treatment

Group 1: mild non-specific vaginitis. 60 patients, diagnosed as having mild non specific bacterial vaginitis (mixed flora) on the basis of vaginal smears, were divided at random into two subgroups of 30 each, one being treated with 1‰ benzydamine vaginal douche and the other with placebo, once daily for 10 days. The two subgroups were similar in age (benzydamine: 20-60 years with a mean of 35.4; placebo: 16-69 years with a mean of 37.9) and in the initial severity of symptoms and signs (see pre-treatment scores, table 1).

Group 2: moderate - severe non-specific vaginitis. 40 patients, diagnosed as having moderate or severe non-specific bacterial vaginitis (mixed flora) on the basis of vaginal smears, were divided at random into two subgroups of 20 each, one being treated with 1‰ benzydamine vaginal douche and the other with placebo, once daily for 10 days, in conjunction with topical antibiotic therapy. The two subgroups were similar in age (benzydamine: 22-57 years with a mean of 36.6; placebo: 20-60 years with a mean of 40.2) and in the initial severity of vaginitis (on the basis of vaginal smears), symptoms and signs (see pre-treatment scores, tables 3, 4 and 5).

Group 3: moderate - severe monilial vaginitis. 10 patients, diagnosed as having monilial vaginitis on the basis of vaginal smears, were divided at random into two subgroups of 5 each, one being treated with 1‰ benzydamine vaginal douche and the other with placebo, once daily for 10 days, in conjunction with oral and topical antimycotic therapy. The two subgroups were similar in age (benzydamine: 24-31 years with a mean of 27.8; placebo: 22-42 years with a mean of 33.6) and in the initial severity of vaginitis (on the basis of vaginal smears), symptoms and signs (see pre-treatment scores, tables 3, 6 and 7).

Group 4: moderate - severe trichomonal vaginitis. 14 patients, diagnosed as having trichomonal vaginitis on the basis of vaginal smears, were divided at random into two subgroups of 7 each, one being treated with 1‰ benzydamine vaginal douche and the other with placebo, once daily for 10 days, in conjunction with oral and topical antitrichomonal therapy. The two subgroups were similar in age (benzydamine: 31-41 years with a mean of 36.5; placebo: 20-47 years with a mean of 32.8) and in the initial severity of vaginitis on the basis of vaginal smears (the trichomoniasis was associated with a mixed bacterial infection in three patients in the benzydamine subgroup and in four in the placebo subgroup, as shown in table 3). They were also similar with respect to the initial severity of symptoms and signs (see pre-treatment scores, tables 8 and 9).

Vaginal douches. Vaginal douches were prepared by diluting the contents of one ampoule of liquid concentrate containing 0.5 g benzydamine hydrochloride or the vehicle alone in 500 ml of water. Douching was performed each morning for 10 consecutive days. The patients were asked to douche in a recumbent position allowing the solution to remain in the vaginal vault for a few minutes.

Assessment and scoring systems

In *patients with mild vaginitis* (group 1) symptoms were assessed before, daily during and at the end of the 10 day treatment period. Gynecological examinations were made before and at the end of treatment period, when the severity of each symptom and sign (itching, burning, dyspareunia, vaginal discharge and vulvovaginal erythema) was scored on a scale ranging from 0 (absent) to 2 (moderate). Smears were taken before treatment and 3-4 days after the last vaginal douche. The scheme used for grading the severity of vaginitis on the basis of smears is reported later.

In *patients with moderate - severe vaginitis* (groups 2, 3 and 4) symptoms were assessed before, daily during and at the end of the 10 day treatment period. Objective findings, obtained from direct gynecological examinations, colposcopy and vaginal and cervical smears were recorded before treatment and 1 week after its termination.

The symptoms assessed were: vaginal discharge, itching, burning, dyspareunia and dysuria. The signs assessed were: (by speculum) vulvovaginal erythema and/or oedema, vaginal discharge, erythema of the urethral meatus, pain provoked by the speculum; (by colposcopy) vaginal inflammation, erosion, bleeding portio vaginalis.

The severity of symptoms was graded on a scale ranging from 0 (absent) to 3 (severe) whereas signs were recorded as being either present or absent.

The severity of vaginitis (or cervicitis) on the basis of the type of bacterial flora and cells

on smear was graded according to the following scheme: (*)

0 (absent) = Type I (only Döderlein's bacilli; few desquamated epithelial cells);

1 (mild) = Type II (mainly Döderlein's bacilli but also some mixed bacterial flora; epithelial cells; a few leukocytes);

2 (moderate) = Type III (few Döderlein's bacilli and many mixed bacterial flora; epithelial cells; many leukocytes);

3 (severe) = Type IV (no Döderlein's bacilli, numerous mixed bacterial flora; epithelial cells; numerous leukocytes).

Before treatment, the smears in monilial and trichomonal vaginitis contained Monilia albicans or Trichomonas vaginalis, with or without numerous mixed bacterial flora.

Randomization code and statistical method

Both the benzydamine and placebo preparations were contained in boxes of 10 ampoules each, identical in appearance and marked with random numbers. Only one box was used for the treatment of each patient. The randomization code was not disclosed until the termination of the study. Therefore, the investigator recorded the data under completely blind conditions.

The data were statistically analysed using the "G" test ([19]).

RESULTS

Group 1 (mild non-specific bacterial vaginitis)

The severity of vaginitis (on the basis of vaginal smears) and of individual symptoms and signs before and after topical therapy with only benzydamine or placebo vaginal douche is shown in table 1. Before traeatment, approximately 60% of the patients in both the benzydamine and placebo subgroups complained of itching, burning and vaginal discharge, 15% of dyspareunia and 25% had vulvovaginal erythema.

The distribution of patients in the benzydamine and placebo subgroups according to the presence or absence of residual symptoms and signs and microscopic evidence of vaginitis is shown in table 2.

All symptoms and signs (itching, burning, dyspareunia, vaginal discarge and vulvovaginal erythema) remitted in a higher proportion (60-80%) of patients treated with benzydamine than with placebo (0-25%). The difference was statistically significant in favour of benzydamine for itching ($P < 0.01$), burning ($P < 0.001$), vaginal discharge ($P < 0.01$) and vulvovaginal erythema ($P < 0.01$). In addition, symptoms were generally relieved more slowly in the placebo than in the benzydamine subgroup.

Vaginitis (on the basis of vaginal smears) was absent in 22 of the 30 patients treated with benzydamine compared to 3 of the 30 treated with placebo, the difference being highly significant statistically ($P < 0.001$). The microscopic cure rate was consequently 73% in the benzydamine subgroup.

Groups 2, 3 and 4 (moderate to severe non-specific, monilial and Trichomonal vaginitis).

Vaginal smears

Table 3 shows the severity of vaginitis (with or without cervicitis) on the basis of vaginal (and cervical) smears, before and after treatment with benzydamine or placebo vaginal douche associated with specific antimicrobial therapy.

Before treatment, the distribution of moderate and severe inflammation for each type of vaginitis was similar in the benzydamine and placebo subgroups.

After treatment non-specific vaginitis on the basis of smears disappeared in 13 of the 20 patients in the benzydamine subgroup, compared to 8 of 20 in the placebo subgroup, i.e. the microscopic cure rate was 65% and 40% respectively. *Monilial vaginitis* was cured in all patients in both subgroups. *Trichomonal vaginitis* was completely cured in all 7 patients in the benzydamine subgroup (both the trichomoniasis and any associated mixed bacterial infection) whereas complete cure oc-

(*) In post-menopausal women the reference to Döderlein's bacilli should obviously be disregarded.

Table 1. — *Mild non-specific bacterial vaginitis. Distribution of patients in the benzydamine and placebo subgroups (30 each) according to pre- and post-treatment scores.*

Symptoms and signs	Treatment	Pre-treatment score [a]			Post-treatment score [a]		
		0	1	2	0	1	2
Itching	benzydamine	12	16	2	24	6	0
	placebo	10	18	2	15	13	2
Burning	benzydamine	15	13	2	27	2	1
	placebo	17	12	1	19	10	1
Dyspareunia	benzydamine	25	5	0	28	2	0
	placebo	27	3	0	26	3	0
Vaginal discharge	benzydamine	11	16	3	24	6	0
	placebo	13	13	4	16	10	4
Vulvovaginal erythema	benzydamine	23	7	0	28	2	0
	placebo	22	7	1	22	7	1
Vaginitis (on the basis of vaginal smear)	benzydamine	0	30	0	22	8	0
	placebo	0	30	0	3	27	0

[a] Score of severity: 0=absent, 1=mild, 2=moderate.

Table 2. — *Mild non-specific bacterial vaginitis. Distribution of patients in the benzydamine and placebo subgroups after treatment, according to the presence or absence of residual symptoms and signs and microscopic evidence of vaginitis.*

Symptoms and signs	Treatment	Residual symptoms and signs		Total No. of cases [a]	"G" test
		Present	Absent		
Itching	benzydamine	6	12	18	6.85 **
	placebo	15	5	20	
Burning	benzydamine	3	12	15	12.64 ***
	placebo	11	2	13	
Dyspareunia	benzydamine	2	3	5	
	placebo	3	0	3	
Vaginal discharge	benzydamine	6	13	19	9.92 **
	placebo	14	3	17	
Vulvovaginal erythema	benzydamine	2	5	7	10.72 **
	placebo	8	0	8	
Vaginitis (on the basis of vaginal smear)	benzydamine	8	22	30	27.20 ***
	placebo	27	3	30	

[a] Number of cases in whom the corresponding symptoms and signs were present before treatment.
* $P<0.05$; ** $P<0.01$; *** $P<0.001$.

Table 3. — *Vaginal smears in moderate to severe vaginitis. Distribution of patients in the benzydamine and placebo subgroups according to pre- and post-treatment scores.*

	Treatment	Pre-treatment score [a]				Post-treatment score [a]			
		0	1	2	3	0	1	2	3
Non-specific bacterial vaginitis	benzydamine	0	0	10	10	13	4	2	1
	placebo	0	0	12	8	8	7	5	0
Monilial vaginitis	benzydamine	0	0	2	3	5	0	0	0
	placebo	0	0	2	3	5	0	0	0
Trichomonal vaginitis	benzydamine	0	0	4 [b]	3	7	0	0	0
	placebo	0	0	2 [c]	5 [d]	3	2 [e]	1 [e]	1

[a] Score of severity: 0=absent, 1=mild, 2=moderate, 3=severe. [b] Trichomonas+mixed bacterial flora present in 3 patients. [c] Trichomonas+mixed bacterial flora present in both patients. [d] Trichomonas+mixed bacterial flora present in 2 patients. [e] Only mixed bacterial flora present.

curred in only 3 of the 7 patients in the placebo subgroup (trichomoniasis persisted in 1 patient and mixed bacterial infection in 3).

The *pooled data* of all the patients in whom benzydamine vaginal douche and placebo were used as adjuncts to specific antimicrobial therapy are reported in table 11. Vaginitis (bacterial, monilial and trichomonal) on the basis of smears was cured in 25 of the 32 patients (78%) in the benzydamine subgroup compared to 16 of the 32 (50%) in the placebo subgroup, the difference being statistically significant in favour of benzydamine ($P<0.02$).

Symptoms

The distribution of patients in the benzydamine and placebo subgroups according to the pre- and post-treatment scores of symptoms are shown in table 4 (non-spe-

Table 4. — *Symptoms of moderate to severe non-specific bacterial vaginitis. Distribution of patients in the benzydamine and placebo subgroups (20 each) according to pre- and post-treatment scores.*

Symptoms	Treatment	Pre-treatment score [a]				Post-treatment score [a]			
		0	1	2	3	0	1	2	3
Vaginal discharge	benzydamine	0	1	14	5	14	5	1	0
	placebo	0	3	13	4	8	10	2	0
Itching	benzydamine	6	6	5	3	16	4	0	0
	placebo	7	6	6	1	14	5	1	0
Burning	benzydamine	6	10	2	2	16	2	2	0
	placebo	7	8	5	0	14	6	0	0
Dyspareunia	benzydamine	13	2	4	1	16	3	1	0
	placebo	12	4	4	0	16	4	0	0
Dysuria	benzydamine	17	2	1	0	19	1	0	0
	placebo	14	4	2	0	17	3	0	0

[a] Score of severity: 0=absent, 1=mild, 2=moderate, 3=severe.

Table 5. — *Clinical signs of moderate to severe non-specific bacterial vaginitis. Distribution of patients in the benzydamine and placebo subgroups (20 each) according to the presence or absence of signs before and after treatment.*

	Signs	Treatment	Before treatment signs		After treatment signs	
			Present	Absent	Present	Absent
By speculum	Vaginal discharge	benzydamine	20	0	3	17
		placebo	20	0	6	14
	Vulvo-vaginal erythema and/or oedema	benzydamine	10	10	3	17
		placebo	8	12	5	15
	Pain provoked by speculum	benzydamine	8	12	2	18
		placebo	10	10	4	16
	Erythema of urethral meatus	benzydamine	5	15	1	19
		placebo	7	13	2	18
On colposcopy	Vaginitis	benzydamine	13	7	3	17
		placebo	12	8	5	15
	Erosion	benzydamine	2	18	1	19
		placebo	1	19	0	20
	Bleeding portio vaginalis	benzydamine	3	17	1	19
		placebo	4	16	1	19

cific bacterial vaginitis), table 6 (monilial vaginitis) and table 8 (trichomonal vaginitis).

Before treatment, all patients in both the benzydamine and placebo subgroups complained of vaginal discharge (moderate to severe in most patients), about 70% of burning and itching (more marked in monilial vaginitis), 50% of dyspareunia (more marked in trichomonal vaginitis) and 30% of dysuria. The distribution of patients within each grading of severity was similar in the 2 subgroups.

After treatment, in each type of vaginitis, a higher proportion of patients in the benzydamine than in the placebo subgroup were completely relieved of each symptom.

The *pooled data* are reported in table 10. Vaginal discharge remitted in 78% (25/32) of cases treated with benzydamine and in 43% (14/32) treated with placebo, itching in 84% (21/25) and 54% (12/22) respectively, burning in 80% (20/25) and 52% (12/23), and dysuria in 90% (9/10) and 58% (7/12). The response rate of dyspareunia was similar (about 70%) in the two subgroups.

The difference was statistically significant in favour of benzydamine for vaginal discharge ($P < 0.01$), itching ($P < 0.05$) and burning ($P < 0.05$). There was a trend towards significance for dysuria ($P < 0.10$). Moreover the daily assessment of symptoms showed that in bacterial and in monilial vaginitis they were relieved within the first few days of treatment with benzydamine, but only some days later with placebo; in trichomonal vaginitis, they were almost completely relieved towards the end of treatment with benzydamine and again some time later with placebo.

Table 6. — *Symptoms of moderate to severe monilial vaginitis. Distribution of patients in the benzydamine and placebo subgroups (5 each) according to pre- and post-treatment scores.*

Symptoms	Treatment	Pre-treatment score [a]				Post-treatment score [a]			
		0	1	2	3	0	1	2	3
Vaginal discharge	benzydamine	0	0	2	3	5	0	0	0
	placebo	0	1	2	2	3	2	0	0
Itching	benzydamine	0	0	3	2	5	0	0	0
	placebo	0	0	1	4	4	1	0	0
Burning	benzydamine	1	1	2	1	5	0	0	0
	placebo	2	0	2	1	4	1	0	0
Dyspareunia	benzydamine	4	0	1	0	5	0	0	0
	placebo	2	2	1	0	5	0	0	0
Dysuria	benzydamine	3	1	0	1	5	0	0	0
	placebo	3	1	1	0	5	0	0	0

[a] Score of severity: 0=absent, 1=mild, 2=moderate, 3=severe.

Table 7. — *Clinical signs of moderate to severe monilial vaginitis. Distribution of patients in the benzydamine and placebo subgroups (5 each) according to the presence or absence of signs before and after treatment.*

	Signs	Treatment	Before treatment signs		After treatment signs	
			Present	Absent	Present	Absent
By speculum	Vaginal discharge	benzydamine	5	0	0	5
		placebo	5	0	2	3
	Vulvo-vaginal erythema and/or oedema	benzydamine	4	1	0	5
		placebo	4	1	2	3
	Pain provoked by speculum	benzydamine	2	3	0	5
		placebo	3	2	0	5
	Erythema of urethral meatus	benzydamine	2	3	0	5
		placebo	1	4	0	5
On colposcopy	Vaginitis	benzydamine	5	0	0	5
		placebo	5	0	0	5
	Erosion	benzydamine	0	5	0	5
		placebo	1	4	0	5
	Bleeding portio vaginalis	benzydamine	1	4	0	5
		placebo	0	5	0	5

Table 8. — *Symptoms of moderate to severe trichomonal vaginitis. Distribution of patients in the benzydamine and placebo subgroups (7 each) according to pre- and post-treatment scores.*

Symptoms	Treatment	Pre-treatment score [a]				Post-treatment score [a]			
		0	1	2	3	0	1	2	3
Vaginal discharge	benzydamine	0	0	6	1	6	1	0	0
	placebo	0	2	2	3	3	3	0	1
Itching	benzydamine	1	4	2	0	7	0	0	0
	placebo	3	1	3	0	4	2	1	0
Burning	benzydamine	0	2	4	1	6	1	0	0
	placebo	0	3	3	1	3	3	0	1
Dyspareunia	benzydamine	0	1	5	1	7	0	0	0
	placebo	0	0	4	3	5	1	1	0
Dysuria	benzydamine	2	3	2	0	7	0	0	0
	placebo	3	2	1	1	5	1	1	0

[a] Score of severity: 0=absent, 1=mild, 2=moderate, 3=severe.

Signs

The distribution of patients in the benzydamine and placebo subgroups according to the presence or absence of signs before and after treatment are shown in tables 5, 7 and 9.

In *non-specific bacterial vaginitis* (table 5), *before treatment* a profuse vaginal discharge was present on examination with a speculum in all 20 patients in each subgroup, vulvovaginal erythema and/or oedema associated with intense pain on introduction of the speculum in around 50% and erythema of the urethral meatus in around 30%. On colposcopy, vaginitis was present in about 60% of cases in each subgroup, but erosion and bleeding portio vaginalis only sporadically.

After treatment, all clinical signs disappeared in a higher proportion of patients in the benzydamine than in the placebo subgroup.

In *monilial vaginitis* (table 7), *before treatment* clinical signs were marked in each case. All or most of the patients in each subgroup showed a vaginal discarge and vulvovaginal erythema and/or oedema on inspection with a speculum and vaginitis on colposcopy. Other signs were present less frequently. *After treatment*, clinical signs remitted completely in all the patients in the benzydamine subgroup. Vaginal discharge and vulvovaginal erythema and/or oedema persisted in the placebo subgroup, but they were less marked than initially.

In *Trichomonal vaginitis* (table 9) *before treatment*, most of the cases in each subgroup showed a vaginal discharge, vulvovaginal erythema and/or oedema, tenderness on introduction of the speculum, and erythema of the urethral meatus on examination with a speculum and vaginitis on colposcopy. Erosion and bleeding of the portio vaginalis were present less frequently. *After treatment*, clinical signs tended to remit in a higher proportion of cases in the benzydamine than in the placebo subgroup.

Table 11 shows the distribution of patients in the benzydamine and placebo subgroups according to the presence or absence, after treatment, of residual clinical signs in moderate to severe vaginitis (*pooled data*).

Table 9. — *Clinical signs of moderate to severe trichomonal vaginitis. Distribution of patients in the benzydamine or placebo subgroups (7 each) according to the presence or absence of signs before and after treatment.*

	Signs	Treatment	Before treatment signs		After treatment signs	
			Present	Absent	Present	Absent
By speculum	Vaginal discharge	benzydamine	6	1	1	6
		placebo	6	1	3	4
	Vulvo-vaginal erythema and/or oedema	benzydamine	4	3	1	6
		placebo	6	1	3	4
	Pain provoked by speculum	benzydamine	4	3	1	6
		placebo	5	2	2	5
	Erythema of urethral meatus	benzydamine	5	2	0	7
		placebo	5	2	1	6
On colposcopy	Vaginitis	benzydamine	7	0	0	7
		placebo	7	0	1	6
	Erosion	benzydamine	1	6	0	7
		placebo	2	5	1	6
	Bleeding portio vaginalis	benzydamine	2	5	0	7
		placebo	3	4	1	6

Table 10. — *Symptoms of moderate to severe non-specific bacterial, monilial and trichomonal vaginitis (pooled data). Distribution of patients in the benzydamine and placebo subgroups (32 each [a]) according to the presence or absence of residual symptoms after treatment.*

Symptoms	Treatment	Residual symptoms		Total number of cases [b]	"G" test
		Present	Absent		
Vaginal discharge	benzydamine	7	25	32	8.15 **
	placebo	18	14	32	
Itching	benzydamine	4	21	25	4.95 *
	placebo	10	12	22	
Burning	benzydamine	5	20	25	4.24 *
	placebo	11	12	23	
Dyspareunia	benzydamine	4	11	15	N. S.
	placebo	6	12	18	
Dysuria	benzydamine	1	9	10	2.98 ***
	placebo	5	7	12	

[a] Each group consisted of 20 patients with non-specific, 5 with monilial and 7 with trichomonal vaginitis. [b] Number of patients in whom the corresponding symptoms were present before treatment. * $P<0.05$; ** $P<0.01$; *** Trend ($P<0.10$).

Table 11. — *Clinical signs and vaginal smears in moderate to severe non-specific bacterial, monilial and trichomonal vaginitis (pooled data). Distribution of patients in the benzydamine and placebo subgroups (32 each [a]) according to the presence or absence, after treatment, of residual clinical signs and vaginitis on the basis of smears.*

Clinical and microscopic findings		Treatment	Residual findings		Total No. of cases [b]	"G" test
			Present	Absent		
By speculum	Vaginal discharge	benzydamine	4	27	31	4.44 *
		placebo	11	20	31	
	Vulvo-vaginal erythema and/or oedema	benzydamine	4	14	18	4.31 *
		placebo	10	8	18	
	Pain provoked by speculum	benzydamine	3	11	14	N. S.
		placebo	6	12	18	
	Erythema of urethral meatus	benzydamine	1	11	12	N. S.
		placebo	3	10	13	
On colposcopy	Vaginitis	benzydamine	3	22	25	N. S.
		placebo	6	18	24	
	Erosion	benzydamine	1	2	3	N. S.
		placebo	1	3	4	
	Bleeding portio vaginalis	benzydamine	1	5	6	N. S.
		placebo	2	5	7	
Smear	Vaginitis	benzydamine	7	25	32	5.60 **
		placebo	16	16	32	

[a] Each group consisted of 20 patients with non-specific, 5 with monilial and 7 with trichomonal vaginitis. [b] Number of patients in whom the corresponding signs were present before treatment. * $P<0.05$; ** $P<0.02$.

Vaginal discharge completely remitted in 87% (27/31) of the cases treated with benzydamine, compared to 64% (20/31) treated with placebo and vulvovaginal erythema and/or oedema in 78% (14/18) and 44% (8/18) respectively. The difference in favour of benzydamine was statistically significant for both signs ($P<0.05$).

The remission rate for provoked pain was 79% (11/14) in the benzydamine subgroup and 67% (12/18) in the placebo subgroup, for erythema of the urethral meatus 92% (11/12) and 77% (10/13) respectively, for vaginitis (on colposcopy) 88% (22/25) and 75% (18/24) respectively. The difference between the two products was not statistically significant for any of these signs.

The response of the remaining clinical signs was similar in the two subgroups.

DISCUSSION

When used alone for the treatment of mild non-specific vaginitis, 1‰ benzydamine vaginal douche was found in our experience to be significantly superior to placebo in its therapeutic effect on the basis of microscopic findings. It was also faster and significantly more effective in relieving symptoms and signs (itching, burning, vaginal discharge and vulvovagi-

nal erythema). Similar results have been obseved in other controlled clinical studies ([20, 21, 22]).

We found benzydamine vaginal douche to be clinically well tolerated in all cases and able to revert type II vaginal flora (Döderlein's bacilli + some mixed bacterial flora) to type I vaginal flora (only Döderlein's bacilli).

Its good tolerance in this study was in agreement with the findings of other investigators. Facchini ([23]) reported a good tolerance even in patients who had shown allergic reactions to other drugs (antibiotics). Scavo and Pallucchini ([24]) commented on the fact that the affinity of cells for specific stains was not modified even within a few hours from vaginal douching with benzydamine (a particularly important finding for oncological and hormonal studies). The same investigators also noted that even relatively prolonged treatment for up to 20 days caused no important changes in the normal vaginal flora, exfoliated cells or pH.

In a controlled trial ([21]) it was found that benzydamine vaginal douche + specific antimicrobial therapy had a significantly greater symptomatic effect within the first two days of treatment than placebo + antimicrobial agents.

In our study, when used as adjunct to specific antimicrobial therapy in different types of vaginitis, 1‰ benzydamine vaginal douche was found to be significantly superior to placebo in producing a microscopic cure of vaginitis (on the basis of smears). It was also either significantly superior or tended to be superior in relieving most symptoms and some of the clinical signs (superior on itching, burning, vaginal discharge and vulvovaginal erythema and/or oedema and tending to be superior on dysuria). The relief of symptoms also occurred more quickly in the benzydamine group.

On the basis of these findings benzydamine vaginal douche enhances the therapeutic effect of antimicrobial agents used routinely for the treatment of vaginal infections.

In conclusion, bezydamine facilitates the remission of both symptoms (pain, burning, irritation, itching, etc.) and objective findings (mucosal congestion, vaginal discharge, altered vaginal flora, etc.). In moderate and severe vaginitis (non-specific bacterial, monilial and trichomonal) benzydamine douche is an useful adjunct to the local or systemic treatment of the aetiological factor since it potentiates and accelerates the control of symptoms and signs.

In mild non-specific vaginitis, on the other hand, it provides an effective therapy on its own, causing the remission of both subjective and objective inflammatory manifestations.

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