Therapeutic Results of Defined Pollen-Extract in Patients with Chronic Prostatitis or BPH Accompanied by Chronic Prostatitis

L. Ebeling
Pharma Stroschein Hamburg, FRG

Introduction

Depending mainly upon analysis of prostatic fluid and angloamerican classification divides the benign painful diseases of the prostate into four categories: Acute bacterial prostatitis, chronic bacterial prostatitis, non-bacterial prostatitis, and prostatodynia (1).

According to findings of *Weidner* (2) the largest group, the prostatodynia (vegetative urogenital syndrome), covers 52.4%. Besides clinical symptoms and normal laboratory findings the following urodynamics changes are characteristic: Elevation of the maximum urethral closure and reduced peak urine flow rates (3,4,5).

In approximately 40% of non-bacterial prostatitis the microbiological examination is negative (2) whereas by definition leucocytosis in the prostatic fluid can be demonstrated. The prostatic congestion, pathomorphologically considered as congestion of secretion and edemas in the prostate (6) can appear in every form of prostatism (7).

This demonstrates that antibiotics are indicated for a small number of patients only. Predominantly an anti inflammatory resp. symptomatic therapy is required.

The use of the pollen-extract in the treatment of benign prostatic diseases as BPH and prostatitis has already been described since 1960 and leads to clinical improvement of symptoms and positive changes by objective parameters.

In a double-blind study with 61 patients and a simultaneously carried out open examination with 118 patients *Leadner* (9) stated in the verum-group a normalization of initially pathological palpation findings and leucocytosis of prostatic fluid in 94% of patients with chronic prostatitis who were treated with pollen-extract. 6% of the patients showed unchanged results, aggravations were not observed. In the placebo-group 48% showed normalization, 34% demonstrated an unchanged status and in 18% of the patients the findings were deteriorated. The results of treatment in the open trial revealed only small differences in comparison to therapeutic effects in the verum-group which can be rated as accidental. *Takeuchi* (10) demonstrated in a clinical study with 25 BPH-patients in stage 1 or 2 under treatment with pollen-extract besides the elevation of peak urine flow rate a significant ($p < 0.05$) decrease of maximum urethral closure pressure with a corresponding diminished resistance of the prostatic part of the urethra.

Pharmacologically the pollen-extract is characterized by antiinflammatory and prostate cell selective growth inhibiting properties. Furthermore a specific affinity to the prostate could be demonstrated (11,12).

The aim of this field study was to control the acceptance and effectiveness of this drug on a large number of patients with chronic prostatic complaints, i.e. symptoms of chronic prostatitis or BPH, and to evaluate the possible role of the pollen-extract in their conservative treatment.

Methods

2,289 patients were divided according to the diagnoses given by 170 urologists based on clinical symptoms, palpation and laboratory findings as well as residual urine volume resp. uroflow measurements into three groups: 583 (25,4%) cases of chronic prostatitis (P), 590 (25,8%) cases of BPH accompanied by prostatitis (BP) and 1116 (48,8%) cases of BPH (B). The BP- and B-group was subdivided into stage 1, 2, and 3 (14).

The treatment with pollen-extract was in 84% of the cases in a dosage of 3 x 2 tablets/ day in the first week and continued in 78.5% with 3 x 2 tablets/ day up to twelve weeks.

Typical symptoms and palpation findings classified as light, medium or severe were recorded and evaluated before, during, and after therapy up to twelve weeks.

The residual urine volume determined by sonography, X-ray or catheterization, uroflow measurements as peak urine flow rate, urine volume voided and flow time, laboratory parameters as leukocytes in urine sediment or expressed prostatic secretions were controlled before and during treatment.

The courses of clinical signs and symptoms and the change of the objective parameters were documented. A further assessment was carried out by comparing the data before and after treatment.

Side effects, statements regarding the tolerance and a general assessment about the treatment with pollen-extract were investigated. Statistical analysis was performed as chi-square tests, variance analysis, split-plot variance analysis and factor analysis.

Results

[1] 1 tabl. Contains: Extr Pollin. sicc. (Cernitin T60) 60mg, Extr. Pollin. dialys. (Cernitin GBX) 3mg.

The age distribution showed a prevalence of the chronic prostatitis in the 4th and 5th decade whereas the BPH with prostatitis was diagnosed mainly in 60-70 years old men. The B-group represented the oldest patient-group (table 1).

Typical for patients with chronic prostatitis are also symptoms other than difficulties on micturition. These complaints reappeared in the BP-group in a less extensive form but compared to the B-group the significant difference is obviously (figure 1a). The correspondence between the P- and BP-group was similar regarding the leukocytes in prostatic expressate (figure 1b) and the >>painful prostate<< on palpation (figure 1c).

Depending on the respective complaints improvement or absence of symptoms were stated in 64% to 82%.

The palpated size of the prostate diminished more markedly in the BP-group compared to the B-group. A significant reduction in the P-group was found in 55.9% of the patients with initially enlarged prostate (n=169, n=302). The changes regarding the >>painful prostate<< on palpation are demonstrated by table II. The microscopic estimates of leucocytes in the prostatic expressate after therapy revealed for all diagnostic groups a decreased number of leucocytes ≤ 10/ HPF in 59% of the cases with initial findings >10 leucocytes/ HPF (n=291, n=493).

The residual urine volume diminished significantly ($p < 0.001$) in all stages (figure 2a) and showed a continuous decrease with the length of therapy (table III).

The peak urine flow rate increased in all groups significantly ($p < 0.001$) about 3 to 4 ml/sec comparing the pre/post-values (figure 2b and table IV). Concomitantly the urine volume voided increased and the flow time was reduced.

The general assessment of the therapy with pollen-extract by physician and patient was very good or good in 72.2% resp. 75%. Side effects (i.e. slight and temporary GIT disturbances)

were described in 66 cases (2.9%), in 1.2% the treatment was discontinued.

Table I. Age distribution in the diagnostic groups (P = chronic prostatitis, B = BPH, BP = BPH with prostatitis).

Parameter	Age range/Statistic	P	B	BP
Patients		583	1.116	590
Age, years	minimum	17	21	22
	maximum	85	97	94
	median	40.3	67.0	60.3
	mean	40.6	66.6	60.3
	standard deviation	12.0	9.3	11.7
	≤ 30	126	2	6
	31–40	170	4	22
	41–50	184	48	87
	51–60	61	210	182
	61–70	26	440	160
	71–80	12	328	113
	> 80	1	67	17
	negative	3	17	3
Stage of BPH	1		324	259
	2		598	244
	3		109	40
	negative		85	47

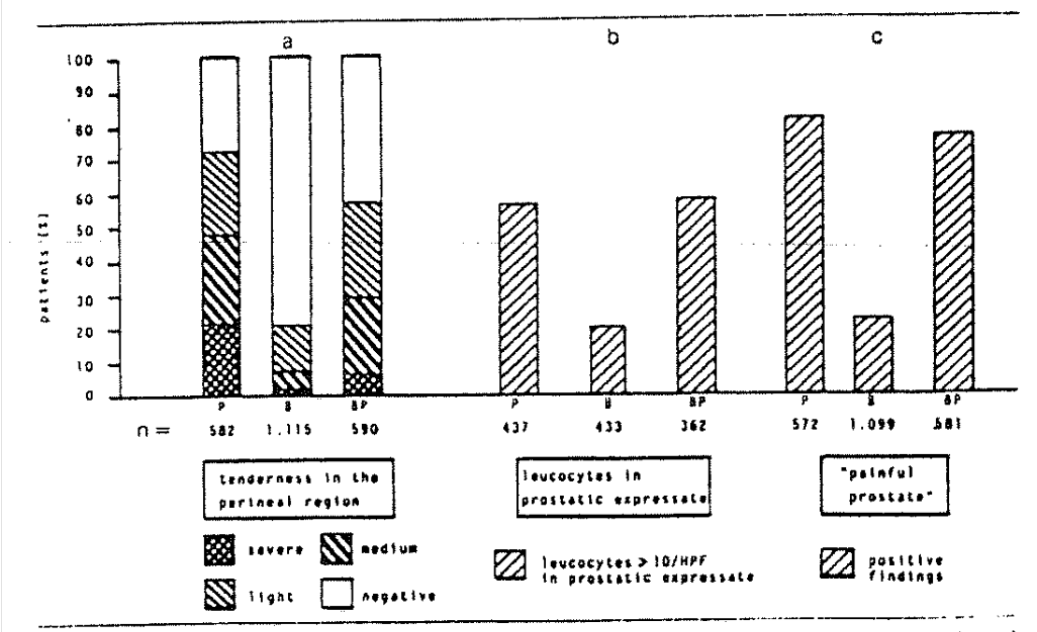

Figure 1a–c. Differences between the diagnostic groups regarding clinical symptoms (a), laboratory (b) and palpation findings (c) before therapy (P = chronic prostatitis, B = BPH, BP = BPH with prostatitis).

Table II. »Painful prostate« on palpation. Comparison of the pre/post-data. Significant ($p < 0.001$) differences in the findings before and after treatment with pollen-extract.

Intensity, scores	Chronic prostatitis		BPH		BPH with prostatitis	
	pre, n	post, n	pre, n	post, n	pre, n	post, n
Severe	96	4	12	–	56	3
Medium	196	26	62	5	186	22
Light	164	159	174	68	194	128
Negative	95	362	812	987	124	407
% negative	17.2	65.7	76.6	93.1	22.1	72.7

Course under therapy	Chronic prostatitis		BPH		BPH with prostatitis	
	n	%	n	%	n	%
Unchanged (all)	93		811		123	
Aggravated	4	0.9	1	0.4	3	0.7
Unchanged positive	50	10.9	41	16.5	47	10.8
Improved	135	29.5	31	12.4	103	23.6
Asymptomatic	269	58.7	176	70.7	284	65.0

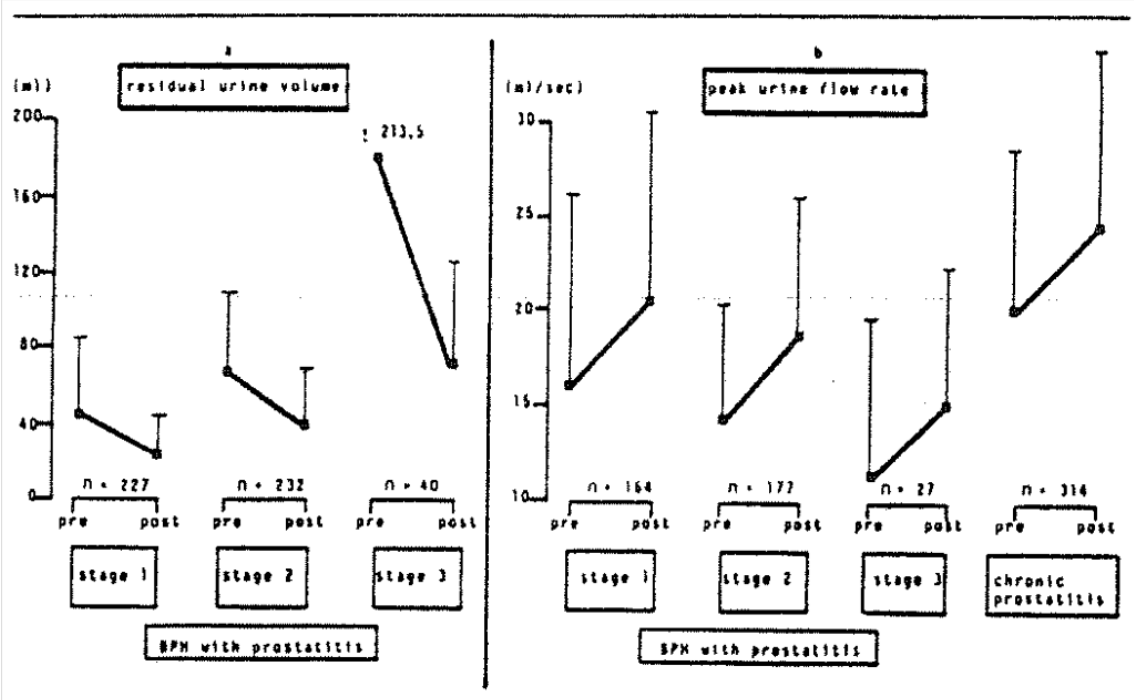

Figure 2a–b. Comparison of pre/post-findings regarding residual urine volume (a) and peak urine flow rate (b). Significant ($p < 0.001$) decrease of residual urine volume in BPH (stage 1–3) with prostatitis, significant ($p < 0.001$) increase of peak urine flow rate in patients with chronic prostatitis or BPH (stage 1–3) with prostatitis under the treatment with pollen-extract.

Table III. Residual urine volume (ml) under treatment with pollen-extract. Continuous decrease with the length of therapy. Significant ($p < 0.001$) differences in the findings before and after treatment.

	Time of control	BPH with prostatitis	
		$\bar{x}$	s
Treatment over 12 weeks (n = 175)			
	pre	67.3	73.6
	2 weeks	50.0	46.2
	6 weeks	41.7	42.0
	12 weeks	32.0	35.7
Pre/post-comparison (n = 542)			
	pre	62.9	76.6
	post	34.2	34.2
	difference	−28.7	

Table IV. Peak urine flow rate (ml/sec) under treatment with pollen-extract. Continuous increase with the length of therapy. Significant ($p < 0.001$) differences in the findings before and after treatment.

	Time of control	Chronic prostatitis		BPH with prostatitis	
		$\bar{x}$	s	$\bar{x}$	s
Treatment over 12 weeks		n = 95		n = 119	
	pre	20.7	9.6	14.6	7.9
	2 weeks	22.6	8.8	16.3	7.5
	6 weeks	24.2	8.8	18.8	9.2
	12 weeks	26.1	8.8	20.0	9.3
Pre/post-comparison		n = 314		n = 403	
	pre	19.8	8.5	15.0	8.2
	post	24.1	8.9	19.3	8.9
	difference	+4.3		+4.3	

Discussion

The objective criteria for therapeutic effectiveness as residual urine volume, peak urine flow rate, urine volume voided, flow time and leucocytes findings show in their course and by comparison the status before and after therapy significant changes which are accompanied by improved palpation findings and a continuous decline of symptom-scores indicating the subjective relief in patients.

Under differential therapeutic aspects the conservative treatment of benign and chronic prostatic diseases is to consider as a predominantly antiinflammatory resp. symptomatic one. The findings of *Weidner* (2) regarding the various forms of chronic >>prostatitis<< confirm that at least in 68.3% of patients an antibiotic therapy is not primarily indicated.

The pre/post-comparison of leucocyte findings in the prostatic expressate reveals a decrease on ≤ 10 leucocytes/ HPF in 59% of all cases with initial values > 10/ HPF.

These results confirm previous findings by *Leander* (9). The differences regarding the percentage of improvement resp. normalization

are explainable by his definition of the pathological value as ≥ 10 leucocytes/ field (x 240).

Therefore it can be concluded that the pharmacologically demonstrated antiinflammatory property leads to clinical effects in human too.

The etiology of the prostatodynia remains uncertain. Whereas *Vahlensieck* (6) distinguishes between the static, vegetative and sexual dependent causes of prostatic congestion, a primary abnormality involving the pelvic sympathetic nervous system in most patients or tension myalgia of the pelvic floor is suggested by *Meares* et al. (4, 5).

The urodynamic findings in this study, i.e. significant ($p < 0.001$) increase about 3 to 4 ml/ sec of peak urine flow rate with concomitantly higher values of urine volume voided and reduced flow time, are investigated in the P- and BP-group, suggesting a homogenous effect of the pollen-extract on the bladder outflow obstruction.

Under treatment with pollen-extract a significant ($p < 0.05$) decrease of maximum urethral closure pressure with decreased resistance of the prostatic part of the urethra was demonstrated in BPH-patients (10).

These findings, due to the antiinflammatory and decongestive effects of this drug, give evidence for the therapeutic benefit of the pollen-extract in patients with non-bacterial prostatitis or prostatodynia since improvement of clinical symptoms and palpation findings occurs concomitantly.

The investigated parameter, evaluated before, during and after treatment with pollen extract, show in the B- and BP-group a reduction of residual urine volumes, elevated peak urine flow rates and voided urine volumes at simultaneously reduced flow times with improvement of both obstructive and irritative symptoms as well as laboratory and palpation findings.

Comparing the course of kinetics between the two hyperplasia-groups B and BP in regard of clinical symptoms, residual urine volume, uroflow and palpation findings it demonstrated even in different before findings a parallel development. This allows the conclusion, that within the BPH frame besides hyperplastic obstruction edematous resp. inflammatory as well as congestive changes in the prostatic tissue reach clinical effectiveness.

These results indicate an applicability of the pollen-extract in patients with BPH (with or without concomitant prostatitis) and suggest in addition therapeutic effects on the so-called non-pathogen post TURP-prostatitis, which is pathohistologically demonstrated in over 50% of patients after prostatectomy (8).

Due to the large number of substances in pollen the identification of (the) active substance(s) of the pollen-extract is difficult and not yet succeeded, but the demonstration of 5 different phytosteroles and of a biological active peptide looks promising as it is known that both peptides and sterols can influence the intracellular metabolism in biological systems (13).

In summary, the results of the multi-center study suggest a rationality for application of the pollen-extract in patients with non-pathogen dependent chronic prostatitis, prostatodynia, prostatic congestion, BPH with and without concomitant prostatitis and TURP-prostatitis.

The positive tolerance of the pollen-extract meets the requirement for a satisfying compliance in chronic and benign prostatic diseases and in thus indicated long-term treatment.

Further investigations with double-blind test design have to establish these encouraging results also to evaluate the degree of spontaneous improvement and placebo-effect.

Acknowledgements

I thank Dr. J. Schnitker and his staff, Institute for Applied Statistics, Bielefeld, Federal Republic of

Germany, for their biometrical evaluation of the data.

References

1 Drach GW, Fair WR, Meares EM, Stamey TA (1978) J Urol 120: 266
2 Weidner W (1984) Fortschr MED 43: 1113
3 Blacklock NJ (1985) Urodynamic observations and their implication in the management of the prostatodynia. Lecture presented on the 3rd Int Meet >>Therapy of Prostatitis<<, Giessen/Bad Nauheim
4 Meares EM (1985) Prostatodynia: Clinical findings and therapy. Lecture presented on the 3rd Int Meet >>Therapy of Prostatitis<<, Giessen/Bad Nauheim
5 Barbalias GA, Meares EM, Sant GR (1983) J Urol 130:514
6 Vahlensieck W (1986) In: Helpap B, Senge T, Vahlensieck W (eds) Prostatakongestion and Prostatitis. Die Prostata 3. pmi-Verlag, Frankfurt/M, pp 1-9
7 Weidner W (1984) Moderne Prostatitisdiagnostik. In: Schmiedt F., Altwein JF, Bauer H-W (eds) Klin exp Urol 7. W. Zuckschwerdt, Munchen Bern Wien
8 Helpap B (1985) In: Helpap B, Senge T, Vahlensieck W (eds) Prostatakongestion and Prostatitis. Die Prostata 3. pmi-Verlag, Frankfurt/M, pp 27-48
9 Leander G (1962) Svensku Lakartidningen 59: 3296
10 Takeuchi 11, Tamauchi A, Ueda T, Hiraga S (1981) Acta Urol Jap 27:317
11 Itoh R (1970) La Clin Ther 54: 205
12 Habib FK (1985) Experimental findings on pollen extracts. Lecture presented on the symp >>New Perspectives in the Treatment of Benign Prostate Diseases, Edinburgh
13 Cholcha W (1985) Cernitin T60 and Cernitin GBX – two pollen-extracts: structure and composition. Lecture presented on the Symp >>New Perspectives in the Treatment of Benign Prostate Disease<<, Edinburgh
14 Alken CE, Sokeland J (1979) Urologie, 8th ed. Georg Thieme, Stuttgart

Corresponding address: I .. Ebeling, Pharma Stroschein, Frohmestrabe 110, 10-2000 Hamburg 61, FRG