

Treatment of Benign Prostatic Hyperplasia with Phytosterols

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Summary - In a randomised, double-blind study, the preparation Curbicin, obtained from pumpkin seeds and dwarf palm plants (*Curcubita pepo* L. and *Sabal serrulata*), was compared with a placebo in the treatment of symptoms caused by prostatic hyperplasia; 53 patients took part in the study, which was carried out over a 3-month period. Urinary flow, micturition time, residual urine, frequency of micturition and a subjective assessment of the effect of treatment were all significantly improved in the treatment group. No untoward side effects were noted.

For many years, particularly in Europe, extracts from pumpkin seeds (*Curcubita pepo* L.) and the fruits of dwarf palms (*Sabal serrulata*) have been used in folk medicine as remedy for micturition problems caused by the prostate (Madaus, 1979). During the past few years, clinical studies carried out under medical supervision with these preparations have shown them to be beneficial (Mandressi et al., 1987; Pannunzio et al., 1987; Carbin and Eliasson, 1989).

The exact mechanism of action of Curbicin is not clear, but it has been shown to decrease the binding capacity of androgen receptors to testosterone (Andersson et al., 1977; Schmidt, 1984), while in some studies Sabal extract has been shown to have an inhibitory effect on 5 α -reductase (Carilla et al., 1984; Sultan et al., 1984; Pannunzio et al., 1987). Thus Curbicin appears to have a dual action in influencing the development of prostatic hyperplasia. The competitive binding of phytosterols to androgen receptors could be explained by the similarity of their chemical structure to androgens and oestrogens (Ourisson et al., 1964; Schöpflin et al., 1966).

In a double blind pilot study in 26 patients it was shown that a preparation with extracts of both *Curcubita pepo* L. and *Sabal serrulata* (Curbicin) significantly decreased nocturia, but other variables, (e.g. residual urine, urinary flow rate and frequency of diurnal voiding) were not significantly different between the 2 groups (Carbin and Eliasson, 1989). However, the sample studied was small and randomisation was not stratified. The study reported here was carried out in a larger group of patients with early symptoms of outflow obstruction due to benign prostatic hyperplasia.

Patients and Methods

A double-blind, placebo-controlled study was carried out in conjunction with 6 general practitioners (4 in Sweden and 2 in Denmark) to assess the value of Curbicin in the treatment of patients with voiding problems due to BPH.

The criteria for the inclusion of patients in the study, after having obtained informed consent, were as follows: males between the ages of 50 and 80 years with symptoms of at least 3 months' duration; the presence of benign prostatic hyperplasia on the basis of a history, clinical examination of the prostate and acid phosphatase determination; patients not previously treated with Curbicin. Patients in imminent need of surgery because of the severity of symptoms or residual urine >300 ml were excluded from the study.

The series included 55 patients. Curbicin contains 160 mg of standardised extract PS6 from *Curcubita pepo* L. Seeds (80 mg) and *Sabal serrulata* fruits (80 mg). The 2 extracts separately standardised with respect to a batchwise controlled total content of specific phytosterols.

The placebo tablets were identical in smell, consistency, shape, colour and taste to the active compound. The tablets were swallowed whole in a dose of 2 tablets 3 times a day. The duration of treatment was 3 months.

The patients were randomly allocated to receive either active compound or placebo according to a centrally controlled code list. At the conclusion of the study 26 patients had received active therapy and 27 placebo, the 2 groups being stratified.

The subjective variables studied were (1) difficulties with voiding, (2) frequency of urination during the day, (3) nocturia. The subjective symptoms were assessed as follows: much better, better, the same, worse.

The objective parameters were (1) urinary flow rate measured in ml/s, (2) voiding time measured in seconds, (3) residual volume. In most patients this was determined by catheterisation, but in 9 cases (5 in the active treatment group and 4 in the placebo group) residual urine was determined by ultrasound. For each individual patient the same method was used both before and after treatment.

The subjective variables were tested for significance with the Mann Whitney U test and the objective variables with Student's t test, first through pairwise comparisons before and after treatment within each group. Thereafter an intergroup comparison of the respective mean differences was done. Non-parametric tests gave the same results as the t test.

Results

Of the 55 patients entered into the study, 2 were withdrawn: 1 because of alcoholism and the other because of acute urinary retention requiring operative treatment. The result of the randomisation of patients is shown in Table 1. The 2 groups were evenly matched, with no significant differences in the variables ($P < 0.1$).

The results of the subjective and objective parameters studied showed a statistically significant improvement in patients treated with Curbicin and no change in those receiving placebo (Table 2).

No untoward side effects were reported.

Discussion

The results of this study showed a significant subjective and objective improvement in patients treated with Curbicin. The difference between these results and those of the earlier pilot study (Carbin and Eliasson, 1989), where improvement was found in only 1 variable, nocturia, may be explained by poor satisfaction between the groups and by the fact that in the present study the preparation contained an increased amount of extract from *Sabal serrulata* (80 instead of 15 mg). There was also a refinement of the extraction process for *Sabal serrulata*.

These findings compare favourably with those of earlier reports on the use of extracts from dwarf palms (Mandressi et al., 1987). The treatment of pronounced symptoms of prostatic outflow tract obstruction is undoubtedly surgical. However, milder symptoms may be present for a considerable period of time while the patient is awaiting surgery because of coexisting disease. In both of these situations there is need for effective medical treatment to alleviate symptoms. Further long-term studies with Curbicin will indicate the benefits of this compound in the treatment of patients with mild symptoms of outflow tract obstruction due to prostatic hyperplasia.

Table 1 Results of randomisation

	<i>Curbicin (n=26)</i>			<i>Placebo (n=27)</i>		
	<i>Mean</i>	<i>Range</i>	<i>SD</i>	<i>Mean</i>	<i>Range</i>	<i>SD</i>
Age (years)	62.0	52-72	±6.7	61.2	51-72	±5.8
Flow (ml/s)	6.8	4.2-9.8	±1.4	6.6	4.1-9.2	±1.3
Micturition time (s)	16.2	12.2-20.7	±1.7	15.6	12.2-22.0	±2.4
Residual volume (ml)	135	55-225	±44	128.0	75-220	±39
Diurnal frequency	7.3	5-9	±1.3	7.8	5.5-10	±1.1
Nocturnal frequency	1.9	0.5-4	±0.6	2.1	1.5-3	±0.6
Duration of illness (years)	3.0	1-7	±1.8	3.2	1-8	±1.9

Table 2 Effect of Treatment on the Variables (means and standard deviations)

	<i>Preparation</i>	<i>Mean value before treatment</i>	<i>Mean value after 3 month</i>	<i>Difference between mean values</i>	<i>P value within the groups</i>
		Urinary flow (ml/s)	Curbicin	6.7±1.4	9.7±3.6
	Placebo	6.6±1.3	6.9±1.8	+0.3±1.7	NS
Micturition time (s)	Curbicin	16.2±1.7	13.8±2.8	-2.4±3.6	<0.01
	Placebo	15.4±2.4	14.9±1.9	-0.7±2.9	NS
Residual volume (ml)	Curbicin	135.0±43.9	92.5±48	-42.5±62.1	<0.01
	Placebo	127.6±39.0	120.0±37.5	-7.6±22.9	NS
Diurnal frequency	Curbicin	7.3±1.3	6.3±1.0	-1.0±1.5	0.05
	Placebo	7.8±1.1	7.9±0.8	+0.1±0.8	NS
Nocturnal frequency	Curbicin	1.9±0.6	1.4±0.7	0.6±0.7	+-
	Placebo	2.1±0.7	2.0±0.9	-0.1±0.6	NS

<i>Subjective variables</i>	<i>Preparation</i>					<i>P value between groups</i>
		<i>Much better</i>	<i>Better</i>	<i>The same</i>	<i>Worse</i>	
Dysuria	Curbicin	10	11	4	1	<0.001
	Placebo	1	4	14	8	
Patient's evaluation of therapy	Curbicin	6	16	3	1	<0.001
	Placebo	0	3	19	5	

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