A double-blind trial of an extract of the plant *Serenoa repens* in benign prostatic hyperplasia

The prostate is a hormonodependent gland under the control of dihydrotestosterone acting at the level of the prostatic androgen receptor (Wilson, 1980). Thus castration has long been known to result in an atrophy of the prostate, an effect which can be reversed by the administration of testosterone. Benign prostatic hyperplasia (BPH), an enlargement of the prostate, results in a restriction of the urinary tract giving rise to dysuria, nocturia and frequent and poor urinary flow. BPH has been shown to result from an accumulation of dihydrotestosterone in the prostate (Siiteri & Wilson, 1970; Hammond, 978) acting at the level of the androgen receptor. To date the use of androgen receptor antagonists in the treatment of BPH has been complicated by their severe side-effects.

The hexane extract (PA109) of the fruit of the American dwarf palm tree *Serenoa repens B* has been shown to have antiandrogenic properties (Stenger *et al.*, 1982) through a direct action at the level of the androgen receptor (Briley *et al.*, 1983; Carilla *et al.*, 1984) and the inhibition of the enzyme testosterone-5-α-reductase (Sultan *et al.*, 1984).

We report here the results of a double-blind clinical trial of the efficacy of PA109 (commercialised in France as Permixon®) in prostatic hyperplasia.

The double-blind, placebo-controlled study was performed with 110 outpatients (55 PA109, 55 placebo). The symptoms of dysuria, nocturia and frequent and poor urinary flow, present in all subjects, were assessed. Investigations involved were flow rate and cystographic post-micturition residual volume. Exclusion criteria included: patients with an acute or unstable episode, adenomas requiring early surgery, carcinoma of the prostate or prostatic syndromes associated with other genito-urinary conditions. Patients were assigned to two comparable groups and received 320 mg per day (2 × 80 mg × 2) of PA109 or placebo. Before, and after 30 days' treatment the following were assessed; nocturia, intensity of dysuria, flow rate, post-micturition residue, self-rating by the patient and global rating by the physician.

PA109 (Permixon®) was used as tablets containing 80 mg of the liposterolic extract of *Serenoa repens*. Permixon is produced by P. F. Médicaments, 125 rue de la Faisanderie, 75116 Paris (French marketing authorisation number 324.808.3; 26 juin 1981). The usual dosage is 2 tablets twice daily.

Ninety-four patients were included in the analysis (44 placebo and 50 PA109). Eight patients were not available for terminal examination (six placebo and two PA109) and eight

Table 1 Effect of treatment with PA109 on the objective and subjective signs of benign prostatic hyperplasia

Criteria		n	*Before treatment* Mean ± s.e. mean	*After treatment* Mean ± s.e. mean	*% difference*	*Intragroup* P	*Intergroup* P
Nocturia (number of times)	PA109	47	3.12 ± 0.84	1.69 ± 0.82	− 45.8	< 0.001	< 0.001
	Placebo	41	3.20 ± 0.77	2.72 ± 0.89	− 15.0	< 0.001	
Flow rate (ml/s)	PA109	46	5.35 ± 1.51	8.05 ± 2.47	+ 50.5	< 0.001	< 0.001
	Placebo	39	5.04 ± 1.64	5.29 ± 2.10	+ 5.0	NS	
Post-micturition residue (ml)	PA109	44	94.7 ± 26.9	55.1 ± 39.6	− 41.9	< 0.001	< 0.001
	Placebo	34	91.3 ± 45.2	100.0 ± 60.9	+ 9.3	NS	

Evaluations		n	*Greatly improved*	*Improved*	*Unchanged or worsened*	χ^2	P
Dysuria	PA109	45	16	22	7	23.8	< 0.001
	Placebo	44	0	22	22		
Patient self-rating	PA109	50	11	33	6	39.1	< 0.001
	Placebo	44	0	30	14		
Physician's rating	PA109	50	14	31	5	53.4	< 0.001
	Placebo	44	0	16	28		

patients received antibiotic treatment during the study (five placebo and three PA109). Data were analysed using the paired *t*-test for quantitative values or the chi-squared test for qualitative results (Table 1).

As can be seen from Table 1 both objective and subjective signs were improved. This improvement was significantly superior to that achieved with placebo. Thus as predicted by pharmacological and biochemical studies PA109 would therefore appear to be a useful therapeutic tool in the treatment of benign prostatic hyperplasia.

PA109 was extremely well tolerated with less side-effects being reported during the study by patients receiving PA109 (five reports) than those receiving placebo (11 reports). All side-effects reported were minor (e.g. headache). In addition standard blood chemistry measurements showed no alterations.

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Information, compliance and side-effects in patients on dothiepin

Myers & Calvert (1984) planned their study to determine whether it is the factual content of verbal and written information or the extra attention given to the patient in providing the information which improve compliance. Their results suggest that the 'attention-placebo' effect seems more important, but the differences between their experimental groups were small and cannot be regarded as conclusive.

There are two ways in which the analysis of their data could be sharpened to yield a clearer and probably more reliable interpretation. One factor that must be considered is dose. The patients were prescribed 'dothiepin 50–100 mg at night'. It does not make sense to lump patients taking 50 mg at night with patients taking twice as much. The larger dose would be likely to cause more frequent and more troublesome side-effects, and so a lower rate of compliance. An analysis of these two dose groups within groups A, B and C is therefore necessary. The data for patients in whom the dose was changed would need to be analysed separately.