

THE EFFECT OF PERMIXON ON ANDROGEN RECEPTORS

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Abstract. Permixon, the liposterolic extract of the plant *Serenoa Repens* is a recently introduced drug for the treatment of benign prostatic hyperplasia. The effect of Permixon on dihydrotestosterone and testosterone binding by eleven different tissue specimens was tested. The drug reduced the mean uptake of both hormones by 40.9% and 41.9% respectively in all tissue specimens. Since hirsutism and virilism are among other gynecological problems caused either by excessive androgen stimulation or excess endorgan response, we suggest that Permixon could be a useful treatment in such conditions and recommend further investigations of the possible therapeutic values of the drug in gynecological practice.

INTRODUCTION

Recently it was reported that the liposterolic extract of the plant *Serenoa Repens* functions as a competitive inhibitor of the binding of androgens to the cytosolic receptors in rat prostate (1). In a double-blind trial on humans the drug, was found to be more effective than placebo therapy in the treatment of benign prostatic hyperplasia (2).

We decided to investigate the possible antiandrogenic effect of Permixon on a variety of human tissues.

METHODS

Eleven specimens of different tissues were recovered from patients during the normal course of surgery (Table 1). Specimen 1 was obtained from the uterus of a 42-year-old patient who had undergone a vaginal hysterectomy operation for prolapse. Specimens 2 and 3 were those of vaginal skin removed during the course of anterior colporrhaphy procedures in 30 and 33-year-old patients, respectively. Specimens 4 and 5 were obtained from abdominal wall wound edges during the course of surgery for Fallopian tube reconstruction in a 30-year-old and minilaparotomy procedure for tubal ligation in a 32-year-old patient. None of the above 5 cases was known to have received any medication prior to surgery.

The last 5 specimens were recovered following circumcision of newborns. The procedure, a part of Moslem tradition, is carried out routinely at this hospital within 3 days of the birth of a male baby.

All tissue specimens were stored in liquid nitrogen (Dewar

container) at -196°C . At the time of processing, 500mg of each specimen was homogenized in 1 ml of a buffer solution (alcohol buffer) using an Ultra-turrax for 3 minutes at 0°C , centrifuged for one hour (100,00 g) at 4°C temperature and the supernatant of the tissue extract (S.F.T.) was kept at 0°C , for further use.

The amount of dihydrotestosterone required for obtaining a full saturation of cytosol receptors in tissue extract was determined. Increasing quantities (50 K-200 μl) of radioactive dihydrotestosterone (Radio Immune Assay RIA kit, Amersham, Amersham International PLC, Amersham, Bucks, England), were added to 100 μl of tissue extract (S.F.T.) of the first 4 specimens. An LKB counter (Compu Gamma Counter) was used to determine the radioactive dihydrotestosterone (RADT) uptake. Maximum cytosol receptor saturation was obtained with 100 μl of RADT for 100 μl of SFT.

The liposterolic extract of the plant *Serenoa Repens* (Permixon) was dissolved (0.080g) in ethyl alcohol 5% and two different concentrations of the drug were prepared (P1=1/100 and P2=1/250). P1 and P2 were tested with different samples of tissues and RADT. We decided to use P1 for the test as it produced more dislodgement of RADT. Two assay tubes were prepared from each of the eleven SFT.

Group A (11 tubes) each contained the following: 100 μl of SFT + 100 μl RADT and 100 μl of P1. Group B (11 tubes) each contained 100 μl of SFT and 100 μl of RADT only. Both groups (22 tubes) were incubated for one hour at 20°C , then 300 μl of charcoal dextran was added to each tube. The mixture was then centrifuged (5000 g) for 15 min at 4°C . A 500 μl sample of the supernatant in each tube was added to 10 ml of liquid scintillator and RADT uptake was measured and compared in both groups.

Permixon effect was also tested on testosterone receptors using radioactive testosterone (RAT) with alteration of the pro-

Table I. Tissue type and radioactive dihydrotestosterone uptake with and without perimixon.

Specimen No.	Type of tissue	Sex	Age	RADT* uptake (group B) CPM**	RADT uptake (group A) CPM**	RADT uptake (blockage) (%)
1	Myometrium (hysterectomy)	F	42 yrs	2 866.5	1 706.0	36
2	Vaginal skin	F	30 yrs	6 866.5	4 845.0	30
3	Vaginal skin	F	33 yrs	3 147.0	1 800.0	43
4	Abdominal wall skin	F	30 yrs	5 189.0	3 617.0	31
5	Abdominal wall skin	F	32 yrs	6 035.0	3 440.0	43
6	Prepuce (circumcision)	M	3 days	2 841.0	1 264.0	57
7	Prepuce (circumcision)	M	3 days	2 830.0	1 641.0	42
8	Prepuce (circumcision)	M	3 days	2 821.0	1 394.0	61
9	Prepuce (circumcision)	M	3 days	2 302.0	1 120.0	61
10	Prepuce (circumcision)	M	3 days	1 838.0	1 199.0	35
11	Prepuce (circumcision)	M	3 days	1 587.0	1 105.0	31
Total mean				3 483.9	2 102.82	40.62
S.D.				+ 1 747.9	2 102.82	9.2

* RADT: Radioactive dihydrotestosterone.

** CPM: Counts per minute.

cedures according to manufacture's instructions (Radio Immune Assay Kit, Amersham International, Burks England) using the same methodology as for RADT. Seven specimens were tested for testosterone receptors; four specimens were not tested because of inadequacy of SFT. The amount of RAT uptake was measured and compared in both groups.

All the above results were statistically evaluated using the Student's t-test.

RESULTS

Eleven different specimens were tested with (Group A) and without (Group B) the drug Perimixon, to deter-

mine the effect of the drug on dihydrotestosterone binding by the cytosol receptors. All tested specimens showed 2 significant ($P < 0.01$) decrease in RADT uptake (Table I). P1 concentration of the drug decreased RADT uptake by up to 30–57% (Mean + S.D., 40.09% + 9.2).

P1 concentration of the drug also reduced significantly ($P < 0.005$) the radioactive testosterone (RAT) uptake by the different tissue specimens. Table II, RAT uptake decreased by 31–48% (mean + S.D., 41.9% + 6.4). With the use of P1 concentration of the drug.

Table II. Effect of Perimixon on radioactive testosterone uptake.

Specimen No.	Type of tissue	RAT* uptake (group B) CPM**	RAT uptake (group A) CPM**	RADT uptake (blockage) (%)
5	Abdominal wall skin	3 209.0	2 007.0	38
6	Prepuce (circumcision)	3 415.0	2 015.0	31
7	Prepuce (circumcision)	3 240.0	1 701.0	48
8	Prepuce (circumcision)	2 656.0	1 395.0	48
9	Prepuce (circumcision)	2 325.0	1 418.0	39
10	Prepuce (circumcision)	4 009.0	2 133.5	47
11	Prepuce (circumcision)	2 005.0	1 182.0	42
Total mean		2 979.9	1 893.0	41.9
S.D.		+ 689.5	+ 370.0	+ 6.4

* RAT: Radioactive testosterone.

** CPM: Counts per minute.

DISCUSSION

Our study showed that the drug reduces significantly the RADT and RAT uptake by cytosol receptors of human skin and other tissues in-vitro. This finding could be of great therapeutic value in the management of female hirsutism, acne androgenic effect of polycystic ovary syndrome and probably other endocrine disorders.

CRPF Laboratories Fabre, France (manufacturing company of Permixon) have suggested that among other physiological effects of the drug on animals is a reduction of capillary permeability. Also they claimed that the drug has no effect on normal secretion of gonadotrophins on the weight of uterus in mice, no estrogenic effect, and no effect on the normal menstrual cycle of female mice.

We would like to introduce this drug to gynecologists and advocate further research in its clinical usefulness. At this time we are considering a double-blind controlled trial of the drug on hirsute patients

and watching for further reports of any possible side effects observed by urologists using the drug on males with senile enlargement of the prostate.

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