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Effect of Phenoxybenzamine on Penile Tumescence in Diabetic Men

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Summary. 10 diabetic men complaining of impotence were treated with phenoxybenzamine. Nocturnal penile tumescence was monitored. No statistically significant changes occured.

Key words: Diabetes mellitus, Sexual dysfunction, Nocturnal penile tumescence, Response to alpha adrenergic blockaders.

Introduction

Many diabetic patients present with a chief complaint of impotence [4, 6]. The work of Karacan et al. [10, 11] and Hursch [9], demonstrating the characteristics of nocturnal penile tumescence (NPT) in the general male population, and the work of Karacan et al. [12] in the diabetic male in particular, have enabled a more objective evaluation of this impotence.

Penile erection is a vascular engorgement phenomenon whose control is primarily mediated by the autonomic nervous system. Ahlquist [1] showed the existence of alpha and beta adrenergic receptors, alpha stimulation causing smooth muscle contraction, beta stimulation causing smooth muscle relaxation. Domer et al. [5] have shown in cats that beta-adrenergic stimulation and alpha adrenergic blockade produced penile engorgement. Levin and Wein [11] have shown an alpha adrenergic receptor density ten times greater than beta adrenergic density in the human corpus cavernosum tissue. However, the exact adrenergic role in tumescence is as yet unknown. Using the diabetic male as a model for impotence possibly caused by autonomic peripheral neuropathy, we have treated 10 diabetic males complaining of impotence with phenoxybenzamine, an alpha adrenergic blocking drug and monitored penile response using the NPT monitor.

Materials and Methods

Ten diabetic men from ages of 34–68 years with a mean of 48 ± 11.5 years having no known vascular complications of the disease were studied (Table 1). All patients presented with complaints of impotence characterised by either total loss of erections, erections insufficient for penetration, or decrease in tumescence with a marked decrease in erectile duration. No patient had any urinary complaints or signs referable to autonomic neuropathy other than that of impotence. All patients described the presence of ejaculations. Patients were hospitalised for one night and were monitored for NPT using the AMSI 7600 nocturnal penile tumescence monitor, using two mercury filled rubber strain gauges at the penile tip and base. Sleep was reported through hourly nursing staff inspections.

The following criteria were recorded before and after treatment: number of erectile episodes; total tumescence time; % time in erectile activity; mean erection duration; erection of maximum duration; mean circumferential change for all episodes (penile tips and penile base) and greatest circumferential change (penile tip and base). Patients were then given 10 ml of phenoxybenzamine at night prior to sleep for thirty nights. They were again hospitalised for another night of monitoring NPT.

Total time of monitoring is reported as examination time. An erectile episode is defined as a deflection of at least 10% of the maximal erectile circumference change. Average and maximal circumference changes are reported in millimeters. Statistical analysis was by the paired *t*-test comparing the mean difference for each variable

Table 1. Patient data

Patient	Age	Children	Years diabetic	Treatment
1	48	3	22	Oral hypoglycemics
2	34	2	1/2	Insulin
3	51	3	10	Oral hypoglycemics
4	47	3	5	Oral hypoglycemics
5	68	3	1/12	Diet
6	59	3	3	Insulin
7	44	3	12	Oral hypoglycemics
8	40	2	15	Insulin
9	59	2	3	Diet
10	32	0	5	Insulin

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Table 2. Post minus pre-therapy differences

Patient	1	2	3	4	5	6	7	8	9	10	Mean	±S.D.
Number of erectile episodes	−8	−8	−4	8	2	0	5	−1	−3	0	0.9	5.3
Total tumescence time (min)	−5	33	−107	67	69	77	−78	2	−119	−14	−7.5	72.7
% time in erectile activity	−6	9	−22	13	11	17	−25	1	−23	−4	−2.9	15.9
Mean erection duration (min)	9.2	6.7	−2	−19.7	2.4	14.5	−13.9	−1.7	−6.5	−2.3	−0.99	10.4
Erection of maximum duration (min)	1	33	23	−13	1	17	−54	−17	−2	−27	−3.8	25.5
Mean circumferential change for all erectile episodes (mm)												
Penile tip	4	1	−2	−6	6	6	0	0	−10	4	0.3	5.2
Penile base	3	−1	2	−2	5	0	0	1	− 8	5	0.5	7.7
Greatest circumferential change (mm)												
Penile tip	−4	−1	−7	1	2	8	7	−1	−15	−4	−1.2	6.6
Penile base	4	−8	2	1	−9	−2	−2	0	−8	−2	−2	4.7

before and after treatment to zero. The consistancy of trends for all variables in each patient was tested by the non-parametic Quade test [3] based on ranking the individuals for each variable and comparing the sum of the ranks for each individual.

Results (Table 2)

Before and after treatment with phenoxybenzamine all patients had at least one erectile episode lasting at least 30 min and one erection with an increase in circumference of 20 mm. No patient reported any improvement in his subjective complaints during treatment with phenoxybenzamine. Three patients reported dizziness from the medication but were able to continue therapy. The only measured variables showing improvement after treatment were the mean post minus pre-therapy mean circumferential difference for all erectile episodes. Here the penile tip showed a mean 0.3 ± 5.2 mm increase and the penile base showed a mean 0.5 ± 7.7 mm increase. The mean post-minus pre-therapy circumferential difference for the single most tumescent episode showed a mean of 1.2 ± 6.6 mm decrease for the penile tip and a 2 ± 4.7 mm decrease for the penile base. The post-minus pre-therapy difference in the number of erectile episodes showed a mean decrease of 0.9 ± 5.3 erectile episodes.

The post-minus pre-therapy difference in % time in erectile activity showed a mean decrease of 2.9 ± 15.9%, while the mean difference in total time in tumescence decreased by 7.5 ± 72 min. The mean duration of all erectile episodes showed a post-minus pre-therapy difference decrease of 0.99 ± 10.4 min. The mean time interval difference for the tumescent episode of maximum duration post minus pre-therapy decreased 3.8 ± 25.5 min. Mean differences for post-minus pre-therapy did not differ significantly for any of the above variables, paired t-test $p > 0.50$.

There were two patients, number 5 and 6, who showed improvement in eight of the nine variables post therapy and one patient, number 9, whose post treatment results were worse in all variables. In all other patients the trend was inconsistent for all variables. The Quade test showed no statistically significant consistent trend in individuals for the variable tested.

Discussion

The work of Domer et al. [5] and Levin and Wein [14] seems to suggest that theoretically a trial of alpha blockaders might augment erectile function in the psychogenically impotent patient whose sole problem is conscious initiation of the erectile event. The phenomenon of NPT should be uneffected here, augmentation should theoretically occur as the local physiological system, i.e. the penis, sacral cord, peripheral nerve supply and vascular perfusion, are intact.

Diabetes with its concommitant complication of small vessel disease and peripheral neuropathy certainly seems to offer an organic aetiology for impotence. Hence, depending upon the severity of the disease, erectile augmentation via alpha adrenergic blockaders may or may not occur.

Karacan et al. [12] have shown that in diabetic men there is a decrease in erectile duration, tumescence and total time in tumescence.

Hosking et al. [8] showed that in 30 diabetic patients the NPT was affected in 20% (6 patients). Here the maximal

penile circumferential change was less than 15 mm. All six of these patients had peripheral neuropathy.

In our group of patients, despite complaints of impotence, NPT monitoring revealed a functioning erectile mechanism.

No statistically significant effect occured with phenoxybenzamine treatment in any of the variables measured. Nor were there any statistically significant trends within individual patients for all the measured variables concerning duration or circumferential changes. Several factors may have contributed to this lack of response. There is the possibility that the dose of phenoxybenzamine was too low; attempts to increase the dose, however, were met with patient non-compliance because of the side effect of orthostatic hypotension. The complication of retrograde ejaculation at high doses of phenoxybenzamine introduces a further complication in a patient population whose sexual function is already impaired. It is possible that higher doses may indeed have a beneficial effect. Phenoxybenzamine in low doses may be more active in vivo at the $alpha_2$ pre-synaptic receptors rather than at the $alpha_1$ post-synaptic receptors [7]. This would inhibit the autoregulatory mechanism of norepinepherine resulting in the presentation of more norepinepherine to the $alpha_1$ post-synaptic receptors. This in turn would neutralise the beta activity thus preventing vasodilation and augmentation of the engorgement of the corpora cavernosa. Finally, without entering into the discussion concerning the aetiology of impotence in diabetes [13] it is possible that a diabetic population with impotence and/or neuropathy might have sufficient arteriosclerotic changes to effect penile erection where the mechanical obstruction to blood flow is the main cause.

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