

Sildenafil Citrate In Diabetics With Hypertension And Erectile Dysfunction

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Citation

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Abstract

With the introduction of effective pharmacological agents for treatment of erectile dysfunction, more men are seeking treatment. The underlying cause of the erectile dysfunction is usually a chronic medical illness.

(1) Atherosclerosis of the penile artery or the drugs used to reduce

cardiovascular risk factors have been implicated in its causation. (2) Sildenafil, acts by activation of nitric oxide (NO)- Cyclic guanosine monophosphate (cGMP) pathway during sexual stimulation. Sildenafil alone can cause mean peak reduction in systolic/diastolic blood pressure of 10/7 mm that are not dose related, where as heart rate remains unchanged. (3) Diabetics with ED do have concomitant hypertension. Many anti hypertensive drugs are known to cause and aggravate ED. Sildenafil is known to reduce blood pressure in healthy adults (3). In one study concomitant use of amlodipine & Sildenafil show synergistic reduction in blood pressure (3). We thought of utilizing sildenafil citrate to treat ED in patients with type 2 diabetes mellitus & note its effect on blood pressure.

SUBJECTS AND METHODS

To study the blood pressure lowering effect of sildenafil in male diabetic patients with erectile dysfunction (ED), 68 male patients having type 2 diabetes mellitus were screened in the medical OPD. The baseline data regarding the duration of diabetes, duration of ED was recorded. Complications of diabetes like neuropathy, nephropathy, retinopathy, hypertension and sexual dysfunctions were looked for. Patients without significant hypertension, having postural hypotension, without erectile dysfunction, and those already on anti hypertensive drugs were excluded. 26 Patients with moderate hypertension along with erectile dysfunction were enrolled for the study. All these patients were on oral hypoglycemic agents and had a good control of diabetes. A written consent was taken and they were explained the details of the study as well as the side effects of sildenafil citrate. All these willing patients were then prescribed sildenafil citrate in the dose of 25 mg to be taken once a day at bedtime. The blood pressure was recorded in the OPD at the beginning of the study and after 2 weeks of

drug therapy. Two readings were taken 15 minutes apart and the mean of these two readings was recorded on both the occasions. Patients were taught to record their blood pressure. They were then asked to record their blood pressure every other day and bring the record to the OPD at the end of two weeks. This was done to look for any precipitous fall in blood pressure. The improvement in erectile dysfunction was noted by recording patient's response, at the beginning and at the end of 2 weeks, on a scale of 1 to 10 with 1 denoting no erection and 10 denoting adequate erection. The sexual performance satisfaction was also noted on a scale of 1 to 10 with 10 being adequate sexual performance.

RESULTS

26 male diabetic patients were enrolled for the study but only 24 were taken up for analysis. Two patients dropped out due to severe adverse effects from day 2 onwards. Mean age was 44 ± 12.5 years. All of them had type 2 diabetes mellitus and were well controlled on oral hypoglycemic

agents. Mean Duration of diabetes mellitus 8.5 \pm 1.75 years. All of them had moderate hypertension. All the patients enrolled had erectile dysfunction since some time. Mean Duration of erectile dysfunction was 4 \pm 1.5 years. Associated complications noted in these patients were background retinopathy in 14, nephropathy, in the form of micro albuminuria in 8 and neuropathy, predominantly sensory (distal symmetrical) in 6. There were no symptomatic macro vascular complications in these patients. The systolic blood pressure was in the range of 150-160 mm Hg (mean SBP 156 \pm 4.5 mmHg) and diastolic blood pressure between 100-105 mm Hg (mean DBP 102 \pm 2.5 mmHg). Decline in BP was noted from 2nd day onwards. The blood pressure recorded at the end of two week showed a mean decline of -8.5 ± 3.5 mm Hg systolic and -5.4 ± 1.4 mm Hg diastolic. Severe side effects as headache & giddiness noted in 2 patients on day 2 & both of them dropped out from the study. Minor adverse effects noted were Flushing in 6 / 24 (25%), Headache in 5 / 24 (16.5%) & Dizziness in one patient (2.4%).

The improvement in erectile dysfunction was noted in 16 out of 22 patients with the 25 mg dose. The mean score for erectile response at the start of the study was 1.5 which improved at the end of 2 weeks to 5.8 ± 1.0 , in 16 patients and in the rest the improvement was marginal up to 2.0 ± 0.5 only. The performance satisfaction rose from 1.0 to 6.5 in 16 patients and in the rest it failed to improve.

Figure 1

SBP before therapy (BT) & after 2 weeks of therapy (AT)

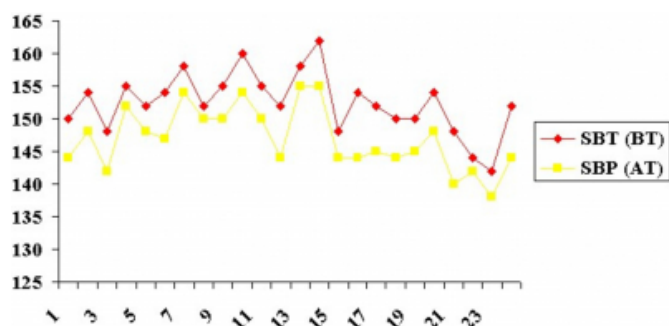
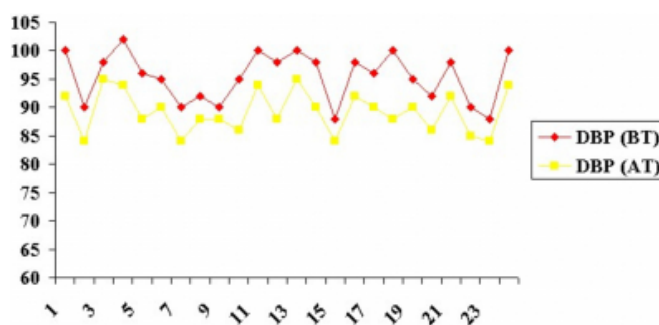


Figure 2

DBP before (BT) & after 2 weeks of therapy (AT)



DISCUSSION

Our study results have shown that sildenafil if used regularly alone may be responsible for small yet significant decrease in blood pressure in diabetics with hypertension and ED.

It is known that in diabetic as well as non-diabetic patients, correcting hypertension reduces incidence of fatal, non-fatal strokes & risk of MI (4). The risk of hypertension causing microvascular disease and accelerating progression of retinopathy & nephropathy in diabetics are also well known. It is now clear that effective lowering of blood pressure can definitely slow the rate of decline in renal functions and with good control of blood pressure renal dysfunction may improve. The UKPDS trial (5) has proven beyond doubt that lowering blood pressure in diabetic patients significantly reduces the risk of cardiovascular mortality in diabetic-hypertensive patients. Similar results were reported in HOT study (6), where lowering blood pressure to less than 85 mm diastolic resulted in significantly lower cardiovascular risk in diabetic subset of study population.

Since a small decrease in blood pressure may be beneficial in diabetics in preventing the progression of renal and cardiovascular dysfunction (7), sildenafil can be used in these patients to achieve double benefit.

In one study where sildenafil was co administered with 5 or 10 mg/day of amlodipine, the mean maximum change from base line in systolic and diastolic blood pressure between sildenafil plus amlodipine and placebo from amlodipine treatment group were -8 mm and -7 mm respectively. Indicating that amlodipine had synergistic reduction in blood pressure when sildenafil was added. (8) This decrease in blood pressure is comparable to the decrease reported in healthy men taking sildenafil alone. (8) Barring 2 patients, our patients did not develop any significant, incapacitating side effects.

Endothelial dysfunction and inactivation of nitric oxide (NO) by advanced glycation end products, glycosylated hemoglobin, free radicals & oxidized LDL have been implicated in causation of diabetic microvascular complications (9). A drug acting through nitric oxide synthase-cGMP pathway, increasing the level of nitric oxide at tissue level may therefore might be helpful in retarding progression of diabetic microvascular complications too. This makes sildenafil an ideal drug for diabetics with hypertension and other complications. However, this drug is not approved by FDA for use as an anti hypertensive drug. Further research is needed in this regard.

Since the drug is costly and better, cheaper alternative agents are available for lowering blood pressure, its use alone as blood pressure lowering agent is debatable. However it can safely be administered in diabetics with ED & mild to moderate hypertension. It can also be combined with other anti hypertensive drugs relatively safely to get synergistic effect.

This is just a small study of limited duration, however we need larger trials to evaluate the role of sildenafil citrate alone, in type 2 diabetic males with hypertension and erectile dysfunction.

CONCLUSIONS

Sildenafil Citrate, if used regularly may be responsible for small yet significant decrease in blood pressure in diabetic hypertensive patients with erectile dysfunction along with improvement in their sexual dysfunction.

This is just an observation, however we need larger trials to evaluate the role of sildenafil citrate alone, in type 2 diabetic males with co-existent hypertension and erectile dysfunction.

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