

# The Use of Sildenafil in Patients with Erectile Dysfunction in Relation to Diabetes Mellitus – A Study of 1,511 Patients

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## ABSTRACT

**Erectile dysfunction (ED) seriously impairs the quality of life. Patients with diabetes mellitus (DM) are prone to ED due to various factors, including vasculopathy, neuropathy and sex hormone abnormalities. This is a retrospective study involving 1,511 patients taking sildenafil. Patients with DM have significantly more comorbidities like hypertension and ischaemic heart disease. They are also more likely to be on medications which may affect erectile function, including various antihypertensive drugs. 77.9% of patients with DM reported success with sildenafil, as compared to 86.5% of patients without DM. A significant number of patients with DM require a higher dose of sildenafil as compared to those without DM.**

**Keywords: Sildenafil, Viagra, diabetes, erectile dysfunction, impotence**

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## INTRODUCTION

Erectile dysfunction (ED) is a condition which seriously impairs quality of life<sup>(1)</sup>. Recently, sildenafil has been proven to be an effective and well tolerated treatment of ED of various aetiologies, including diabetes mellitus (DM)<sup>(2)</sup>. ED in men with DM is often associated with diabetic neuropathy and peripheral vascular disease<sup>(3)</sup>. ED also occurs at an earlier age in men with DM compared to men in the general population<sup>(4)</sup>. There is also a high prevalence (35% to 75%) of ED with diabetes<sup>(5-7)</sup>. Moreover, in men with treated diabetes, the age-adjusted prevalence of complete ED (no erections) is 28%, which was approximately three times higher than that observed in the entire sample of men (10%)<sup>(8)</sup>.

Our study is a retrospective study involving all the patients taking sildenafil, comparing patients with ED and DM and those with ED without DM in terms of demographics, hormonal profile as well as the efficacy of sildenafil.

## METHOD

The population of our multi-centre study involved all the patients taking sildenafil for a period of at least six months from the three hospitals – Changi General Hospital, National University Hospital and Tan Tock Seng Hospital. All the patients were aged 21 years or older. All of them have ED for a duration of at least six months. Those with DM have a disease duration of at least one year. The diagnosis of ED is based on the patient's medical history, physical examination, standard laboratory testing (including hormonal profiles) and other diagnostic procedures (e.g. intracavernosal PGE<sub>1</sub> injections, duplex scans, cavernosometry and cavernosography). Exclusion criteria included the following: penile anatomical deformities that significantly impair erection; a primary diagnosis of sexual disorder other than ED; a major psychiatric disorder that was not well controlled with treatment; spinal cord injury; a history of major haematological, renal, or hepatic abnormalities; stroke or myocardial infarction within the previous six months; active peptic ulcer; hypotension; active proliferative diabetic retinopathy; or regular treatment with nitrates.

The patients were given sildenafil at doses ranging from 12.5 mg to 100 mg. A higher dose of sildenafil was given if the initial dose was ineffective and if they were able to tolerate it. The patients were followed up after six months regarding their assessment of the efficacy of sildenafil on ED. Success in penetration and increased sustenance of erection were taken as target outcomes. The patients were given a global efficacy questionnaire (GEQ), that is whether they thought that their erection has improved, pertaining to the above points. Although various scoring systems have been devised for erectile dysfunction, like the IIEF scores, most of our investigating doctors do not use such scores in their notes, this being one of the limitation of a retrospective study.

The statistical analysis was performed with the aid of SPSS version 9.0.

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Fig. 1 Frequency histograms for age of patients with and without DM.

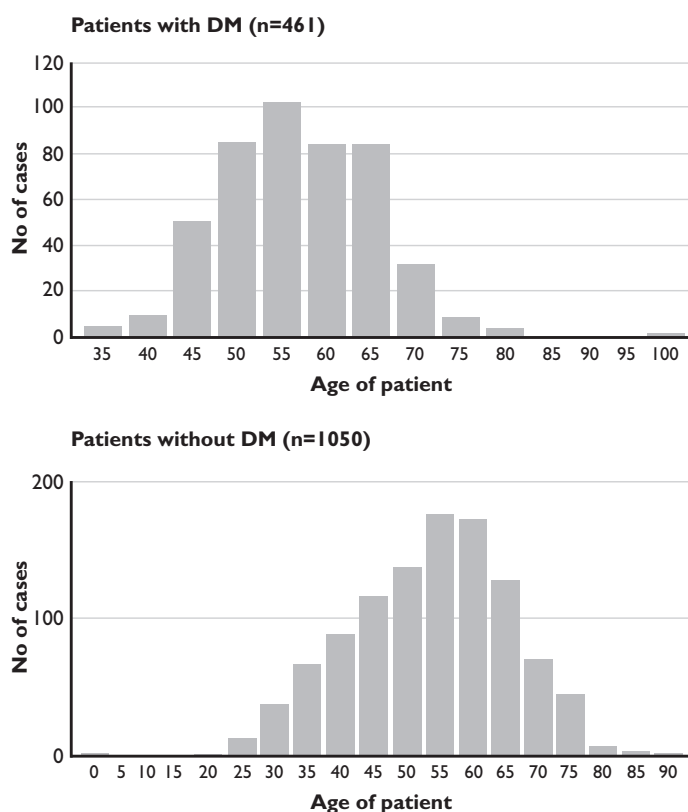
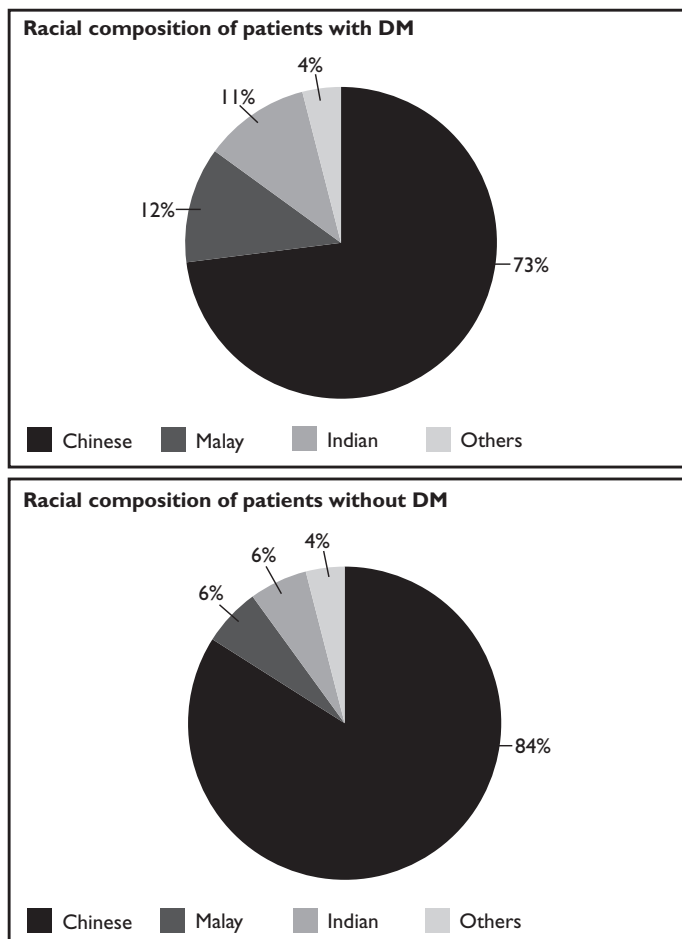


Fig. 2 Racial composition of patients with and without DM.



**RESULTS**

A total of 1,511 patients were studied. Four hundred and sixty-one patients have DM and 1,050 patients do not have DM. The demographics of these two populations in terms of age distribution, racial composition and marital status were similar. The mean ages of patients with DM and those without DM were 56.9 years and 53.5 years respectively. The frequency histograms for the age of these two populations are illustrated in Fig. 1. The racial compositions of these two populations are illustrated in Fig. 2. 64.0% of the patients with DM were married while 63.5% of the patients without DM were married. Mean ages of patient's partners were 65.9 years and 49.5 years respectively for patients with DM and those without DM.

The mean and median durations of DM were 6.5 years and 3 years respectively. For patients with DM, 91.2% were type 2 DM (NIDDM) and 8.8% were type 1 DM (IDDM). Of patients with type 2 DM, 9.9% were on dietary control and 90.1% were on oral hypoglycaemic drugs.

Patients with DM also have significantly more co-morbidities. 40.5% and 10.3% have hypertension and ischaemic heart disease respectively as compared to 28.3% and 4.1% for those without DM.

Patients with DM were more likely than those without DM to be on various drugs that might affect potency, like drugs for hypertension (e.g. ACE inhibitors, beta-blockers and diuretics). 31.9% of patients with DM received antihypertensive drugs as compared to 24.8% of patients without DM. Also patients with DM were more likely to be on multiple drugs – 9.1% were taking two antihypertensive drugs and 1.2% were taking three antihypertensive drugs; whereas the corresponding figures for patients without DM were 5.3% (double drugs) and 0.4% (triple drugs). The drugs used and the number taking these drugs are shown in Fig. 3.

The duration of erectile dysfunction for both populations was similar. The median durations of erectile dysfunction for those with DM and those without DM were both 12 months. The frequency histogram of the erectile dysfunction is illustrated in Fig. 4. Prior to sildenafil being approved for use in Singapore, many patients with ED had tried various other treatments, as illustrated in Fig. 5. Low levels of testosterone were found in 10.6% of patients with DM and 8.3% of patients without DM. FSH, LH and prolactin were also assayed in our patients, and the results are shown in Fig. 6.

Out of the 1,511 patients studied, 912 (60.4%) patients came back for follow-up. The outcome for these patients who returned for follow-up showed

that 77.9% (211/271) of the patients with DM responded to sildenafil while 86.5% (555/641) of the patients without DM reported success ( $p < 0.01$ ).

Our results showed that among the diabetic patients, patients who were insulin dependent diabetics have a lower rate of success (75.0% or 21/28) compared to those on control by diet (78.9% or 15/19) and those on oral hypoglycaemic drugs (82.1% or 184/224). However, the difference was not statistically significant.

Dosages of sildenafil were prescribed as 25 mg, 50 mg and 100 mg. The proportion of patients with DM and without DM taking the higher dose of sildenafil (i.e. 100 mg) were 50.3% and 33.2% respectively ( $p < 0.001$ ). The corresponding proportions taking sildenafil 50 mg were 46.1% (with DM) and 61.2% (without DM). Only one patient without DM (0.1%) used sildenafil 12.5 mg; none of the patients with DM used sildenafil 12.5 mg.

A closer look into the diabetic population showed that the duration of DM of the group reporting success with sildenafil (mean duration 5.7 years, median duration two years) was shorter than the group reporting failure (mean duration 8.4 years, median duration 3.5 years). The data showed that there was a higher proportion of IDDM in the group which do not respond to sildenafil (15.0%) than among the group that do (6.3%), the results however were not statistically significant.

## DISCUSSION

ED is a common complication of diabetes. Despite the increased morbidity associated with ED, the condition remains widely under-diagnosed and inadequately treated. Anecdotal evidence suggests that the loss of self esteem associated with ED may reduce the motivation of patients to manage their diabetes adequately.

The risk of ED increases with both increasing duration of diabetes and metabolic indices of inadequate diabetes control, e.g. concentrations of blood glucose and glycated haemoglobin<sup>(9)</sup>. Vasculogenic ED appears to be the most frequent cause of ED in diabetic men<sup>(10)</sup>. There is a striking overlap between the comorbidities of diabetes and risk factors for ED. Vascular disease, treated or untreated hypertension, peripheral neuropathy and obesity are all significantly more common in diabetic subjects than in their normoglycaemic peers. This is shown by our results as well as other numerous studies<sup>(11-13)</sup>. Also, our results showed that many diabetic patients were more likely to receive long-term treatment with antihypertensive drugs, many of which adversely affect erectile function.

Fig. 3 Antihypertensive drugs taken by patients with and without DM.

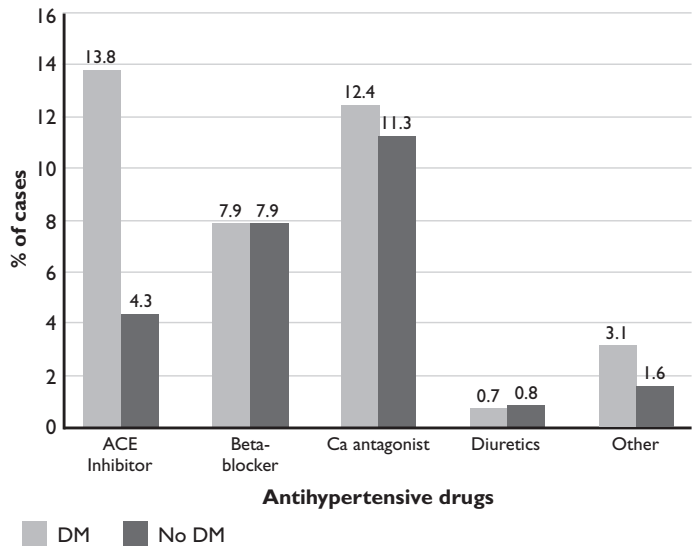
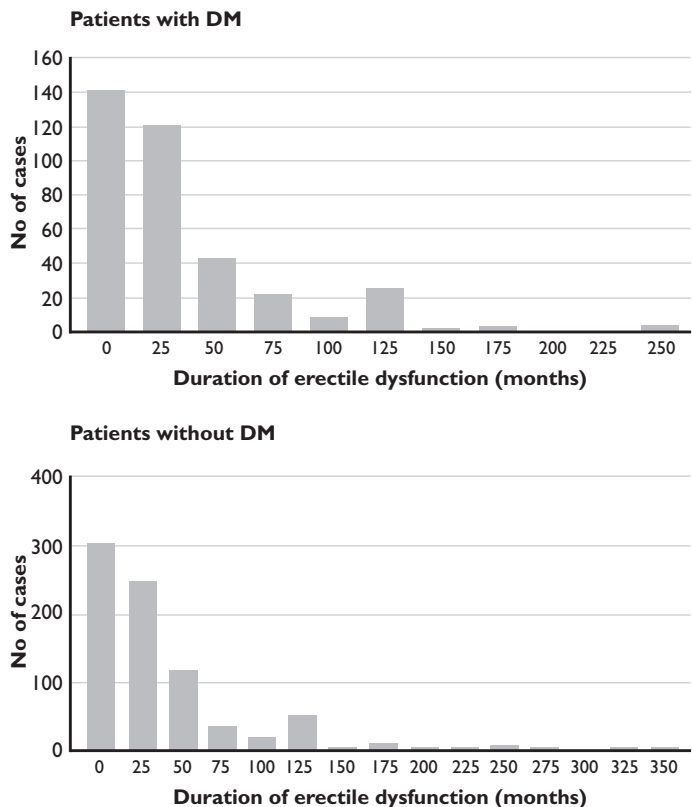
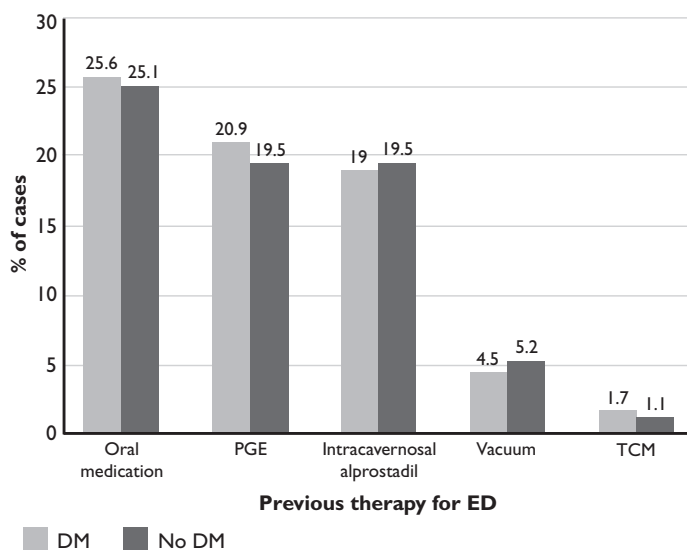
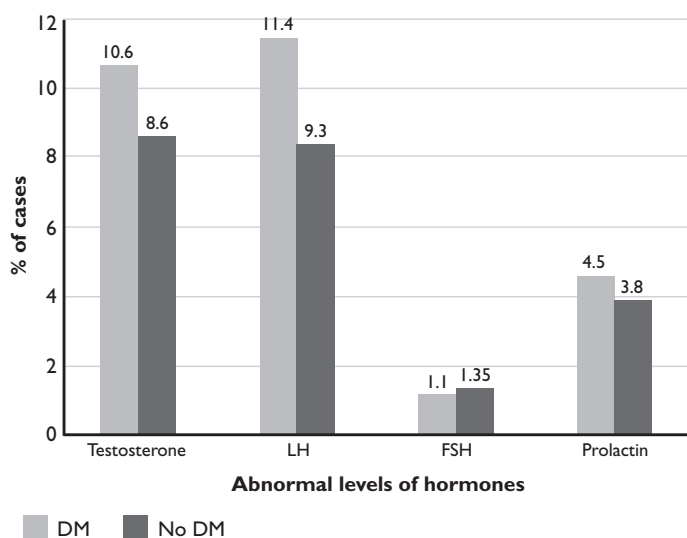


Fig. 4 Frequency histogram for duration of erectile dysfunction for patients with and without DM.



Thiazide diuretics are commonly associated with the development of ED, although their use may be restricted in diabetic patients because of concerns over their adverse metabolic effects. In a study of the treatment of mild hypertension, the effects of five antihypertensive drugs (acebutolol, amlodipine, chlorthalidone, doxazosin and enalapril) on sexual function were studied. It suggested that the only

**Fig. 5** Other treatment for ED prior to the use of sildenafil in patients with and without DM.**Fig. 6** Abnormal levels of hormones in patients with DM and no DM.

group in which ED were not increased was the doxazosin group<sup>(14)</sup>.

Patients with DM are more likely to have sex hormone abnormalities as compared to those without DM. Our study showed that lowered testosterone is found in greater proportion of those patients with DM. Many of the diabetic men with ED may in fact have hypogonadism, which may result from the effect of diabetes on the pituitary gland. It is suggested that some of these patients may benefit from

testosterone therapy, and their response to sildenafil may be better after testosterone replacement<sup>(15)</sup>.

Whilst sildenafil no doubt provides improvement in ED in patients with or without DM, there was a slightly lower success rate for patients with DM (77.9%), as compared to those without DM (86.5%). The success rate among the diabetics with a more severe disease, i.e. the IDDM, was even lower (75.0%). Those patients with DM also required a higher dose of sildenafil.

## CONCLUSION

ED is a common problem in patients with DM. This is due both to vasculopathy as well as neuropathy of DM. There is also a suggestion that sex hormone abnormalities may play a part in the pathogenesis of ED in DM. Sildenafil is an effective treatment in patients with DM, although its success rate is slightly lower and the dose required is higher as compared to patients without DM.

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