Retinal effects of Sildenafil in diabetic patients

Original Article

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Summary:

Background

Sildenafil has been used in the treatment of erectile dysfunction (ED). However it has the disadvantage of many visual disturbances. The aim of this work is to study the effect of sildenafil on diabetic patients which might have ocular problems due to diabetes mellitus.

Materials and Methods:

A total of 30 subjects were enrolled in the study, they were divided into two groups. The control group consisted of 10 healthy subjects but complaining of ED only and the other (20 patients) had diabetes mellitus and ED as well.

All subjects had ocular tests done before and after sildenafil intake.

It was obvious that sildenafil changed visual tests from totally normal for controls, before treatent, to visual abnormality in some of the tests after treatment, such as in colour sense , diplopia & intra ocular pressure (IOP) .

Results:

While certain percentage of diabetic patients had visual disturbances even before sildenafil intake. The abnormalities were in visual acuity, visual field and, in fundus appearance.

Post – treatment led to increase the percentage of patients with already existing ocular problems and extend them to include some other new ones like change in colour sense , diplopia and increased (IOP) .

Conclusions:

Comparing the patient group with the control , pre – treatment tests revealed that diabetic patients had already pre – existing ocular problems due to diabetes such as in the visual acuity , visual field which were statistically not significant ($p>0.05$). The only significant ($p<0.05$) difference was in the fundus appearance.

Post – treatment results indicated more ocular damage in diabetic patients as all tests were abnormal compared to control subjects. So, although not significant but ocular complications do exist and might cause unpredictable eye damage to certain percentage of patients which should be taken into consideration.

Introduction:

Sildenafil is an effective oral treatment for erectile dysfunction (1) . It is a potent inhibitor of phosphodiesterase isoenzyme type 5 (PDE5) in the corpus cavernosum (2,3) .

In vitro studies have shown that PDE6 , found predominantly in retinal photoreceptors (4) a key enzyme in the phototransduction cascade , is also inhibited by sildenafil . The inhibition efficacy is about 1/10 of that for PDES (2) . PED6 is required for the transformation of light into electrical signals , therefore , retinal effects of PDE inhibitors (PDEI) are not unexpected and are well known from studies in cats (5,6) and human - beings (7,8) .

Ocular side effects of sildenafil fall into two major types; those secondary to the inhibition of PDE6 in the retina. These side effects include temporary loss of vision, increased intraocular pressure , green/blue tingeing of vision , increased sensitivity to light and blurred vision (9) .

The other type are due to ocular vascular events such as haemorrhage , venous occlusion and anterior ischaemic optic neuropathy (9) .

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These side effects appear 1 hour after oral administration of 100 mg sildenafil and the changes disappeared 5 hours later .

There is a controversy in previous reports whether there is no need for alarm over retinal side effects of sildenafil or whether they should be seriously considered .

Selected cases reported , one case was of a healthy 69 year old man presented with a sudden loss of vision due to brand retinal artery occlusion in the left eye few hours after administration of silindenafil (100 mg) which was considered serious (9) . However , another study involved five healthy volunteers had the same dose recommended that there was no significant effect of the drug (10) . Thus it has been prescribed to cure impotence and proved effective regardless of the etiology .

There are several risk factors for erectile dysfunction (ED) such as : aging , smoking , alcohol drinking , some of the drugs , cardiovascular diseases , chronic renal failure and depression .

Hence , the most common and significant is diabetes mellitus which is associated with impotence and ED due to autonomic neuropathy .

Sildenafil can solve this problem with good results , however , diabetes might be complicated with ocular problems as : blurring of vision , open – angle glaucoma , retinopathy and cataract . These visual disturbances mainly depend on glucose level and duration of the disease (11) .

The aim of this study is to find whether there is alarm over retinal side effects of sildenafil for those elder diabetic patients with pre-existing retinal dysfunction .

Subjects and Methods

A total of 30 male subjects were enrolled in the study . Ten subjects (mean age 55±10 years) were healthy volunteers suffering of ED only and considered as the control group . The rest of the subjects (mean age 57±10 years) were diabetic patients having ED . Table – 1 shows the characteristic features of all subjects included in the study .

Cases excluded were : hypersensitivity to the drug , cardiovascular diseases , hepatic or renal dysfunction , those on nitrate group derivatives and enzyme inducers or inhibitors , retinitis pigmentosa and those with anatomical deformation of the penis (12) .

The effect of a single oral dose of 100 mg sildenafil in all 30 volunteers on visual acuity (Snellen's test) , visual field (Goldman perimetry) , colour vision (Ishihara's test) , fundus appearance (ophthalmoscopy) , Intraocular pressure (Tonemetry) , and diplopia were studied (13) . All tests were done immediately before medication (pretreatment) and 1 hour afterwards .

Statistical analysis :

All data were based on the mean of two readings , expressed as percentages or SD , and the Chi test was used for statistical evaluation of significance between control and patient groups .

A P-value of <0.05 was regarded as significant .

Results :

Table – 2 reveals that , before treatment , all the control group subjects (who are totally healthy but with ED) had normal vision tests done for visual acuity , visual field , color sense , fundus appearance , diplopia , and lOP . However , one hour after a single high dose intake of sildenafil (100 mg) , although not significant , but there was a change in their vision tests as 10% of the control subjects suffered of change in the colour sense and had diplopia while 20% of them had raised lOP .

As for the patient's group (diabetics with ED) , these had abnormal results in some of the vision tests done even before they had the drug . As shows in table – 3 that 10% of patients had visual acuity , 5% had abnormal visual field , & 50% of them had abnormal fundus appearance .

After they took the medicine the damage was more intense as the percentage of patients with changed vision raised to 20% in case of acuity , 10% of them suffered of change in their color sense , 5% had diplopia & 15% increased lOP . As for the visual field and the funds appearance these remained at the same degree of damage. But statistically all changes were insignificant .

In comparison with each other (the control and the patient groups) pretreatment results clarified that (table – 4) , unlike the control subjects , patients with diabetes had changed visual tests regarding visual acuity , visual field and fundus appearance . The only

significant change was in the fundus appearance .

After drug administration (post-treatment,table-5) , 20% of diabetic patients had abnormal visual acuity while remained perfect for all subjects in the control group . Visual field remained the same while there was more damage in the colour sense , these were raised to 10% in both groups . As for the fundus appearance remained the same significant change in the patient group .

Although not significant , more subjects in the control group suffered of diplopia as 10% of them had double vision problem while only 5% of the other group had double vision . Also more percentage of control subjects had increased lOP (20%) than patients in the second group (15%) , the difference was statistically not significant .

Discussion

Are the visual disturbances , of which some patients having sildenafil complain of , considered alarming side effects ? Are patients with preexisting visual abnormalities at higher risk of ocular damage ?

The data obtained in this study revealed that , some of the tests indicated visual damage due to sildenafil intake and exacerbation of visual abnormalities in pre-existing cases of ocular damage .

Thus some of the subjects suffering of ED but are healthy otherwise , had changed colour sense , deplopia and increased lOP after administration of sildenafil (100mg) but the change was statistically insignificant .

However diabetic patients with ED had already disturbed vision , before sildenafil administration , which is quite common in cases of uncontrolled diabetes .Visual acuity ,visual field were abnormal in 10% and 5 % of patients respectively which are found to be not significant . But 50% had a change in the fundus appearance which was statistically significant .

After drug administration vision abnormalities worsened except for vision field and fundus appearance which remained unchanged .

Although not significant , but the percentage of patient suffering of abnormal vision acuity had raised from 10 to 20 % .Colour sense , diplopia , lOP which were not a claim of any patient before drug administration , 10% , 5% and 15% of patients respectively had these problems after medication .

These results reflected the effect of sildenafil (100 mg) one hour after oral intake . The dose and time of doing the vision tests (1 hr. after administration) were important factors in determining the extent of damage (10,14) . Because of the weak inhibitory effects of sildinafil on the isoenzyme PDE6 in the retina which is the basis for abnormalities related to retinal dysfunction those were usually observed at high doses of sildenafil (100 mg) one hour after oral intake . These changes were reversible and completely disappeared 5 hrs later (10,15) .

This was followed by another report of a potentially blinding complication due to the development of a retinal artery occlusion (9) .

For all these side effects , sildinafil was avoided in cases of inherited retinitis pigmentosa (a genetic disorder of retinal PDE enzyme) (12,16) .

Table – 4 clarifies the extent of damage due to diabetes by comparing vision tests between the control and the patient groups (healthy with ED and diabetic patients with ED respectively) before sildenafil intake .

In comparison with the control group which all had perfect vision , diabetics had non significant abnormalities like in visual acuity and visual field , but the significant difference was in the fundus appearance . This reflects the function of the optic disc which lead to several changes in patients suffering of diabetic retinopathy such as increased capillary permeability , microaneurysm , dilated veins , hemorrhage (dot – blot) , cotton wool spots and hard exudates (17) .

After medication , diabetic patients had all their vision tests abnormal while the control group had the change only in the colour sense , diplopia and lOP . Although not significant except for the fundus appearance but from these results it is clear that the pre – existing abnormalities due to diabetes are exacerbated and extended to include more vision problems when sildenafil was administered .

Thus ocular side effects should be seriously considered with all patients using this medication and are at high risk because of a pre – existing disease .

Further work should be done on the long term effect of sildenafil in patients with pre – existing retinal problems or diseases. Also to check whether these side effects are temporary or permanent.

Table (1) : baseline features of control & patient groups .

Baseline features	Control (ED) N=10	Patient (ED+D.M) N=20	Significance (P-value)
Age (year)	40 – 65	43 – 68	NS
Weight (kg)	63 – 86	61 – 88	NS
Alcohol drinkers	Zero %	Zero %	NS
Smokers	2 (20%)	5 (25%)	NS

N= number of subjects
NS= not significant (p>0.05)

Table (2) : Visual tests for the control group (healthy but with ED) , before and after treatment with sildenafil .

Test	% normal visual test (% abnormal)	
	Before treatment	After treatment
Visual acuity	100 (zero)	100 (zero)
Visual field	100 (zero)	100 (zero)
Colour sense	100 (zero)	90 (10)
Fundus appearance	100 (zero)	100 (zero)
Double vision	100 (zero)	90 (10)
Iop	100 (zero)	80 (20)

Table (3) : Visual tests for the patient group (diabetics with ED) , before and after treatment with sildenafil .

Test	% normal visual test (% abnormal)	
	Before treatment	After treatment
Visual acuity	90 (10)	80 (20)
Visual field	95 (5)	95 (5)
Colour sense	100 (zero)	90 (10)
Fundus appearance	50 (50)	50 (50)
Double vision	100 (zero)	95 (5)
Iop	100 (zero)	85 (15)

Table (4) : Comparison between visual tests of the *control and **patient groups before sildenafil administration .

Test	% normal visual test (% abnormal)		Significance (p)
	Control group	Patient group	
Visual acuity	100 (zero)	90 (10)	NS
Visual field	100 (zero)	95 (5)	NS
Colour sense	100 (zero)	100 (zero)	NS
Fundus appearance	100 (zero)	50 (50)	S
Double vision	100 (zero)	100 (zero)	NS
Iop	100 (zero)	100 (zero)	NS

* Control : healthy but with ED .
** Patient : diabetic with ED .
NS : not significant .
S : significant .

Table (5) : Comparison between visual tests of the *control and **patient groups after sildenafil administration .

Test	% normal visual test (% abnormal)		Significance (p)
	Control group	Patient group	
Visual acuity	100 (zero)	80 (20)	NS
Visual field	100 (zero)	95 (5)	NS
Colour sense	90 (10)	90 (10)	NS
Fundus appearance	100 (zero)	50 (50)	S
Double vision	90 (10)	95 (5)	NS
Iop	80 (20)	85 (15)	NS

* Control : healthy but with ED .
** Patient : diabetic with ED .
NS : not significant .
S : significant

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