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SILDENAFIL *(VIAGRA)* IN THE TREATMENT OF MALE ERECTILE DYSFUNCTION IN NAIROBI
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ABSTRACT

Objective: **To evaluate the effectiveness of sildenafil *(Viagra)* in the treatment of male erectile dysfunction in Nairobi.**
Design: **Prospective open label extension study.**
Setting: **Urology clinics at the Nairobi Hospital, Kenyatta National Hospital and the author's private clinic in Hurlingham, Nairobi.**
Participants: **Two hundred and nineteen adult male patients with erectile dysfunction.**
Results: **The age range was 33-80 years with a mean of 62.5 years and a peak incidence in the 60-69 year age group. One hundred and nineteen patients (54.34%) had organic causes, 85 patients (38.81%) had pyschogenic causes and 15 patients had mixed causes. Two hundred patients (91.32%) had improved sexual function after treatment with *viagra.* This improvement was sustained during the study period of sixteen weeks and included improved erectile and orgasmic functions and overall sexual satisfaction. One hundred and fifty seven of these patients responded to therapy with 50mg of *viagra;* 40 patients with 25mg and three patients with 100mg of therapy. Nineteen patients (8.68%) had no improvement in sexual function after *viagra* administration. Seven patients (3.2%) had adverse effects which were mild and transient. They included mild headaches in three patients, mild dyspepsia in two patients and facial flushing and nausea and vomiting in one patient, respectively.**
Conclusion: **Oral sildenafil *(Viagra)* is an effective well tolerated and simple treatment for male erectile dysfunction in the majority of cases. The cost of treatment at about ten United States dollars for the 50mg tablet is prohibitive and may limit its wide use by many deserving patients in this locality.**

INTRODUCTION

Erectile dysfunction is the persistent inability to achieve and maintain an erection sufficient for satisfactory sexual performance(1). Traditionally this condition has been called impotence, but the term erectile dysfunction is more precise because it refers specifically to the clinical problem of an erection. Furthermore, men with erectile dysfunction usually retain other sexual functions such as sexual desire and the ability to achieve orgasm and ejaculation. Although regarded as a benign condition, erectile dysfunction has a profound impact on the quality of life of many men(2). It is estimated that it affects upto 30 million men in the United States and is age-associated with estimated prevalence rates of 39% among men 40 years old and 70% among those over 70 years old(3). In this locality, although no epidemiological study similar to the Massachusetts male ageing study has been carried out, erectile dysfunction is presumed to be common. However, until recently, most patients did not consult the medically trained doctors. They preferred to consult the traditional medical practitioners because of the stigma and socio-cultural taboos associated with erectile dysfunction.

It was once thought to be a primarily psychological and lifestyle disorder. More recently it has become clear that erectile dysfunction is often attributed to organic disease(4-7). Damage to arteries, smooth muscle and fibrous tissue resulting in altered blood flow to and from the penis are the most common causes(2). This is often the result of chronic disease such as diabetes, kidney disease, artherosclerosis, and vascular disease(8,9). The results of the Massachusetts male ageing study, a large population based random sample study confirmed that erectile dysfunction is highly correlated with such disease as hypertension, heart disease and diabetes mellitus(3). The available methods of treatment include vacuum constriction devices(10,11), intracavernosal injection of vasoactive substances including alprostadil (prostaglandin El)(12), transurethral delivery of alprostadil(13), implantation of penile prostheses, venous or arterial surgery(15,16) and psychotherapy.

Normal penile erection depends on the relaxation of smooth muscles in the corpora cavernosa. In response to sexual stimuli, cavernous nerves and endothelial cells release nitric oxide which stimulates the formation of cyclic guanosine monophosphate(c-GMP) by guanilate cyclase(17). The mechanism by which cyclic GMP stimulates the relaxation of smooth muscle remains to be elucidated(18). Sildenafil (Viagra) is a selective inhibitor of cyclic GMP specific phosphodiasterase type 5, the

predominant isoenzyme metabolising cyclic GMP in the corpus cavenosum. By selectively inhibiting cyclic GMP catabolism in cavernosal smooth muscle cells, sildenafil would be expected to restore the natural erectile response to sexual stimulation but not cause erections in the absence of such stimulation(19,20). Currently in this locality, no effective and affordable oral therapy for erectile dysfunction is widely available. It is against this background that a prospective open label extension study on the efficacy of oral sildenafil (Viagra) in the treatment of male erectile dysfunction in this locality was carried out.

MATERIALS AND METHODS

This is a prospective open label extension study of two hundred and nineteen male patients with erectile dysfunction. At the first visit during evaluation informed consent was obtained from all patients. A detailed general medical history was obtained followed by sexual history. Sexual function was established using a sexual function questionnaire which was completed by each patient answering from the 15 question international index of erectile dysfunction (IIEF), a validated multidimensional self-administered questionnaire used for the clinical assessment of erectile dysfunction and treatment outcomes in clinical studies(21). Patients were also asked about the existence of additional systemic diseases and any drugs used. They were also asked about heart disease and whether or not they were on nitrate therapy. Complete physical examination including neurological examination was performed on all patients by the same investigator. Routine blood chemistry and haematological laboratory tests and urinalysis were performed on every patient. Special investigations such as colour doppler ultrasound of the penis were performed only if clinically indicated as is the practice by the investigator. Patients were excluded from the study if they had anatomical deformities of the penis, a primary diagnosis of premature ejaculation, had uncontrolled diabetes mellitus, on nitrate therapy or had erectile dysfunction of less than four months duration.

The men were instructed to take 50mg, 25mg or l00mg of sildenafil (Viagra) orally approximately one hour before the planned sexual activity but not more than once every 24 hours. Patients were reviewed at the outpatient urology clinics at four weekly intervals for sixteen weeks by the same investigator. During this period each patient had at least twelve tablets of viagra. At each visit the patients reported on their responses regarding erectile function, orgasmic function and overall sexual satisfaction. The patients were also examined and asked about any adverse effects during the administration of sildenafil. The assessment of efficacy was effected by using patient responses to question 3 (frequency of vaginal penetration) and question 4 (maintenance of erection after penetration) of the 15 question IIEF questionnaire(21). All relevant data collected were analysed and tabulated.

RESULTS

A total of 250 patients were seen at the urology clinics by the same investigator but only 219 of them satisfied the inclusion criteria for this study on the efficacy of sildenafil in the treatment of erectile dysfunction undertaken between November 1998 and August 1999 in Nairobi, Kenya. One hundred of the patients were referred by other health practitioners including pharmacists but the majority (150 patients) came directly to the investigator as a result of the massive publicity given to sildenafil in the local press since its launch on 31st October 1998.

The age range was 33-80 years with a mean of 62.5 years (Table 1). The causes of erectile dysfunction are illustrated in Table 2 with organic causes in 119 patients (54.34%), psychogenic causes in 85 patients (38.81%) and mixed causes in 15 patients (6.85%). A detailed distribution of organic causes of erectile dysfunction is illustrated in Table 3.

Table 1

Age distribution in erectile dysfunction in Nairobi

Age group in years	No. of patients	% of total
30 - 39	5	2.28
40 - 49	25	11.41
50 - 59	69	31.51
60 - 69	99	40.20
70 - 79	19	8.67
80- 89	2	0.91

Table 2

Causes of erectile dysfunction in Nairobi

Causes of dysfunction	No. of patients	% of total
Organic causes	19	54.34
Psychogenic causes	85	38.81
Mixed causes	15	6.85

Table 3

Organic causes of erectile dysfunction in Nairobi (n= 119)

Causes of erectile dysfunction	No. of patients	% of total
Cardiovascular (controlled hypertension on antihypertensive therapy e.g. calcium channel brokers)	38	31.93
Cardiovascular (uncontrolled hypertension diagnosed by the surgeon)	19	15.97
Diabetes mellitus	20	16.81
Other endocrine disorders	3	2.52
Chronic alcoholism	4	3.36
Excessive tobacco consumption	5	4.20
Other prescription drugs (e.g. antiandrogens, cimetidine, NSAIDS etc)	9	7.56
Non prescription drugs (e.g. antihistamines)	2	1.68
Prostate surgery (TURP and open prostatectomy)	11	9.24
Radical pelvic surgery (e.g. abdominoperineal excision of rectum).	3	2.52
Spinal cord injury	4	3.36
Neurological disorders	1	0.84

The effective sildenafil dose variation indicated in Table 4 indicated that the dose of 50mg was effective in 157 patients (71.69%) compared to 25mg and 100mg which were effective in 40 patients (18.26%) and three patients (1.37%), respectively. A total of 200 patients had improved erectile function, 198 had improved orgasmic function and 200 patients had improved overall sexual satisfaction indicating an efficacy rate of 91.32% as shown in Tables 4 and 5. No improvement in erectile function, orgasmic function and overall sexual satisfaction was reported in 19 patients respectively (8.68%).

Table 4

Effective sildenafil dose response variation in the treatment of male erectile dysfunction

Dosage	No. of patients given	No. of responses	No. of non responses	% of responses	% of non responses
25mg	60	40	20	66.67	33.33
50mg	159 + (20 non responders to 25mg)= 179	157	22	87.71	12.29
100mg	22 (all non responders to 25mg and 50mg)	3	19	13.64	86.64
Total for all doses (25,50 and 100MG)	219	200	19	91.32	8.68

Table 5

Effect of (sildenafil) viagra administration on sexual function of men with erectile dysfunction

Effect of viagra administration	Number of patients	% of total
Improved erectile function	200	91.32
Improved orgasmic function	198	90.41
Intercourse satisfaction	199	90.87
Improved overall sexual satisfaction	200	91.32
No improvement in erectile, function orgasmic function and overall sexual satisfaction	19	8.68

Table 6

Adverse effects of sildenafil administration

Adverse effect	Number of patients	% of total
Mild headaches	3	1.37
Mild dyspepsia	2	0.91
Nausea and vomiting	1	0.46
Facial flushing	1	0.46

Seven patients (3.2%) had adverse effects related to *viagra* administration (Table 6). The adverse effects include mild headaches in three patients, dyspepsia in two patients and facial flushing, and nausea and vomiting in one patient, respectively. All the adverse effects were mild and transient and no patient discontinued treatment because of them. No patient experienced visual disturbances, myalgia or priapism.

DISCUSSION

The oral administration of drugs is known to be the easiest and most acceptable form of treatment for male erectile dysfunction compared with other successful modalities such as external vacuum devices, topical creams, intracavernosal injection and intraurethral application of vasoactive drugs and different penile reconstructive vascular and prosthetic surgical techniques developed over the last three decades(22). Unfortunately, until recently, yohimbine hydrochloride was the most widely used oral medication for erectile dysfunction, but the outcome has been disappointing even when used in high doses(23). Currently, there is a worldwide increase in the prevalence of male erectile dysfunction which is associated with rapidly ageing populations. The newly available and highly publicised oral medical treatments such as sildenafil and vasomax are now raising challenging policy issues in many countries including Kenya(24). The results of clinical studies on a selective 5- phosphodiasterase inhibiting sildenafil *(Viagra)* have particularly continued to be promising and form the basis of this study(25).

The age range was 33-80 years with a mean of 62.5 years and a peak incidence in the 60-69 year age group. The number of men with erectile dysfunction increased steadily with age from five (2.28%) in the 30-39 year age group to 99 (40.20%) in the 60-69 year age group (Table 1). These findings are similar to previous reports in the Massachussetts male ageing study in which strong association between age and male erectile dysfunction was observed(3,26). The apparent decrease in the number of patients with erectile dysfunction in the 70-79 year age group in this locality is because of reduced life expectancy resulting in reduced numbers in this age group.

One hundred and nineteen patients (54.34%) had organic causes for the erectile dysfunction, eighty five patients (38.81%) had pyschogenic causes and fifteen patients (6.85%) had mixed causes. The distribution of the various organic causes is illustrated in Table 2.

The responses of individual patients to sildenafil administration is illustrated in Tables 4 and 5. Sixty patients were placed on 25mg of sildenafil. At the end of four weeks, 40 patients (66.67%) had shown improvement

in sexual function. These consisted of improved erectile function as indicated by achieving and sustaining an erection sufficient for vaginal penetration; and maintaining the erection after penetration; improvement in orgasmic function, and improvement in overall sexual satisfaction. Treatment was continued for sixteen weeks for the 40 responders but discontinued after four weeks for the 20 non responders (33.33%). A total of 179 patients including the 20 non responders to 25mg sildenafil were placed on 50 mg sildenafil for four weeks. One hundred and fifty seven patients (87.71%) had improved sexual function and continued on the treatment for the duration of the study period of sixteen weeks. Treatment was discontinued in the 22 patients (12.29%) who reported no improvement in sexual function after four weeks of therapy. All the 22 patients were placed on 100 mg sildenafil for a further period of four weeks. In this group three patients (13.64%) had improved sexual function and continued with the therapy for sixteen weeks. The other 19 patients (86.64%) were categorised as non responders to 25mg, 50mg and l00mg of sildenafil therapy. Therefore in this study out of the 219 patients who had various doses of sildenafil therapy, 200 patients (91.32%) had improved erectile function, orgasmic function and overall sexual satisfaction (Table 5). These findings are similar to previous reports by other investigators elsewhere(25,27-29).

The main adverse effects of *viagra* (sildenafil citrate) administration recorded in this study included mild headaches in (1.37%), dyspepsia in (0.91%), nausea and vomiting in (0.46%) and facial flushing in (0.46%). These adverse effects were mostly mild and transient and no patient discontinued treatment during this study because of the adverse effects. There were no episodes of myalgia, visual disturbances or priapism. The adverse effects reported in this study almost certainly reflect the presence of phosphodiasterase type 5 in other tissues such as platelets and vascular smooth muscles(30). These findings indicate a high level of tolerability and acceptance of sildenafil as has been previously reported by others(25,31).

Although oral sildenafil in the treatment of male erectile dysfunction was only introduced recently in this locality, it has proved to be an effective, well tolerated and simple treatment for erectile dysfunction in the majority of cases as has been previously reported by others(25,31). However, the high cost of sildenafil which at present is about ten US dollars per 50 mg tablet is bound to limit its very much desired availability to a large number of deserving patients in this locality.

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REFERENCES

1. NHI. Consensus development panel on impotence. *J. Amer. Med. Ass.* 1993; **270:** 83-90.
2. Krane, R.J. Goldstein I. and Saenz de Tejada I. Impotence. *N. Engl. J. Med.* 1989; **321:** 1648.
3. Feldman H.A., Goldstein, I. Harzichristou, D.G., Kraine R.J. and Mc Unley J.B. Impotence and its medical and psychosocial: Results of the Masachusetts male aging study. *J. Urol.* 1994; **151:**54-61.
4. Plaud, J. Dubbert P.M., Lolm J. *et al.* Erectile dysfunction in men with chronic medical illness. *J. Beh. Ther. Exp. Psychiat* 1996; **27:** 11-19.
5. Morley, J. Impotence. *Amer. J. Med.* 1986; **80:** 897-905.
6. Slag, M. Morley, J.E., Elson M.K. *et al* Impotence in medical clinic outpatients. *J. Amer. Med. Ass.* 1983; **249:** 736-740 .
7. Spark, R. White, R.A. and Connolly P.B. Impotence is not always psychogenic: Newer insights into hypothalamic pituitary gonadal dysfunction. *J. Amer. Med. Ass.* 1980; **1980:** 750-755.
8. National institute of diabetes, digestive, kidney diseases. National kidney and urologic diseases information clearing house. NIH publishing NO. 95-3923, 1995.
9. Jevitch M.J. Edson N., Jarman W.D. *et al* Vascular factors in erectile failure in diabetics. *Urology*, 1982; **19:** 163-168.
10. O'sullivan D.C., Munson K.W. and Chilton C.P. Impotence: First line treatment with vacuum device. *J. Urol.* 1994; **151:** 347-349.
11. Baltaci, S., Aydos, K., Kosar *et al.* Treating erectile dysfunction with vacuum tumsense device: A retrospective analysis of acceptance and satisfaction. *Brit. J. Urol.* 1995; **76:** 757-760.
12. Linet, O.I. and Ogrinc F.G. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. *N. Engl. J. Med.* 1996; **334:** 873-877.
13. Padma-nathan, H. Hellstrom, W.J.G., Kaiser, F.E. *et al.* Treatment of men with erectile dysfunction with transurethral alprostadil. *New. Engl. J. Med.* 1997; **336:** 1-7.
14. Evans, C. The use of penile prosthesis in the treatment of impotence. *Brit J. Urol.* 1998; **81:** 591-598.
15. Freedman, A.L., Costa neto, F. Mehringer, C.M. and Rajfer J. Long term results of penile vein ligation for venous leakage. *J. Urol.* 1993; **149:** 1301-1303.
16. Wespes, E., Corbusier A., Delcour, C. *et al.* Deep vein arterialization in vascular impotence. *Brit. J. Urol*. 1989; **64:** 535-540.
17. Burnett, A.L. The role of nitric oxide in the physiology of erection. *Biol. Reprod.* 1995; **52:** 485-489.
18. Rajfer, J., Aronson, W.J. Bush, P.A. Dorey, F.J. and Ignarro L.J. Nitric oxide as a mediator of relaxation of the corpus caernosum in response to nonadrenergic, noncholinergic neurotransmission. *N. Engl. J. Med*. 1992; **326:** 90-94.
19. Moreland, R.B., Goldstein, I. and Traish, A. Sildenafil, a novel inhibitor of phosphodiasterase type 5 in human corpus cavernosum smooth muscle cells. *Life sci.* 1998; **62:** PL309-318.
20. Boolel, M., Allen, M.J., Ballard, S.A. *et al*. An orally active type cyclic GMP specific phosphodiasterase inhibitor for the treatment of penile erectile dysfuntion. *Int. J. Impot. Res.* 1996; **8:** 47-52.
21. Rosen, R.C., Riley, A., Wagner, G., Osterloh, I.A., Kirkpatrick, J. and Mishra A. The international index of erectile function (11EF): A multidimentional scale for assessment of erectile function. *Urology*, 1997, **49:** 822-830.
22. Chen, J., Wollman, Y., Chernichovsry, T. *et al*. Effect of oral administration of high dose nitric oxide donor L-arginine in men with organic erectile dysfunction: Results of a double blind randomized placebo controlled study. *Bju International.* 1999; **83:** 269-273.
23. Kunelius, P., Hakkinen, J. and Lukkarinen, O. Is high dose yohimbine hydrochloride effective in the treatment of mixed type impotence? A prospective randomized controlled double blind crossover study. *Urology.* 1997; **49:** 441-444.
24. Aytac, L.A., Mckinlay, J.B. and Krane, R.J. The likely worldwide increase in erectile dysfunction between 1995 and 2025, some possible policy consequences. *Bju International.* 1999; **84:** 50-56.
25. Goldstein, I. Lue, T.F. and Padma-nathan H. Oral sildenafil in the treatment of erectile dysfunction. *N. Engl. J. Med.* 1998; **338:** 1397-1404.
26. Spector, I.P. and Carey, M.P. Incidence and prevalence of sexual dysfunction: A critical view of the empirical literature. *Arch. Sex. Bhav*. 1990; **19:** 389.
27. Eardley, I., Brook, J. Yates, P.K., Wulff, M.B. and Boolel, N. Sildenafil (Viagra), A novel oral treatment with rapid onset of action for penile erection dysfunction. *Brit. J. Urol*. 1997; **4:** 66.
28. Lue T.F. and The sildenafil study group. A study of Sildenafil (Viagra) a new oral agent for the treatment of male erectile dysfunction. *J. Urol.* 1997; **157:** 701.
29. Eardley, I. Morgan, R.J., Dinsmore, W.W. Pearson, J. Wulff, M.B. and Boolel, M. UK-92.480, a new oral therapy for erectile dysfunction. A double blind placebo controlled trial with treatment taken as required. *J. Urol*. 1996; **155:** 495A.
30. Eardley, I. New oral therapies for the treatment of erectile dysfunction. *Brit. J. Urol.* 1998; **81:** 122-127.
31. Boolell, M., Gepi—Atee, S., Ginger, J.C. and Allen, M.J. Sildenafil. A novel effective oral therapy for male erectile dysfunction. *Brit. J. Urol*. 1996; **78:** 257-261.