

## Diabetes Mellitus associated Erectile Dysfunction.

N. Gopakumar, Jose Mon Thomas

Division of Urology and General medicine, PRS Hospital Killipalam, Trivandrum, India

**Abstract :** Erectile dysfunction is common in diabetic patients and occurs at a younger age group than non diabetic population. Both neurogenic and vascular factors are important in the pathogenesis of erectile dysfunction.  
**Keywords:** Pathophysiology , evaluation and management of erectile dysfunction is discussed.

### INCIDENCE AND PREVALENCE

Erectile dysfunction is more common in diabetic than in the general population and occurs at a younger age group and is often associated with ejaculatory problems<sup>1</sup>. Vast majority of diabetic patients have an organic basis for their erectile dysfunction . Both neurogenic and vascular factors are important in the pathogenesis of erectile dysfunction. Autonomic neuropathy is almost certainly the cause of ejaculatory failure but may be present in upto 40% of men with Diabetes mellitus<sup>2,14-17</sup>.

The frequency of erectile dysfunction in diabetes was evaluated in a survey of 541 men aged 20 to 59 years with diabetes mellitus attending a large community diabetes clinic. The prevalence of ED increased progressively with age from 6 percent in men aged 20 to 24 years to 52% in men aged 55 to 59 years. In addition to increasing age the main factors associated with ED were peripheral or autonomic neuropathy, retinopathy, long duration diabetes and poor glycemic control<sup>6,9</sup>. In a similar study ED severity increased with diabetes duration, poor glycemic control, presence of microvascular and cardio vascular disease. This study suggests that the presence of ED is a predictor of cardio vascular events in men with diabetes<sup>3,4,5</sup>. Men with diabetes who develop ED experience significant decline in quality of life as well as increase in depressive symptoms.

### PATHO PHYSIOLOGY

Erection is a neurovascular event that involves spinal and supra spinal pathways. The final common pathway involves the release of Nitric Oxide (NO) from both endothelial cells and neurons, which acts as a vasodilator causing penile engorgement and erection. NO is degraded by Phospho diesterase type 5 enzyme in the penis<sup>7</sup>. When the neurovascular pathways are inhibited by medical conditions or drugs, results in ED . The development and maintenance of a normal erection requires an increase in parasympathetic activity and a reduction in sympathetic activity and these changes increase the blood flow into the Corpora Caverosa of the penis and relax the trabecular smooth muscle of Corporal caverosa thereby decreasing venous drainage. ED can result from local nerve damage (eg : Neuropathy or surgical trauma ), impaired blood flow to the penis or psychological factors. Cavemosal muscle degeneration is found in diabetic men with ED<sup>2,3,4</sup>.

All men with diabetes should be asked about erectile dysfunction. The other causes of ED such as drugs, vascular disease, endocrine dysfunction, depression, alcohol consumption should be looked into. Men should be examined for retinopathy, peripheral or autonomic neuropathy, hypertension peripheral vascular disease, hypogonadism and gynaeomastia<sup>12,14,15</sup>. Some expert groups suggest that men with diabetes and erectile dysfunction who are planning to start vasoactive drugs should first undergo evaluation of CHD . Depression is an important cause of ED in men with Diabetes. In a study the prevalence of mild or moderate and severe ED was 24 and 34% respectively<sup>15,17</sup>.

### EVALUATION

Laboratory testing should include haemoglobin A1C, Serum creatinine,

**Correspondence:** N. Gopakumar, Chief Urologist, Department of Urology & Radiology, PRS Hospital, Killippalam, Trivandrum -695002, India e-mail : drungkumar uro @ rediffmail.com

Cholesterol, testosterone, prolactin, thyrotropin and Urinary protein excretion<sup>14</sup>.

In one study of 1022 men with ED, persistently low serum testosterone (less than 300ng /ml) were found in 4% of men under age 50 yrs and 90% of those age 50yrs or older<sup>8</sup>. If testing had been restricted to men with symptoms of low sexual desire and signs of hypogonadism 40% of the men with low serum testosterone would have been missed. Some of them may respond to treatment with testosterone .

Specific tests of peripheral or autonomic nerve function are not necessary<sup>12</sup>.

### TREATMENT

Several treatment option are available for ED none of which is specific for diabetes. Intensive glycemic control reduces the development of ED. There are no data to suggest intensive therapy for blood sugar can reverse or improve ED once it has developed<sup>9</sup>.

Most men with diabetes have one or more organic causes for their ED. Psychologic factors are also often present. Psychosexual counseling alone is not often effective in diabetic men with ED but it may be helpful as an adjunct to drug therapy with Phospho diesterase Inhibitors<sup>10,13</sup>.

The first line therapy for ED are a class of drugs that are cyclic GMP PDE 5 inhibitors (Sildenafil, Tadalafil, Vardenafil) that prolong the vasodilatory effect of Nitric oxide to initiate and maintain an erection. Analysis of 8 trials with 976 diabetic men taking sildenafil vardenafil or tadalafil reported improvement in several indices of erectile dysfunction. The adverse effects were headache, flushing, dyspepsia, abnormal vision, backpain etc. PDE 5 inhibitors are contra indicated in patients taking nitrates<sup>10</sup>.

With Intra urethral alprastodol (Prostaglandin E1) the success rate was 65%<sup>14,18</sup>.

Intra cavemosal injection with papaverine phentolamine and prostaglandin E1, either alone or in combination are effective men with ED<sup>18,19</sup>.

The patients who are not getting benefit from these treatments are considered for Penile prosthesis implantation. Semirigid and inflatable penile implants are available. Men with peyronies plaque with ED benefit from dermal grafting and Penile prosthesis implantation. Incidence of infection is more in diabetic men who undergo penile prosthesis implantation<sup>11,20,21</sup>.

### REFERENCES

- NH consensus conference Impotence JAMA - 1993 : 270: 83.
- MacCulloch DK, Campbell IVY, Wu FC etal. The prevalence of diabetic impotence Diabetologia 1987; 18: 279.
- MacCulloch DE, Young RJ, Prescott J etal. The natural history of impotence in diabetic man Diabetologia 1984; 26:437.
- Kater Leibovicio, Wainstein J etal clinical parameters associated with erectile dysfunction in diabetic men Diabetes care 2005; 28:1739
- MaRC, SoWY, Yang X etal. Erectile dysfunction predicts coronary heart disease in Type 2 diabetes J Am Coll Cardiol 2008; 51: 2045
- Giuliano FA, Leriche A, Jaudinot EO et al . Prevalence of ED among 7689. Men with diabetes or hypertension or both. Urology 2004;64:1196
- Andersson KE, Wagner G Physiology of penil erection phsioyol Rev 1995; 76:191
- Buvat Lemaire A. Endocrine screening in 1022 men with ED clinical significance and cost effective strategy. J Urol. 1997; 158:1764
- Wessels H, Renson DF etal. Effect of intensive glycemic therapy on erectile function in men with Type 1 diabetes. J Urol 2011; 185:1828
- Vardim, NiniA. PDE inhibitors for ED in patients with diabetes mellitus. Cochrane data base syst Rev 2007; (D00218)
- Garber BE : Inflatable penile prosthesis results of 150 cases. Br. J Uro 1996; 78: 933
- The aetiology and management of erectile, ejaculatory. Problems in with diabetes mellitus. Dunsmuir WD, Holmes SA Diabet Med 1996 ; Aug 13 (8) 700-8
- New treatment options for ED in men with diabetes mellitus. Basu A, Ryder RE Drugs 2004; 64(23) 2667 - 88
- Erectile dysfunction : anatomical parameters , etiology , diagnosis and therapy Hafes ES, Hafe 35D Arch Androl 2005 Jan 51 (1) 15 - 31
- ED in diabetes mellitus Malavige LS, Lew JC. J. Sex Med 2009 May 6 (5) 1232 - 47
- Diabetic Autonomic neuropathy. ViniKAL, Maser RE, Freeman R. Diabetes care 2003 May 26 (6) 1553 - 79
- Diabetic sexual dysfunction. Hakim LS, Goldstein I Endocrin Metab Clin North Am. 1996 Jun 25 (2) 379: 400.
- Therapy Insight : Sexual dysfunction associated with diabetes mellitus. Fedele D. Nat. Clin Pract urol. 2005 Jun 2 (6) 282 -90.
- Treatment strategies for diabetic patients suffering from ED. Chen Y, Dai Y, Wang R Expert opin Pharmacoo 2008 Feb 9 (2) 257 - 88
- Management of ED in diabetes an update for 2008. Price D, Hackett G, Curr Diab Rep 2008 De 8 (6) : 437 - 43
- Cambell Walsh Urology 10<sup>th</sup> edition, Vol 1 chapter 27 Prosthetic. Surgery for ED. Drogo. K. Montague MD

**SYMPOSIUM :****PRACTICAL APPROACH TO PARKINSONISM****OUR GUEST EDITOR**

**Dr. (Prof.) Kuljeet Singh Anand, MBBS, DM (Neurology), MNAMS, FIAN, FAMS, FRCP (London), FICP, FIMSA, FIAMS, MBA (HCA)**, pioneer in the field of neuroscience is known across the country for his valuable contributions in the field. He graduated from Maulana Azad Medical College (MAMC), New Delhi and received his neurology training from National Institute of Mental Health and Neuroscience (NIMHANS) which is one of the premier and prestigious neurosciences institute of India. He did a fellowship in movement disorders from The Centre for Parkinson's disease and other Movement Disorders, Presbyterian Medical Center, New York, USA & Baylor Medical College of Medicine, Houston, Texas, USA. He is currently academic professor and head of faculty of neurology at PGIMER and Dr. RML hospital, New Delhi. Dr. Kuljeet Singh Anand is an invited Faculty at various conferences and is known for his vibrant and informative talks. He has keen interest in dementia, movement disorders, epilepsy and stroke. He has published several original articles in leading professionally reputed journals and contributed multiple chapters in books on these topics. In recognition of his achievements in the field of neurology, Royal College of Physicians, London conferred upon him FRCP.

**EDITORIAL**

**P**arkinsonian disorders encompass a heterogeneous group with a marked clinical and pathological overlap. These may be broadly classified as synucleopathies (PD, DLB, and MSA) and tauopathies (PSP and CBD), however making a pathological diagnosis is not always feasible. Genetic studies CSF biomarkers and functional imaging may be helpful in diagnosing these disorders at an early stage when a clinical differentiation is difficult.

**Role of Genetics**

Recent advances in genetics have shed light on the underlying pathophysiology of various parkinsonian syndromes<sup>1</sup>. The genome wide association studies have found more than 16 PARK loci associated with PD and 11 genes for PARK loci with new insights gained every year. Five of the identified genes present as typical Parkinsons disease [a-synuclein, parkin, PTEN induced putative kinase 1, DJ-1, and leucine-rich repeat kinase 2 (LRRK2)] while mutations of ATP13A2 (PARK 9) cause Kufor-Rakeb disease characterized by both Parkinsonism and many atypical features<sup>2</sup>.

**Cerebrospinal fluid biomarkers<sup>3</sup>**

The Cerebrospinal fluid (CSF) represents a potentially reliable biomarker source for diagnosing various parkinsonian syndromes. Total - $\alpha$ -syn is a promising marker in differentiating PD, DLB and MSA from other neurodegenerative diseases. Similarly Neurofilament light chain (NF-L) may be helpful in differentiating PD from atypical parkinsonian syndromes. CSF AB-42 might be helpful in predicting cognitive decline in patients with PD.

**Functional imaging - positron emission tomography (PET)/single photon emission computed tomography (SPECT)**

Dopamine transporter imaging (DAT) has largely been employed with SPECT using 123I-ioflupane or DATSCAN. This typically reveals normal DAT levels in caudate and putamen of healthy people and patients with essential tremor & drug induced parkinsonism but reduced DAT levels in PD, PDD, MSA or PSP. Hence it has high sensitivity in differentiating patients with parkinsonian syndromes from those with ET and healthy controls<sup>4</sup>.<sup>11</sup>Craclopride (<sup>11</sup>C-RACLO)

PET is employed in order to estimate D2 receptor and various studies showed that these receptors are more reduced in MSA than in PD. FDG PET (18 Fluorodeoxy glucose) directly assesses synaptic activity. In PD metabolism in putamen and globus pallidus is increased whereas parietal associated cortices show decreased glucose utilization. In contrast in MSA bilateral putaminal hypometabolism and decreased pontocerebellar activity is observed and PSP is characterized by decreased activity in premotor, motor cortices and mid brain.

Each of these markers may be helpful in selected cases for clinching an early diagnosis. However further research may be warranted before these can be incorporated in routine testing.

This issue on Parkinsonism discusses briefly about clinical approach to differentiate various parkinsonian disorders followed by their neuroimaging findings, clinical features of atypical parkinsonian disorders and management issues.

**Bibliography**

1. Antonini A, Leenders KL, Vontobel P, et al. (1997) Complementary PET studies of striatal neuronal function in the differential diagnosis between multiple system atrophy and Parkinson's disease. *Brain* 120: 2187-2195.
2. Benamer TS, Patterson J, Grosset DG, et al. (2000) Accurate differentiation of parkinsonism and essential tremor using visual assessment of [123I]FP-CIT imaging: The [123I]FP-CIT Study Group. *MovDisord.* 15:503-510
3. Brooks DJ, Ibanez V, Sawle GV, et al. (1992) Striatal D2 receptor status in patients with Parkinson's disease, striatonigral degeneration, and progressive supranuclear palsy, measured with 11C-raclopride and positron emission tomography. *Ann Neurol.* 31:184-192.
4. Cerebrospinal fluid biomarkers in parkinsonian conditions: an update and future directions. Magdalinou N, Lees AJ, Zetterberg H. *J Neurol Neurosurg Psychiatry.* 2014 Oct;85(10):1065-75.
5. Coppede F. (2012). Genetics and epigenetics of Parkinson's disease. *Scientific World Journal* 2012, 489830.
6. Polymeropoulos MH, Lavedan C, Leroy E, et al. Mutation in the alpha-synuclein gene identified in families with Parkinson's disease. *Science* 1997;276:2045-7.

**Kuljeet Singh Anand**

Department of Neurology,

Dr. RML Hospital & PGIMER, New Delhi, India

e-mail: kuljeet\_anand@rediffmail.com

*Presenting*

The proven therapy to delay progression of

## **Chronic Kidney Disease**

# **Ketosteril<sup>®</sup>**

**Protects and Preserves Renal Function**

- **Provides nitrogen sparing effect**
- **Reduces hyperfiltration of nephrons**
- **Improves metabolic complications**



*Recommended for all patients with:*

- **Proteinuria, even micralbuminuria**
- **Creatinine clearance < 50 ml/min**

**Delays the onset of dialysis and Prolongs life expectancy**

**Dose: 1 tab/5kg bw/day**



**Fresenius  
Kabi**  
Caring for Life

For further detailed information please contact

**Fresenius Kabi India Pvt. Ltd.**

Heritage House, 6-E, Ramabai Ambedkar Road, Pune - 411001, India

Ph. : 91-20-26053602-7 Fax : 91-20-26138258

[www.fresenius-kabi-india.com](http://www.fresenius-kabi-india.com)