



RESEARCH ARTICLE

CORRELATION BETWEEN METABOLIC SYNDROME AND VOIDING DYSFUNCTION IN FEMALES – A RETROSPECTIVE STUDY

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ABSTRACT

Aim: Voiding dysfunction is an under evaluated issue in females with metabolic syndrome. Aim of our study was to investigate correlation between voiding dysfunction in females with metabolic syndrome.

Materials and Methods: The study was a retrospective study conducted from January 2015 to December 2016 in the Institute of urology, Madras medical college, Chennai. We investigated 80 female patients who visited the urology department for voiding dysfunction with features of metabolic syndrome. The data included were age, body mass index, diabetic status, blood pressure and lower urinary tract symptoms.

Results: A total of 80 women were included as voiding dysfunction group with metabolic syndrome with mean age of 58.5 years (42 – 75years). 74 (92.5%) females had high blood sugar. Diastolic blood pressure was raised in 71 (88.75%) of patients. Obstructive voiding symptoms were noted in 57 (71.25%) of patients and irritative voiding symptoms in 23(28.75%) of patients. Body mass index more than 25 was noted in 31(38.75%) of patients.

Conclusion: Voiding dysfunction is a highly prevalent in females with metabolic syndrome. Diabetes and obesity cause voiding dysfunction through alterations in the phenotype of bladder. Chronic complications of diabetes especially neuropathy, nephropathy, and presence of metabolic syndrome are important predictors of bladder dysfunction.

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INTRODUCTION

Voiding dysfunction is an under evaluated issue in females with metabolic syndrome. Metabolic syndrome is associated with the risk of developing cardiovascular disease and type 2 diabetes. The syndrome is thought to be caused by an underlying disorder of energy utilization and storage. The cause of the syndrome is an area of ongoing medical research. Patients with metabolic syndrome may have storage problems like urgency and urge incontinence or voiding problems like hesitancy and poor stream. Disordered bladder dysfunction is one of the complications of diabetes mellitus that occurs in the middle aged and elderly diabetic patients. Poor glycemic control leads to production of glycosylated end products that cause axonal degeneration and impairment of nerve conduction. This affects autonomic innervations to the bladder muscles and leads to disordered bladder function. Obese women are found to have more stress urinary incontinence and urge

urinary incontinence compared to normal weight women. Obesity is also a risk factor for type 2 diabetes

MATERIALS AND METHODS

The study was a retrospective study conducted from January 2015 to December 2016 in the Institute of urology, Madras medical college, Chennai. We investigated 80 female patients who visited the urology department for voiding dysfunction with features of metabolic syndrome. The data included were age, body mass index, diabetic status, blood pressure and lower urinary tract symptoms.

RESULTS AND OBSERVATIONS

A total of 80 women were included as voiding dysfunction group with metabolic syndrome with mean age of 58.5 years (42 – 75years). 74 (92.5%) females had high blood sugar. Diastolic blood pressure was raised in 71 (88.75%) of patients. Obstructive voiding symptoms were noted in 57 (71.25%) of patients and irritative voiding symptoms in 23 (28.75%) of patients. Body mass index more than 25 was noted in 31(38.75%) of patients.

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Classification of females with voiding dysfunction depending on age

Age group	Total no of patients
40-50 years	6
50-60 years	22
60-70 years	42
70-80 years	10

Pattern of voiding dysfunction

Lower urinary tract symptoms	Total no of patients
Hesitancy	13
Thin stream	12
Sense of incomplete emptying	9
Post void dribbling	11
Infrequent voiding	12
Urge incontinence	13
Stress incontinence	10

Relation between blood sugar and voiding dysfunction

Fasting blood sugar	Patients with voiding dysfunction
120-150mg%	9
150-180mg%	12
180-200mg%	31
200-250mg%	22

Relation between blood pressure and voiding dysfunction

Diastolic blood pressure	Patients with voiding dysfunction
90-100mmhg	20
100-110mmhg	41
110-120mmhg	10

Relation between obesity and voiding dysfunction

Body mass index	Patients with voiding dysfunction
25-30 kg/m ² (over weight)	10
30-35kg/m ² (obese class 1)	8
35-40kg/m ² (obese class 11)	13

DISCUSSION

Voiding dysfunction is an under evaluated issue in females with metabolic syndrome. Metabolic syndrome is associated with the risk of developing cardiovascular disease and type 2 diabetes. The syndrome is thought to be caused by an underlying disorder of energy utilization and storage. The cause of the syndrome is an area of ongoing medical research. Patients with metabolic syndrome may have storage problems like urgency and urge incontinence or voiding problems like hesitancy and poor stream.

Metabolic syndrome

Metabolic syndrome is a clustering of at least three of the five following medical conditions

- Abdominal (central) obesity
- Elevated Blood Pressure
- Elevated Fasting Plasma Glucose
- High Serum Triglycerides
- Low high-density lipoprotein levels

The exact mechanisms of the complex pathways of metabolic syndrome are under investigation. Most patients are older, obese, sedentary, and have a degree of insulin resistance. Stress can also be a contributing factor. The most important

risk factors are diet, genetics, aging, sedentary behaviour or low physical activity, disrupted sleep, mood disorders/psychotropic medication use and excessive alcohol use. There is debate regarding whether obesity or insulin resistance is the cause of the metabolic syndrome or if they are consequences of a more far-reaching metabolic derangement. A number of markers of systemic inflammation, including C-reactive protein, are often increased, as are fibrinogen, interleukin 6, tumour necrosis factor-alpha, and others. Some have pointed to a variety of causes, including increased uric acid levels caused by dietary fructose. It is generally accepted that the current food environment contributes to the development of metabolic syndrome. Our diet is mismatched with our biochemistry. Weight gain is associated with metabolic syndrome. Rather than total adiposity, the core clinical component of the syndrome is visceral and/or ectopic fat (i.e., fat in organs not designed for fat storage) whereas the principal metabolic abnormality is insulin resistance. The continuous provision of energy via dietary carbohydrate, lipid, and protein fuels, unmatched by physical activity/energy demand creates a backlog of the products of mitochondrial oxidation, a process associated with progressive mitochondrial dysfunction and insulin resistance.

Diabetes and voiding dysfunction

Voiding dysfunction is more common in diabetic patients. It is very difficult to estimate exactly what percentage of diabetic patients suffer from voiding dysfunction. There is no correlation of voiding dysfunction with type and duration of diabetes. In addition, the presence or absence of diabetic retinopathy did not correlate with presence or absence of voiding dysfunction. Diabetic bladder dysfunction presents in a spectrum of clinical symptoms ranging from bladder over activity to impaired bladder contractility. Its prevalence has been estimated as being between 25 and 87%. Diabetic cystopathy was used by Fridodt Moller in 1976 and refers to lower urinary symptoms due to diabetic neuropathy. Diabetic cystopathy is characterized by increased post voiding residual volumes and enhanced bladder capacity that is accompanied by decreased bladder sensation and contraction secondary to damage of visceral afferent fibres in the bladder wall. This insidious process causes gradual changes in patient's voiding patterns, with a reduced desire to void, which usually occurs at a stored urine volume of 300–400 ml in healthy subjects. These patients commonly experience difficulty in initiating and maintaining micturition. Therefore, voiding reflexes appear sluggish and an asymptomatic increase in bladder capacity and urinary retention occurs.

On the other hand, diabetic bladder dysfunction can also present as an overactive bladder syndrome usually described as urgency, with or without incontinence, usually with urinary frequency and nocturia. Indeed bladder hypersensitivity and hyper contractility is much more common than bladder hypocontractility. More than half of diabetic patients have detrusor hyper reflexia, while another 23% have reduced detrusor contractility and a further 10% demonstrate detrusor areflexia with the remaining 11% showing indeterminate findings. Based on both animal studies and human findings, Daneshgari et al. presented the “temporal theory of diabetic bladder dysfunction” which proposes that hyperglycemia-induced polyuria plays a major pathophysiological role during the early stages of diabetes polyuria, causing compensatory bladder hypertrophy and associated myogenic and neurogenic

alterations. This stage is compatible with findings of a hyperactive bladder during urodynamic evaluation when patients present with bladder storage concerns (urgency or urge incontinence). With time and accumulation of toxic metabolites, decompensation of bladder tissue and function ensues, resulting in the classical signs and symptoms of diabetic cystopathy (hypocontractile detrusor or atonic bladder) in patients with urinary voiding problems.

Obesity and voiding dysfunction

Obese women are found to have more stress urinary incontinence and urge urinary incontinence compared to normal weight women. Obese women reported greater symptom distress and impact on quality of life from incontinence symptoms, and experienced more incontinent episodes, suggesting they have worse disease and/or experience other factors which increase the symptom burden. As BMI weight categories increased, subjective and objective urinary incontinence severity seemed to increase. It seems plausible that at rest, urethral pressures are greater in obese women, but the urethra is unable to respond to events that require quick increases in urethral pressure. It is possible that obese women rely on greater muscle contraction and force at rest, thereby recruiting a larger proportion of the motor unit pool to maintain continence at rest. When a stress event occurs they are unable to recruit any additional motor units resulting in urinary leakage. Such a hypothesis is consistent with Hahnemann's principle for motor unit recruitment in striated muscles which states that as the requirement for greater muscle contraction and force increases, more and larger motor units are recruited. Research in other fields has demonstrated that obesity is associated with slower median nerve conduction velocities, which further supports a potential neuromuscular aetiology. Further studies which more precisely assess urethral neuromuscular function in obese and normal weight women are necessary. Obese women had less urethral mobility with straining than normal weight women. Lack of urethral mobility is associated with poorer outcomes after stress urinary incontinence treatments and may contribute to increased urge incontinence severity in obese women despite better measures of intrinsic urethral function. In a case-control study of stress incontinent and continent control women,

Investigations

The history taking and physical examination of patients who have signs and symptoms of bladder dysfunction should be followed by laboratory workup tests. The rate of bacterial cystitis is higher in diabetic subjects, so urinalysis and culture with some additional biochemical tests for the assessment of diabetic control and also screening for end organ damage (such as serum glucose, glycosylated hemoglobin, urea, and creatinine) should be done. Other diseases and conditions that can induce or aggravate vesicourethral dysfunction should also be considered. Thus it is important to rule out neurological disorders, especially cerebrovascular accidents, or lumbar disk disorders that can also cause urinary symptoms mimicking those found in diabetes mellitus. Examination of females should also include a complete uro gynaecological examination to rule out pelvic organ prolapse such as cystocele or other forms of pelvic prolapse; an assessment of the integrity of pelvic floor muscle should be done in females. Urodynamic studies are key components of patient examination, and can include a simple cystometrogram,

simultaneous pressure/flow studies, uroflow, sphincter electromyography, and evaluation of leak point pressures plus measurement of post void residual urine.

Management

Management goals include relief of symptoms, prevention and treatment of urinary tract infections, and adequate bladder emptying. In this regard, the management strategies can be grouped into three classes: behavioural, pharmacological, and surgical.

Behavioural treatment

Weight reduction improves urinary incontinence in obese women and should be considered an initial step for moderately obese women as part of non-surgical treatment of incontinence. A recent study analyzed the results of the Diabetes Prevention Program study and concluded that life style modification consisting of a 5–10% weight reduction substantially lowered symptoms of incontinence. Other recommendations may include changes in diet, assessing the amount and timing of fluid intake, and bladder and pelvic muscle training. Recent research has focused on the supplementation of diet with thiamine or cyclohexanoic long chain fatty acids. Some encouraging results show that these compounds can diminish or even prevent diabetic cystopathy. Patients must be educated to minimize nocturnal polyuria, by confining most fluid intake to the morning or early afternoon, avoiding bladder irritants such as caffeinated beverages, and void before going to bed. Attention should also be given to maintaining regular bowel habits by increasing fibre consumption via appropriate foods or supplements, especially in constipated patients. Emphasizing better glucose control and improving blood pressure control are also very important components in such patients. Pelvic floor exercises, or Kegel exercises, are useful to strengthen the pubococcygeus muscles of the pelvic floor, which support the structures of the bladder and urethra. These exercises are helpful in stress, urge and mixed incontinence.

Pharmacological treatment

Antimuscarinic agents represent the cornerstone of treatment for patients who present with an overactive bladder. These agents inhibit the binding of acetylcholine at muscarinic M_2 and M_3 receptors on detrusor smooth muscle cells and other structures within the bladder wall, thus, reducing the contractions of the detrusor muscle and controlling involuntary detrusor contractions without disturbing normal voiding. In general, anticholinergic drugs cause dry mouth, blurred vision, somnolence, dizziness, cognitive problems, and constipation. Close angle glaucoma is a contraindication for anticholinergic treatment. Imipramine is a tricyclic antidepressant that has been extensively used in the treatment of over active bladder, and appears useful in managing diabetic autonomic dysfunction such as incontinence. This drug inhibits the re-uptake of noradrenaline and serotonin by adrenergic nerve endings, resulting in increased contractile effects of noradrenaline on urethral smooth muscle and enhanced detrusor muscle relaxation. In addition to blocking amine re-uptake, imipramine also has a direct smooth muscle relaxing effect that could contribute to increased storage function. Chronic administration of imipramine has shown to be clinically effective in improving functional bladder capacity by

a reduction in detrusor pressure concurrent with an increased resting sphincter tonus. Pharmacotherapy has a limited role in the treatment of detrusor areflexia. Attempts have been made to simulate detrusor muscle by administration of parasympathomimetic drugs. Such drugs stimulate the autonomic effector cells and postganglionic parasympathetic receptors resulting in increased intravesical pressure and decreased bladder capacity. The side effects of cholinergic agents (such as sweating, salivation, tachycardia, and flushing) limit the daily use of them. Alpha-methyl-dopa and phenoxybenzamine have been studied as other therapeutic options. There were two reasons for trying these drugs. First, the bladder neck and posterior urethra contain a predominance of alpha adrenergic receptors. Agents that block or depress their function promote bladder neck and urethral relaxation. Second, postganglionic sympathetic fibres regulate transmission of cholinergic discharge of the pelvic parasympathetic ganglia. Blockade of this effect facilitates bladder contraction by improving the transmission at the pelvic parasympathetic ganglia. However, these agents have provided limited clinical benefits and are rarely used

Surgical treatment

Patients with the classical signs of diabetic impaired detrusor contractility but who do not benefit from non-pharmacological and pharmacological interventions is candidates for surgical intervention. The aim of these procedures is to minimize the risk of urinary tract infection. Vesical neck resection, which is performed through a transurethral rout and leaves the external sphincter intact to preserve urinary continence, has been advocated by some authors. The rationale for this procedure is based on resistance reduction in the presence of a hypotonic bladder. There is, however, a risk of cysto urethrocele in women. In addition, the function of the external sphincter may be impaired due to diabetic neuropathy and also lead to urinary incontinence. Bladder outlet resistance may also be reduced by selective pudendal nerve block. In this procedure, a solution of 1% lidocaine is used initially to determine if micturition is improved and post voiding residual volume decreased, before a unilateral pudendal neurectomy is considered as a treatment option. Sacral neuromodulation is another approved method for urinary urge incontinence, urge-frequency incontinence, and non-obstructive urinary retention refractory to non-surgical treatment

Conclusion

- Voiding dysfunction is an under evaluated issue in females with metabolic syndrome.
 - Voiding dysfunction is a highly prevalent in females with metabolic syndrome.
 - Diabetes and obesity cause voiding dysfunction through alterations in the phenotype of bladder.
 - Diabetic bladder dysfunction is relatively common and can have different manifestations from detrusor instability to poor bladder sensation and contraction.
 - Diabetic neuropathy plus detrusor muscle and urothelial dysfunctions all have some role in pathophysiology
 - Chronic complications of diabetes especially neuropathy, nephropathy, and presence of metabolic syndrome are important predictors of bladder dysfunction.
- Urodynamic evaluation is the cornerstone of diagnosis and determines the actual type of bladder dysfunction and the therapeutic strategies.
 - Obesity induced diabetes and lower urinary tract fibrosis promote voiding dysfunction
 - Obese women are found to have more stress urinary incontinence and urge urinary incontinence compared to normal weight women

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