Clinical Research in Diabetes and Urinary Incontinence: What We

Know and Need to Know

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Abstract

Purpose

We discuss epidemiological and clinical trial research in women with urinary incontinence and diabetes, and provide directions for future research.

Materials and Methods

Published epidemiological and clinical trial literature examining diabetes and incontinence is presented.

Results

Multiple studies have now confirmed that the prevalence and incidence of incontinence is increased in women with type 2 diabetes. Emerging evidence also suggests higher incontinence rates in women with type 1 diabetes or prediabetes. Clinical trial research suggests that weight loss can decrease incontinence in women with prediabetes. An ongoing multicenter trial will examine the effects of weight loss on incontinence in women with type 2 diabetes. Limited trial data in those with type 1 diabetes suggest that intensive glycemic control does not appear to decrease the long-term risk of incontinence in women with type 1 diabetes.

Conclusions

Future research is needed to identify the risk factors, mechanisms, and most effective treatment and prevention strategies to decrease urinary incontinence in women with type 1 or 2 diabetes, or prediabetes. Physicians should be alert for urinary incontinence because it is often not reported and, therefore, it is under treated in women with diabetes and prediabetes.

Key Words: urinary incontinence, obesity, diabetes mellitus, type 1, diabetes mellitus, type 2, prediabetic state

Abbreviations and Acronyms

AHEAD = Action for Health in Diabetes

DCCT = Diabetes Control and Complications Trial

EDIC = Epidemiology of Diabetes Interventions and Complications

Type 2 diabetes and urinary incontinence in women are common, chronic and costly disorders with major public health implications. Type 2 diabetes affects an estimated 19.3 million American adults and another 54 million who have prediabetes or impaired fasting glucose. Total estimated diabetes costs in the United States in 2002 were \$132 billion, including medical care and services, short-term and permanent disability, and premature death. Urinary incontinence is a similarly prevalent disorder, affecting an estimated 12.7 million women, that has profound consequences on quality of life, including social isolation, stigmatization, depression and the end of independent living for some elderly women. Costs of incontinence may be as high as \$30 billion per year in the United States, greater than the annual direct costs of breast, ovarian, cervical and uterine cancers combined.

Sound epidemiological evidence from several studies has linked these 2 disorders and shown that urinary incontinence is 50% to 200% more common in women with type 2 diabetes than in women with normal glucose. ^{7, 8, 9, 10} For example, in the Nurses' Health Study, a large cohort of women, the prevalence of weekly incontinence was 17% in those without diabetes and 24% in those with diabetes. ¹¹ For severe incontinence the difference in prevalence was also significant, that is 2% in women without diabetes vs 4% in women with diabetes. Data on the incidence of incontinence reflect similar patterns. In the Nurses' Health Study the 2-year incidence of weekly incontinence was 5% in those without diabetes and 9% in those with type 2 diabetes. ¹² In this study the prevalence and incidence of urinary incontinence remained significantly greater in women with type 2 diabetes even after controlling for a wide variety of potential confounding factors, including body mass index. These data complement other research⁹ and establish type 2 diabetes as a strong independent risk factor for prevalent and incident urinary incontinence and urgency incontinence in particular.

There has been less research on type 1 diabetes to estimate the prevalence of incontinence and how it may differ to that in women with normal glucose. Recent data on women with type 1

diabetes from the Urological Complications of EDIC study showed a prevalence rate of almost 20% for weekly incontinence. ¹³ Specifically women with type 1 diabetes in this study had a significant 2-fold increased risk of urgency incontinence compared with those without diabetes after adjusting for age, body mass index, parity, hysterectomy and current smoking (9% vs 4.5%, p = 0.01). Thus, type 1 diabetes may also be a risk factor for urinary incontinence in women.

There is also evidence that women with prediabetes are at higher risk for urinary incontinence. In the National Health and Nutrition Examination Survey 2001 to 2002 women with impaired fasting glucose had an increased prevalence of urinary incontinence similar to that in women with diabetes (33.4% and 35.4%, respectively), and significantly higher than in women with normal fasting glucose (16.8%, p <0.001). ¹⁴ Moreover, 2 microvascular complications caused by diabetes, microalbuminuria and peripheral neuropathic pain, were significantly associated with incontinence. These data suggest that incontinence may be a more common consequence of hyperglycemia than other microvascular complications, such as retinopathy, neuropathy or nephropathy.

Risk Factors and Mechanisms

Well recognized and common risk factors for urinary incontinence in women include increasing age, parity, hysterectomy, excess weight and oral estrogen. However, despite mounting evidence of a link between diabetes and incontinence, little is known about the mechanisms by which diabetes leads to incontinence. Some clues from epidemiological studies provide a few possibilities. For example, investigations in women with type 2 diabetes suggest that microvascular complications further increase the prevalence and incidence of urinary incontinence. ^{11, 14} Physiological, microvascular and neurological complications of diabetes result in changes that may impair the function of continence mechanisms, including damage to the bladder innervation, altered detrusor muscle function or urothelial dysfunction. ^{15,}

^{16, 17} However, at the same time the increase in urinary incontinence in women with prediabetes who generally lack these severe diabetic complications suggests that other unknown processes may also underlie the development of incontinence in women with impaired glucose.

Diabetes appears to be related to an increased risk of incontinence with or without obesity. ¹⁰ However, obesity is clearly a strong risk factor for urinary incontinence and type 2 diabetes. Obesity and abdominal fat in particular may influence urinary incontinence by increasing pressure on the bladder, and straining the muscles and connective tissue that support the urethra. ¹⁸ Also, the strong positive relationship between obesity and insulin resistance ¹⁹ suggests several potential mechanisms linking obesity and incontinence. Improving blood glucose control and promoting weight loss have been identified as potential targets for interventions to prevent or treat urinary incontinence in women with diabetes.

Clinical Trials

Only a few clinical treatment trials have examined ways to decrease or prevent urinary incontinence in women with diabetes. The Diabetes Prevention Program examined whether lifestyle intervention targeting diet and physical activity or metformin therapy could prevent urinary incontinence in overweight women with impaired glucose tolerance. Findings indicated that after 3 years the prevalence of urinary incontinence was significantly lower in women in the intensive lifestyle intervention group than in those receiving metformin or placebo (38.3% vs 48.1% and 45.7%, respectively). The effects of lifestyle intervention on incontinence were observed across various subgroups of age, race and initial body mass index. In terms of incontinence subtypes this overall effect was due to a decreased prevalence of stress rather than urge incontinence, most likely reflecting the age of the trial population. Interestingly weight loss was the most important mediator of the beneficial effect of the lifestyle intervention on incontinence. Although patients and clinicians are concerned that exercise exacerbates incontinence, we found that increased physical activity did not appear to have an adverse effect on incontinence.

Whether a similar lifestyle intervention would have positive effects on urinary incontinence in women with type 2 diabetes is unknown. The Look AHEAD trial is a randomized, controlled study in overweight and obese individuals with type 2 diabetes that is designed to assess the long-term effects of an intensive weight loss program delivered during 4 years vs a control group given diabetes support and education. This study was started in 2001 with planned followup until 2012. The Urinary Incontinence Ancillary Study to Look AHEAD will examine the effects of the intensive lifestyle weight loss program on the incidence and prevalence of urinary incontinence in women with type 2 diabetes. Analysis of baseline data on this cohort indicates that a third of women in this ethnically and racially diverse cohort has weekly urinary incontinence. Moreover, obesity was the strongest modifiable risk factor for overall incontinence and stress incontinence.

There are limited trial data on women with type 1 diabetes. The DCCT compared the effects of intensive treatment (insulin 3 or more times per day) or conventional therapy (insulin 1 to 2 times per day) in 1,441 individuals with type 1 diabetes.²² Results indicated that after 6.5 years intensive treatment decreased the risk of retinopathy, nephropathy and neuropathy by 35% to 90% compared with conventional treatment. In 1994 the EDIC study began after the closeout of the DCCT. The EDIC study is a 20-year observational study of the DCCT cohort and 96% of surviving DCCT participants volunteered to participate in it. In 2001 the Urological Complications of Diabetes Group was formed to examine urological complications in the DCCT/EDIC cohort. Interestingly findings indicate that DCCT intervention had beneficial effects on neuropathy, nephropathy and retinopathy during 20 years of followup but there was no significant decrease in the risk of incontinence in women assigned to intensive treatment.²³ The reasons for this remain unclear.¹³ It is possible that treatment for diabetes does not reverse bladder dysfunction or improvements in incontinence associated with treatment were not apparent in this study, in which controls also had good diabetic management.

Future Research

There are several avenues for future investigation in epidemiological and clinical trial research.

Raising Awareness

Recognizing urinary incontinence as an important medical problem remains an issue. For example, in the Nurses' Health Study (a population of health professionals) only 38% of women with new onset urinary incontinence mentioned the condition to a physician. Although there are only limited data on incontinence in men and in men with diabetes, the number of men with incontinence who seek health care for this condition is also low at about 4%.²⁴ Programs are needed to increase awareness of urinary incontinence in patients with diabetes and facilitate communication about incontinence with their health care providers. Equally, strategies are needed to improve the physician diagnosis of urinary incontinence in the context of primary care. A simple diagnostic tool may aid primary care physicians in detecting and treating urinary incontinence in patients with diabetes.²⁵ This and effectiveness trials of pharmacological treatments for incontinence designed to increase physician involvement in treating urinary incontinence in the context of primary care merit further investigation.

Targets for Intervention

Clearly an important area for future epidemiological and basic science research is the risk factors and causes of urinary incontinence in the population with diabetes or prediabetes. Prior studies investigated mechanisms generally in small samples of men and women, often focusing on elderly populations using insulin with age related neurological or urological conditions, lacking adjustment for common risk factors such as age, parity or prior hysterectomy. The relationship between increased urine production in diabetic and incontinent cases has also received little empirical attention. Prospective research in larger, more diverse samples is needed to help identify the mechanisms of and potential targets for intervention.

Clinical Trials

The clinical trial literature on treating and preventing urinary incontinence in women with diabetes is limited. Clinical outcomes of common treatments for urinary incontinence in women with prediabetes and diabetes have not been critically examined. Thus, it remains unclear whether standard urinary incontinence treatments are equally effective in women with diabetes. Given the increasing prevalence of diabetes, the question is becoming increasingly important. Randomized, controlled trials are needed to assess the efficacy and safety of behavioral, pharmacological and surgical treatments for incontinence in women with diabetes. Comparative effectiveness studies are also needed to examine the effects of standard diabetic treatment, standard urinary incontinence treatment and their combination to decrease or prevent urinary incontinence in women with diabetes or prediabetes.

Weight reduction was recently shown to improve incontinence in obese women. The Look AHEAD study will examine the effects of weight loss in women with type 2 diabetes. However, future research should expand this line of investigation and examine, for example, whether the dual diagnosis of diabetes and urinary incontinence creates a teachable moment to improve long-term weight loss outcomes. Moreover, it remains unclear whether weight loss can decrease or prevent urinary incontinence in women with type 1 diabetes. Since urinary incontinence is common in women with gestational diabetes, future research should also examine whether lifestyle intervention to prevent excessive gestational weight gain could decrease and prevent urinary incontinence related to gestational diabetes.

Conclusions

As the population ages, diabetes and lower urinary tract dysfunction will markedly increase in prevalence. Physicians should be alert for urinary incontinence because it is often unrecognized and, therefore, under treated in women with diabetes and prediabetes. Future research is needed to identify risk factors, mechanisms, and most effective treatment and prevention strategies to decrease the psychosocial, medical and economic costs of this prevalent and chronic disorder affecting many women with diabetes.

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