Study shows benefits, drawbacks, for women's incontinence treatments

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Oral medication for treating a type of incontinence in women is roughly as effective as Botox injections to the bladder, reported researchers who conducted a National Institutes of Health clinical trials network study, with each form of treatment having benefits and limitations.

After six months, women in both treatment groups said that the average number of daily episodes had declined from about five per day to about 1-2 per day.

In the study, the researchers compared the effectiveness of Botox injections to oral anticholinergic medications for treating urge urinary incontinence in women. Nearly 250 women participated in the trial comparing Botox injections with anticholinergic medications. On average, the women were 58 years old. Anticholinergic medications reduce bladder contractions by targeting the bladder muscle through the nervous system. Many women who take anticholinergic medications relate having unpleasant side effects, including constipation, dry mouth and dry eyes

The proportion of women receiving Botox whose urinary leakage completely went away six months after starting treatment (27 percent) was twice that of the group taking oral medication (13 percent). Women in the Botox group were more likely to experience incomplete bladder emptying or bladder infections, while the women taking the medication were a little more likely to report that they had dry mouth— a common side effect of the medication.

The study focused on treatment for urge urinary incontinence— the unpredictable release of urine shortly after feeling the urge to urinate. Information on urge incontinence as well as other kinds of incontinence is available from the National Institute of Diabetes, Digestive, and Kidney Diseases at http://kidney.niddk.nih.gov/kudiseases/pubs/uiwomen/index.aspx.

Women are twice as likely as men to experience urinary incontinence, and older women are more likely to experience it than are younger women. An estimated 15.7 percent of U.S. women experience urinary incontinence. Pregnancy and childbirth, menopause, and the structure of the female urinary tract account for this difference.

"This is the first study to compare the effectiveness of Botox treatments to oral medication," said study senior author Susan F. Meikle, M.D., M.S.P.H., of the Contraception and Reproductive Health Branch of the NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and Program Director of the Pelvic Floor Disorders Network (PFDN). "Previously, Botox was reserved for women who had tried oral medications but found them ineffective. Because we included some women who had not been treated with oral medication before, these results suggest that Botox could be discussed as an option for first line treatment."

First author Anthony G. Visco, M.D., of Duke University Medical Center, in Durham, N.C., was the principal investigator of the study. He collaborated with Dr. Meikle and researchers affiliated with Loyola University Chicago; University of Alabama at Birmingham; University of Utah, Salt Lake City; Cleveland Clinic; Kaiser Permanente San Diego; University of Texas Southwestern Medical Center in Dallas; University of Pittsburgh; Oakwood Hospital and Medical Center, Dearborn, Mich.; Oakland University, Royal Oak, Mich.; University of Michigan, Ann Arbor; RTI International, Research Triangle Park, N.C.;

and other researchers associated with the NICHD-supported PFDN.

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The findings appear online in the *New England Journal of Medicine*.

Urge incontinence results from unpredictable activity of the bladder muscles, the cause of which is often unknown. Botox injections work by relaxing the overactive muscles. In August 2011, the U.S. Food and Drug Administration approved Botox, or onabotulinumtoxinA, for the treatment of urge urinary incontinence when the cause of the overactive bladder is known, and due to spinal cord injury, multiple sclerosis or other nervous system disorders.

OnabotulinumtoxinA is not FDA-approved to treat an overactive bladder without a neurologic cause, even when other therapies have been found to be ineffective.

Women diagnosed with urge urinary incontinence were divided randomly into two groups. One received Botox injections in the bladder muscle and also for six months received placebo (sugar) pills. The other group received a saline injection in the bladder muscle and took oral anticholinergic medication for six months. The study participants— as well as their doctors or other staff— did not know whether the women had received anticholinergics or Botox.

Each month, the women recorded the number of leakage episodes they experienced over a three-day period. They also answered questionnaires about their symptoms and quality of life.

About 90 percent of the women in each group responded to treatment within one month. At the end of six months, about 70 percent of the

women in each group reported that their symptoms were adequately controlled.

All women were instructed to stop taking the pills after six months, but the researchers continued to monitor the effectiveness of both treatments for an additional six months. Nine months after the start of their treatment, 52 percent of the women who had received Botox reported adequate symptom control, compared with 32 percent in the oral anticholinergic drug group. At 12 months, the figures were 38 percent and 25 percent.

In addition, side effects in the two groups differed. Two months after the start of treatment, women in the Botox group needed to use a catheter more often to empty their bladders completely (5 percent vs. 0) and were more likely to experience urinary tract infections (33 percent vs. 13 percent). Women taking the oral anticholinergic medication were more likely to report dry mouth (46 percent vs. 31 percent).

According to Dr. Visco, ongoing studies seek to evaluate the cost-effectiveness of the two approaches.

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