willing to accept a 50% chance of being randomly assigned to hysterectomy, and many were recruited to the study after seeking a hysterectomy and deciding instead to be potentially randomized to an alternative of unknown effectiveness. One can imagine such individuals being more favorably inclined to seek a hysterectomy for persistent symptoms after UAE. In contradistinction, women who viewed hysterectomy as a treatment of last resort would not have participated in the EMMY trial and might have accepted some degree of tradeoff between symptom resolution and hysterectomy avoidance.

To determine how large a difference this might make, we can compare the EMMY trial’s 5-year hysterectomy rate to the results of Kaiser Permanente Northern California’s observational study UAE cited previously. The Kaiser patients were not randomly assigned to treatment and were presumably making preference-based decisions in which they were willing to accept a potential tradeoff in symptom relief by selecting UAE. Nevertheless, nearly 20% in the Kaiser cohort underwent hysterectomy in the 5 years after UAE. Had the Kaiser patients been followed up for 5 more years, it is likely that additional hysterectomies would have occurred for persistent symptoms. Whether that rate would have ultimately reached 30% cannot be determined.

The 10-year findings of the EMMY study improve our ability to accurately counsel patients regarding likely outcomes of UAE. I agree with the authors’ conclusion that women who are candidates for hysterectomy for symptomatic uterine leiomyomata should be made aware of UAE as an effective alternative. It will be crucial for patient counseling to include the possibility of late failures more than 2 years after the procedure. Some patients may find a 30% risk of failure too great, particularly women with medical comorbidities that may worsen over time. For these patients, a hysterectomy now may seem safer than a 30% chance of hysterectomy later.—LAL

A Systematic Review and Meta-analysis on the Efficacy of Intravesical Therapy for Bladder Pain Syndrome/Interstitial Cystitis

Jayanta M. Barua, Ignacio Arance, Javier C. Angulo, and Claus R. Riedl

King George Hospital (BHRUT), Ilford (J.M.B.); Barts and the London School of Medicine & Dentistry, QMUL, London (J.M.B.), United Kingdom; Servicio de Urología, Hospital Universitario de Getafe Universidad Europea de Madrid, Madrid, Spain (I.A., J.C.A.); and Department of Urology, Landesklinikum Thermenregion, Baden, Austria (C.R.R.)

Int Urogynecol J 2016;27:1137–1147

ABSTRACT

Although the precise pathophysiology of bladder pain syndrome/interstitial cystitis (BPS/IC) is unclear, the underlying mechanism appears related to a defect in the urine-tissue barrier (the bladder’s protective mucous lining of glycosaminoglycans [GAG]). This defect has been documented in a subset of BPS/IC patients, and a favorable response to GAG-restoring agents has been reported. A number of agents are widely used in Europe for intravesical BPS/IC therapy. The 2 most commonly used GAGs for intravesical instillation are hyaluronic acid and chondroitin sulfate alone or in combination. Other agents include pentosan polysulfate, which is a semisynthetic heparin-like GAG of low molecular weight, and dimethyl sulfoxide (DMSO). (Dimethyl sulfoxide is the only US Food and Drug Administration (FDA)-approved instillation agent for bladder pain.) The limited research-based evidence supporting therapeutic efficacy of these agents is mainly based on uncontrolled trials.
The aim of this meta-analytical review was to compare the clinical efficacy of available products for intravesical therapy of BPS/IC and to assess their pharmacoeconomic impact in clinical decision making. A comprehensive search was performed for articles on intravesical therapy for BPS/IC published between 1996 and 2014 using the PubMed/MEDLINE database. The MEDLINE search identified 345 publications; 326 of these were excluded because they did not meet study criteria. Assessment of symptom reduction and response rates was quantified statistically using effect size (ES).

The final set of 19 articles included 5 prospective controlled trials (CTs) and 14 observational and uncontrolled trials. Among the 801 patients evaluated in the 19 studies, 208 were enrolled in CTs. The largest ES in all CTs for symptom reduction as well as response rate was found for high-molecular-weight hyaluronic acid (HMW-HA). Similar findings were reported in 2 uncontrolled studies with HMW-HA. To achieve a response to intravesical therapy, the number needed to treat was 2.67 for intravesical pentosan polysulfate and 1.31 for HMW-HA. The number needed to treat for both these agents was superior to all other instillates. Cost efficacy and cost effectiveness were higher for HMW-HA compared with the other instillation regimens.

These meta-analytic findings show an advantage of HMW-HA over other instillation agents when medical and pharmacoeconomic aspects are combined. However, well-designed controlled studies are needed that directly compare these different agents.

EDITORIAL COMMENT

(This interesting meta-analysis is narrowly focused on intravesical therapy with single-agent bladder instillation series for BPS/IC. The findings of both the CTs and uncontrolled trials groups show an impressive favorable ES for hyaluronic acid preparations compared with other agents. Instillation therapy with various agents in the bladder is recognized as second-line therapy in BPS/IC treatment algorithms, right behind nonpharmacologic first-line treatments such as pain management and stress reduction. Most clinical practices use a “cocktail” of medications such as lidocaine, injectable heparin, sodium bicarbonate, gentamicin, and DMSO. Unfortunately, the efficacy of these combined regimens is not well supported by trials, and notably, only DMSO is actually approved by the FDA for use in instillation therapy.

The rub is that hyaluronic acid, although effective in several trials collected in this analysis, whereas FDA approved for other uses, is not approved in a form useful for bladder instillation in the United States. Hyaluronic acid is FDA approved for intra-articular injection (Euflexxa) and dermal injection as a filler (Belotero). In a review of clinicaltrials.gov reviews, there are no ongoing trials focusing on placebo-controlled instillation therapies with traditional medications, and only one using a liposomal therapy composed of a sphingomyelin phospholipid bilayer. It would be great to see a United States–based trial of hyaluronic acid for this type of therapy that might offer both simplification of instillation technique and improved evidence to support use of these treatments for our patients.—ACW)

Phenazopyridine for Evaluation of Ureteral Patency: A Randomized Controlled Trial

Katie Propst, Elena Tunitsky-Bitton, David M. O’Sullivan, Adam C. Steinberg, and Christine LaSala

Department of Women’s Health, Female Pelvic Medicine and Reconstructive Surgery and Research Administration, Hartford Hospital, Harford, CT

Obstet Gynecol 2016;128:348–355

Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.