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CLINICAL TRIAL REPORT

The Scientific Rationale for Using Biomaterials in Stress Urinary Incontinence and Pelvic Organ Prolapse

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Aboushwareb T, Mckenzie P, Wezel F, Southgate J, Badlani G. Is Tissue Engineering and Biomaterials the Future for Lower Urinary Tract Dysfunction (LUTD)/Pelvic Organ Prolapse (POP)? *Neurourol and Urodynam*. 2011; 30:775–82.

Campeau L, Gorbachinsky I, Badlani G, Andersson KE. Pelvic floor disorders: Linking genetic risk factors to biochemical changes. *BJUI*. 2011 (in press).

Rating: • Of importance

Introduction: Stress urinary incontinence (SUI) and pelvic organ prolapse (POP) are pelvic floor disorders (PFDs) that can have profoundly negative effects on a patient's quality of life. In the United States, it has been shown that 16% of women over 20 years old suffer from SUI, while 3% of women of that same age group suffer from POP [1]. Furthermore, over 72% of women with POP will have concomitant SUI [2]. Current research efforts into characterizing the etiologies of SUI and POP go beyond looking solely at the patient's environmental and phenotypic factors. The investigation of potential genetic and biochemical etiologies should provide further insight into the development of better prevention and treatment options. Current standards of surgical treatment of SUI and POP include the use of biomaterials, namely biodegradable or synthetic mesh, to address the anatomical defects. Applying stem cell research and regenerative medicine techniques to existing biomaterials could improve the morbidities associated with current materials.

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Aims: Campeau et al. reviewed the literature regarding etiologies of SUI and POP, but focused on genetic and biochemical factors altering the extracellular matrix, causing PFDs.

Aboushwareb et al. sought to tie in etiologies of SUI and POP, the basis for the use of biomaterials in the surgical treatment of SUI and POP, and reviewed how tissue engineering has played a role in bladder augmentation and replacement.

Methods: Aboushwareb et al. performed a literature review, although their search criteria were not specified. Campeau et al. used PubMed, MEDLINE, and MeSH databases to perform a literature review, searching for the keywords "pelvic organ prolapse," "stress urinary incontinence," "polymorphism," "genetic," "collagen," "elastin," and "extracellular matrix."

Results: Aboushwareb et al. utilized 102 articles in the review. Campeau et al. utilized 65 out of 155 articles considered in the review.

Discussion

The anatomically complex female pelvic floor functions to provide support for pelvic organs as well as maintain fecal and urinary continence. It comprises skeletal and smooth muscle groups, as well as various ligaments and fascia. The extracellular matrix (ECM) within the ligaments and fascia consists primarily of collagen types I and III, supplying tensile strength, as well as elastin, affording elasticity and stretch. The ECM is in a dynamic state, balancing collagen

and elastin synthesis and breakdown, which allows for proper pelvic floor function in the normal state. However, studies have shown an imbalance in this system in patients with SUI and POP. Cardinal ligaments and anterior vaginal wall tissue have been shown to have decreased density of collagen in patients with POP [3, 4]. Similarly, decreased collagen concentrations have been observed in endopelvic fascia, anterior vaginal wall tissue, and round ligaments of patients with SUI as compared to control patients without SUI [5–7]. Whether these findings can be explained by decreased synthesis of ECM components or an increase in the rate of their breakdown has yet to be fully elucidated. Studies examining levels of ECM synthesis have been divergent, with some finding increased synthetic rates in patients with POP [8], while others have found no significant difference in levels of collagen synthesis between patients with POP or SUI as compared to normal control patients [5, 8]. However, there is a more uniform consensus among studies investigating collagenolytic activity. Collagen metabolism is largely regulated by matrix metalloproteinases (MMPs), which are zinc-dependent endopeptidases that degrade collagen; over 20 different MMPs have been identified [9]. Multiple studies have revealed higher MMP activity in patients with SUI and POP as compared to control patients [6, 10–13]. With increasingly more information available regarding the etiologies of pelvic floor dysfunction, there is a need for treatment strategies to incorporate this knowledge and translate it into clinical practice.

Comments

Synthetic biomaterials for surgically treating PFDs are currently preferred over native or natural tissue. Natural biomaterials (auto-, allo-, or xenographs) have limited availability, have inconsistent strength, are subject to breakdown, and also have high rates of recurrent disease when used [14–17]. Even though synthetic biomaterials perform better in these areas compared to natural tissue, they certainly have problems of their own. Perforation into the urethra, bladder, or bowel and extrusion into the vagina are the primary complications observed postoperatively. Also, retraction of synthetic materials can occur as the mesh shrinks in vivo, causing reduction in length. Furthermore, implanted mesh is a foreign body and can serve as a nidus for infection. While postoperative outcomes are multifactorial, all of these complications can lead to dyspareunia, chronic pelvic pain, or failure of the procedure.

There is higher clinical recurrence of POP and SUI when a patient's native tissue is used during surgical repair. Their tissue may have decreased collagen content as well as the genetic link to this defect, suggesting a need for biomaterials to be utilized in treatment. The initial use of biomaterials was based on decreasing recurrence, but they were popularized by the availability of commercial kits, leading to widespread use and complications. It is unclear if these complications are solely due to characteristics of the material itself, or whether the surgical technique or even host factors play a role. Clearly, there is a need for development of new mesh technology that can combine the advantages of both natural and synthetic biomaterials. The model product should be able to maintain mechanical strength over time, enhance tissue repair, and be biocompatible and easily customizable for individual patients [18]. While some efforts have been made to produce hybrid biomaterials that utilize synthetic and natural substances [19, 20], further studies into designing an ideal biomaterial are required. The goal is to find a balance between biomaterials that can be easily produced and tailored to an individual patient's needs while incorporating tissue engineering technology that can provide biodegradable tissue. Another issue that also must be considered is cost of production, as well as cost to the patient. Lastly, an important issue raised by Aboushwareb et al. regards the ability to translate basic science research into the clinical realm. While animal experiments are used for safety concerns and tissue response, an animal model cannot function as a surrogate for demonstrating the inherent ECM defects that exist in these patients, nor the mechanical stress of the upright posture in humans. Once in clinical use, randomized clincal trials that can show the difference in the efficacy would require 2 to 4 years of follow-up and many participants to show a statistical difference. However, this goal is not always easily attainable. In TOMUS (Trial Of Mid-Urethral Slings), for instance, the treatment outcomes between two different SUI procedures were found to be equivocal despite the large number of participants [21]. Similarly, the SISTEr (Stress Incontinence Surgical Treatment Efficacy) trial was a multicenter trial by its duration, but the resulting data could not be used clinically because these techniques are used infrequently by surgeons today [22].

Disclosure

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References

1. Nygaard I, Marber M, Burgio K, et al. Prevalence of symptomatic pelvic floor disorders in US women. JAMA. 2008;300:1311–6.
2. Lowder J, Frankman E, Ghetti C, et al. Lower urinary tract symptoms in women with pelvic organ prolapse. Urogynecol J Pelvic Floor Dysfunct. 2010;21:665–72.

3. Salman M, Ozyuncu O, Sargon M, Kucukali T, Durukan T. Light and electron microscopic evaluation of cardinal ligaments in women with or without uterine prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2010;21:235–9.
4. Lin S-Y, Tee Y-T, Ng S-C, Chang H, Lin P, Chen G-D. Changes in the extracellular matrix in the anterior vagina of women with or without prolapse. Urogynecol J Pelvic Floor Dysfunct. 2007;18:43–8.
5. Chen Y, DeSautel M, Anderson A, Badlani G, Kushner L. Collagen synthesis is not altered in women with stress urinary incontinence. Neurourol Urodyn. 2004;23:367–73.
6. Chen BH, Wen Y, Li H, Polan ML. Collagen metabolism and turnover in women with stress urinary incontinence and pelvic prolapse. Urogynecol J Pelvic Floor Dysfunct. 2002;13:80–7. discussion 87.
7. Ulmsten U, Ekman G, Giertz G, Malmstrom A. Different biochemical composition of connective tissue in continent and stress incontinent women. Acta Bostet Gynecol Scand. 1987;66:455–7.
8. Edwall L, Carlström K, Jonasson AF. Markers of collagen synthesis and degradation in urogenital tissue and serum from women with and without uterovaginal prolapse. Mol Hum Reprod. 2008;14:193–7.
9. Nagase H, Woessner JF. Matrix metalloproteinases. J Biol Chem. 1999;274:21491–4.
10. Connell K, Guess M, Chen H, Andikyan V, Bercik R, Taylor H. HOXA11 is critical for development and maintenance of uterosacral ligaments and deficient in pelvic prolapse. J Clin Investig. 2008;118:1050–5.
11. Jackson S, Aver N, Tarlton J, Eckford S, Abrams P, Bailey A. Changes in metabolism of collagen in genitourinary prolapse. Lancet. 1996;347:1658–61.
12. Gabriel B, Watermann D, Hancke K, et al. Increased expression of matrix metalloproteinase-2 in uterosacral ligaments is associated with pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2006;17:478–82.
13. Phillips C, Anthony F, Benyon C, Monga A. Collagen metabolism in the uterosacral ligaments and vaginal skin of women with uterine prolapse. BJOG. 2006;113:39–46.
14. Nieminen K, Hiltunen R, Takala T, Heiskanen E, Merikari M, Niemi K, et al. Outcomes after anterior vaginal wall repair with mesh: a randomized controlled trial with a 3 year follow-up. Am J Obstet Gynecol. 2010;203(3):235.e1–8.
15. Ignjatovic I, Stojkovic I, Basic D, Medojevic N, Potic M. Optimal primary minimally invasive treatment for patients with stress urinary incontinence and symptomatic pelvic organ prolapse: tension free slings with colporrhaphy, or Prolift with the tension free midurethral sling? Eur J Obstet Gynecol Reprod Biol. 2010;50(1):97–101.
16. Nguyen JN, Burchette RJ. Outcome after anterior vaginal prolapse repair: a randomized controlled trial. Obstet Gynecol. 2008;111 (4):891–8.
17. Withagen MI, Milani AL, den Boon J, Vervest HA, Vierhout ME. Trocar-guided mesh compared with conventional vaginal repair in recurrent prolapse: a randomized controlled trial. Obstet Gynecol. 2011;117(2 Pt 1):242–50.
18. Karlovsky ME, Kushner L, Badlani GH. Synthetic biomaterials for pelvic floor reconstruction. Curr Urol Rep. 2005;6:376–84.
19. Lee SJ, Liu J, Oh SH, et al. Development of a composite vascular scaffolding system that withstands physiological vascular conditions. Biomaterials. 2008;29:2891–8.
20. Tillman BW, Yazdani SK, Lee SJ, et al. The in vivo stability of electrospun polycaprolactone-collagen scaffolds in vascular reconstruction. Biomaterials. 2009;30:583–8.
21. Richter HE, Albo ME, et al. Retropubic versus transobturator midurethral slings for stress incontinence. N Engl J Med. 2010;362(22):2066–76.
22. Richter HE, Burgio KL, et al. Factors associated with incontinence frequency in a surgical cohort os stress incontinent women. Am J Obstet Gynecol. 2005;193(6):2088–93.