Editorial

Amnion/chorion grafts and their applications in urology

Jason Akerman[1], Jason R. Kovac[2]

[1]Department of Urology, McMaster University, Hamilton, Ontario, Canada; [2]Men's Health Center, Indianapolis, Indiana 46260, USA

Correspondence to: Dr. Jason R. Kovac, MD, PhD, FACS, FRCSC. Men's Health Center, 8240 Naab Road, Suite 220, Indianapolis, Indiana 46260, USA. Email: jkovac@urologyin.com.

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The use of human amnion/chorion membranes in wound healing and skin grafting dates back to the early 1900s (1-4). Widespread use of these graft materials has been limited by concerns with sourcing, storage, preparation, and the potential for transmission of infectious diseases (including hepatitis C) (4). Recent developments allowing processed tissue allografts to be stored as dehydrated human amnion/chorion membrane (dHACM) has addressed these issues and led to a revitalized interest in potential applications. The advantages of these processed grafts are that they retain their biologically active growth/regulatory factors over a prolonged shelf life (5,6). This has led to extensive use of dHACM across a variety of fields including ophthalmology, pediatric neurosurgery, gynecology, plastic surgery, wound care, oral/maxillofacial surgery, and urology (7).

The greatest uptake of dHACM has been in wound healing. Several randomized studies have shown significant improvements in healing venous stasis ulcers, diabetic wounds, burns, and dermal injuries (5,8-11). In addition to providing a matrix for cell colonization, dHACM serves as an implantable source of growth factors, cytokines, and chemokines. This leads to increased cell signalling which can promote epithelialization of the wound bed and improved healing (6,12). Furthermore, the non-immunogenic nature of dHACM reduces infection, rejection, inflammation, and scarring (6). There is also growing evidence that dHACM may facilitate nerve healing and axonal regeneration. Indeed, when Liang *et al.* (13) studied the effects of natural denuded human amniotic membrane on transected spinal cords in a rat model, significant improvements in functional recovery and axonal regeneration were seen following placement of the amniotic membrane graft. (13)

There has been a great deal of interest in dHACM as a means of improving outcomes in urological surgery. Studies have highlighted favourable applications in reconstructive surgery, radical prostatectomy, fistula repair, and surgical correction of Peyronie's disease (7,14-21). Burgers *et al.* (14) were one of the first groups to look at a potential application of amniotic grafts in urology. They studied the role of neonatal amniotic membranes in promoting neurogenic recovery following ablation of cavernous nerves in a rat model (14). Those rats who received the amniotic membrane had enhancements in mating behaviour and electrically stimulated erections (14). Patel *et al.* (15) then expanded these results in a sample of 58 men undergoing robot-assisted laparoscopic radical prostatectomy. The effect of dHACM placement on the neurovascular bundle at the time of surgery was examined and graft placement enhanced the mean time to potency (1.34 *vs.* 3.39 months) when compared to computer-matched controls (15). Larger, phase 2 prospective trials are currently recruiting patients to confirm these findings (16).

With its neuro-regenerative properties, dHACM has the potential to improve return to potency and quality of erections in men who have experienced injury to the neurovascular bundle. By promoting re-epithelialization and inhibiting scar formation, dHACM has also produced promising results in reconstructive urology. Amniotic grafts been successfully used in urethral reconstruction in a small number of reports (17). Unfortunately, amniotic membrane alone is too weak to support augmentation urethroplasty and becomes deformed or tears when used as anastomotic tissue (7). As such, simultaneous use of dHACM with an additional supportive graft may allow for expanded use in the field of reconstructive urology. Günes *et al.* (7) looked

at a combination of dHACM and buccal mucosal grafts in a rabbit model of acute urethral injury. The group receiving both dHACM and buccal mucosa as part of their repair demonstrated better epithelial transformation compared to either graft alone. The author suggests that this may translate to use in penile augmentation urethroplasty in the future (7). Adamowicz *et al.* (18) also reported beneficial outcomes using a biocomposite dHACM where, using a rat model, a combination of dHACM and electrospun nanofibers was successfully used to replace urinary bladder wall during partial cystectomy (18).

An animal model has also shown promising results in the use of dHACM in surgical correction of Peyronie's disease. The ability of dHACM to adapt to host tissue characteristics makes it an ideal substitution for the tunica albugenia. In their canine model, Salehipour *et al.* (19) found that dHACM grafts showed increased distensibility and elasticity post-operatively. This was confirmed by the presence of elastin fibers on histopathologic examination. During subsequent stimulation of artificial erections, the dHACM was able to tolerate high intra-cavernosal pressures without leaking or bulging (19). This characteristic of dHACM may make it the ideal substitution graft for penile reconstructive surgery. In addition to dHACM, placental matrix-derived stem cells (PM-MSC) have also been used in the management of Peyronie's disease. In a small series of 5 patients, Levy *et al.* (20) found that men with Peyronie's disease who received PM-MSC injections lead to significant reduction in penile plaques (20).

There is growing data to support many applications of dHACM within the field of urology. The ability of dHACM to serve as an implantable source of pro-healing signaling factors, its non-immunogenic nature, and capacity to adapt host tissue properties makes it particularly effective. Emerging evidence in radical prostatectomy, urethral reconstruction, and correction of Peyronie's disease suggests that dHACM may enhance surgical outcomes by reducing time to potency, improved wound healing, and better tissue epithelialization. Adjunct use of dHACM at the time of penile prosthesis presents an additional potential use in urology that may lead to earlier device activation, decreased risk of erosion and infection along with improved patient outcomes. These grafts could also be particularly valuable in diabetic men post penile prosthesis to improve healing and decrease chance of incisional breakdown and device infection.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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