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Wound healing in urology ☆

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ABSTRACT

Wound healing is a dynamic and complex phenomenon of replacing devitalized tissues in the body. Urethral healing takes place in four phases namely inflammation, proliferation, maturation and remodelling, similar to dermal healing. However, the duration of each phase of wound healing in urology is extended for a longer period when compared to that of dermatology. An ideal wound dressing material removes exudate, creates a moist environment, offers protection from foreign substances and promotes tissue regeneration. A single wound dressing material shall not be sufficient to treat all kinds of wounds as each wound is distinct. This review includes the recent attempts to explore the hidden potential of growth factors, stem cells, siRNA, miRNA and drugs for promoting wound healing in urology. The review also discusses the different technologies used in hospitals to treat wounds in urology, which make use of innovative biomaterials synthesised in regenerative medicines like hydrogels, hydrocolloids, foams, films etc., incorporated with growth factors, drug molecules or nanoparticles. These include surgical zippers, laser tissue welding, negative pressure wound therapy, and hyperbaric oxygen treatment.

Contents

1. Introduction

Urology is the branch of science for diagnosing and curing diseases of the urinary tract, which includes the kidneys, urinary bladder, urethra, penis, prostate and scrotum [1,2]. The disruption of the normal anatomical structure of the tissue is termed as injury or wound [3]. Injuries to the organs of the urinary tract may affect their regular functioning, and lead to further impediments or complications. Urinary tract wounds or injuries include blunt trauma, penetrating wounds or accidental wounds during surgery. These injuries are found to affect the surrounding abdominal organs and lead to continuous urine leakage, bleeding, infection. Urinary tract injuries are classified as kidney injuries, bladder injuries, urethral injuries and ureteral injuries [4,5]. Kidney injuries are caused due to extensive sports activities, motor vehicle accidents, unintentional falls, accidents during kidney biopsy or bullet

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wounds. The patients suffer from high blood pressure, kidney failure, infection, delayed bleeding, blood in urine and pain in the upper abdomen. Their treatment depends on the severity of the injury. Minor kidney injuries can be treated with bed rest and uptake of fluids, whereas major wounds are cured by surgery to repair the damaged tissue [6,7]. Bladder injuries are due to high-impact blows to the pelvis or accidents that occur during the caesarean section, hysterectomy or colectomy. Patients may experience lower abdominal pain, difficulty in urination, haematuria (presence of blood in urine) and urinary incontinence. Minor bladder injuries are treated using catheters whereas, surgical repairs are required in the case of major bladder injuries [8,9]. Ureteral injuries occur during ureteroscopy (diagnosis of ureter), pelvic surgeries, stabbed wounds or gunshots. Patients suffer from abdominal pain, infection, urine leakage, blood in urine, fistula formation, etc. Minor ureteral injuries are cured by placing stents in the ureter and major wounds require surgery to reconstruct the ureter [10–13]. Urethral injuries can arise during procedures such as cystoscopy, bladder catheterization or from pelvic fractures and straddle type falls that mainly affect the area between the legs. The main symptoms include permanent narrowing of the urethra, blood in urine, infection, urinary incontinence, blood discharge from the penis of the male or the urethral opening of the female and erectile dysfunction. Minor urethral injuries are cured by inserting a catheter into the urethra and major wounds are treated by surgery [14,15].

Wound healing is a dynamic and complex phenomenon of replacing devitalized tissues of the body [16–19]. Urethroplasty, hypospadias repairs and other surgical interventions that are used to treat defects or injuries of the urinary tract, rely on functional wound healing to be successful [20]. Impaired wound healing may result in the formation of fistula and strictures (scar formation) due to excessive fibrosis. Recurrent microtrauma caused by continuous displacement of damaged urethral tissue persuades a prolonged inflammatory response and increased metabolic activity during the wound healing process [21]. The different phases of wound healing and the various methods adopted to accelerate the healing process, in the case of urology are discussed in the following paragraphs.

Urethral healing takes place in four phases namely inflammation, proliferation, maturation and remodelling, similar to dermal healing. However, the duration of each phase of wound healing in urology is extended for a longer period when compared to that of the skin (Fig. 1) [22]. In normal tissue, bleeding occurs immediately after an injury. During haemostasis, blood vessels constrict and reduce the blood flow to the injury site. Platelets express sticky glycoproteins on their cell membranes that allow them to aggregate with each other. Fibrin and fibronectin connect together to form a plug that blocks the flow of blood from the wound and trap proteins and other particles [23]. Once the bleeding stops, an inflammatory reaction starts in the injured tissue (Fig. 2). Chemokines and cytokines are released to attract cells that phagocytize bacteria, damaged tissue, and debris. Various signalling molecules are produced to initiate the proliferation phase of wound healing. During this period, the intensity of inflammation is reduced and migration of fibroblasts is observed at the wounded site. Angiogenesis or neovascularisation occurs simultaneously with fibroblast proliferation. Endothelial stem cells move to the wounded area using pseudopodia to develop new blood vessels. Angiogenic factors and fibronectin attract these cells to the wound site [24]. During migration, endothelial cells degrade the clot and part of the extracellular matrix (ECM), using collagenases and plasminogen activator. Granulation tissue starts appearing, which mainly consists of blood vessels, fibroblasts, endothelial cells, inflammatory cells and components of the ECM. Fibroblasts help in collagen deposition (type III collagen) that increases the strength of the wound. Re-epithelialisation occurs in which epithelial cells migrate to form a barrier between the wound and the surrounding. The epithelialisation phase is moderated by basal keratinocytes from the wound edges [25]. Remodelling is the last stage of wound healing, which is characterised by collagen deposition and formation of scar

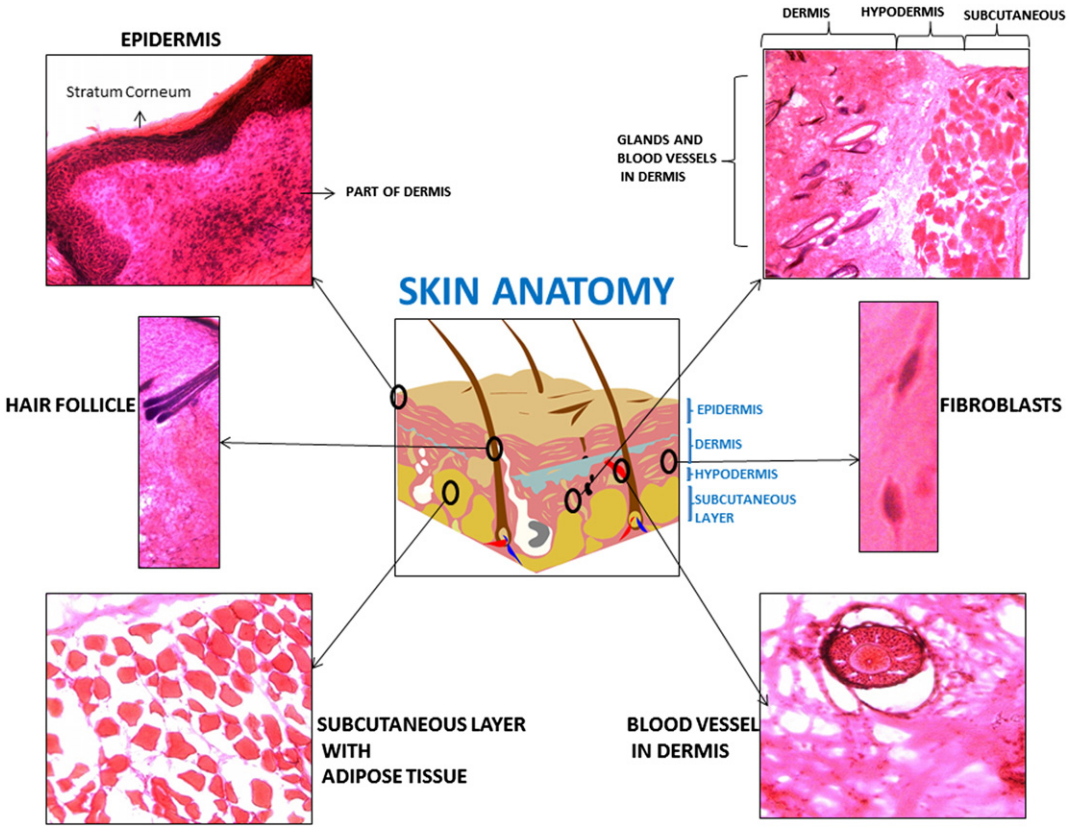

Fig. 1. Haematoxylin and eosin stained images that show different sections of skin.