

ELECTRON MICROSCOPIC STUDY IN THE UROTHELIUM OF INTERSTITIAL CYSTITIS AND KETAMINE RELATED CYSTITIS

Hypothesis / aims of study

In recent an animal study, intact umbrella cell structure in ketamine related cystitis (KC) had been observed by both transmission and scanning electron microscopy (TEM and SEM). Previous human interstitial cystitis/ bladder pain syndrome (IC/BPS) study also revealed no specific urothelium characteristics were detected by SEM. However, urothelium denudation in KC and IC/BPS also had been proved by many H&E or immunochemical stain studies. Current study used TEM and SEM to investigate the urothelium ultrastructure characteristics again in human KC and IC/BPS bladder.

Study design, materials and methods

The KC and IC/BPS patients who were failure to conservative treatment were enrolled into this study. Random cold-cup biopsies of the posterior bladder wall for patients with KC and IC/BPS were obtained after cystoscopic hydrodistention. Bladder muocsa biopsies were also taken from the female patients with stress urinary incontinence, and the specimens were considered as normal control. A portion of each biopsy specimen was immediately placed in 2% glutaraldehyde and 0.1M phosphate buffer, pH 7.4, and within 30 minutes it was cut into 5-mm³ pieces. The tissue was rinsed several times in the buffer for 30 minutes and then dehydrated in an ascending alcohol series. Specimens were oriented and then embedded in critical-point dried. Each bladder specimens were examined both with SEM and TEM.

Results

In the TEM micrograph of normal control urothelium, all cell layers were present and, umbrella cells were intact (Fig. 1A). The invagination of cell membrane and subapical vesicles also could be clearly noted (Fig. 1B). The tight junction complexes were also well-structured (Fig. 1C). In the SEM micrograph, normal control urothelium also revealed intact urothelium uniform umbrella cells (Fig. 2A) and deep folding of cell membrane (Fig. 2B). In the KC bladder, TEM revealed almost totally lost of urothelium, only some basal layer cells and basement membrane could be found (Fig. 1D and 1E).. Collagen deposition in the submucosa was also noted (Fig. 1F). The SEM micrograph of KC bladder revealed lack of umbrella cells and exposed submucosa collagen (Fig. 2C and 2D). In the IC/BPS bladder, multiple layers of urothelium were noted, but the mature umbrella cells were disappeared. The cellular difference between umbrella-intermediate-basal layers seems to be eliminated (Fig. 1G). The tight junctional complexes were also not found in the urothelium cell junction. (Figure 1H). Some microvilli were noted (Fig. 1I). The SEM of IC/BPS urothelium revealed inconsistent size of surface cells (Fig. 2E), and the folding of cell membrane were also decreased (Fig. 2F).

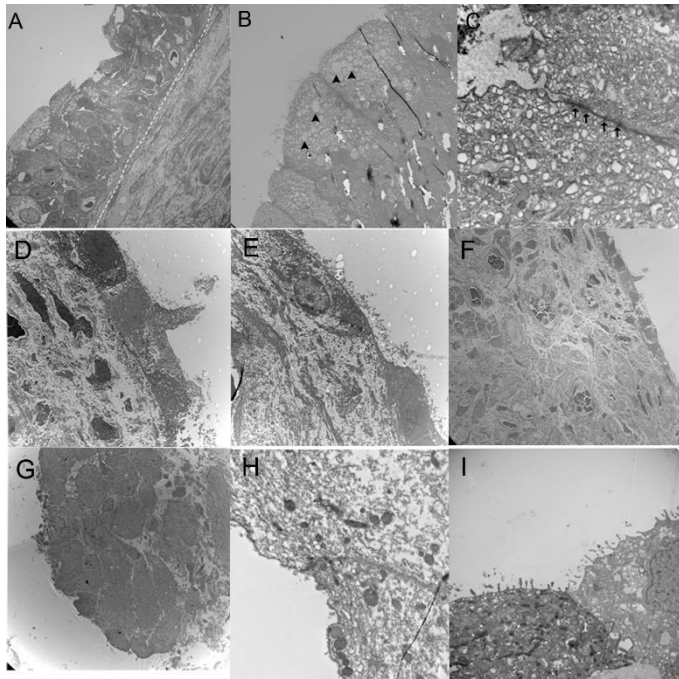


Fig. 1. TEM analysis of urothelium from normal, KC and IC/BPS bladder. A-C normal urothelium: All cell layers were present, and umbrella cells were intact. The invagination of cell membrane and subapical vesicles also could be clearly noted (arrowhead). The tight junction complexes were also well-structured (arrow). D-F urothelium from KC bladder: Urothelium almost totally lost, and only some basal layer cells and basement membrane could be found. Collagen deposition in the submucosa was also noted. G-I urothelium from IC/BPS bladder: Multiple layers of urothelium were noted, but the mature umbrella cells were disappeared. The cellular difference between umbrella-intermediate-basal layers seems to be eliminated. The tight junctional complexes were also not found in the urothelium cell junction. Some microvilli were noted.

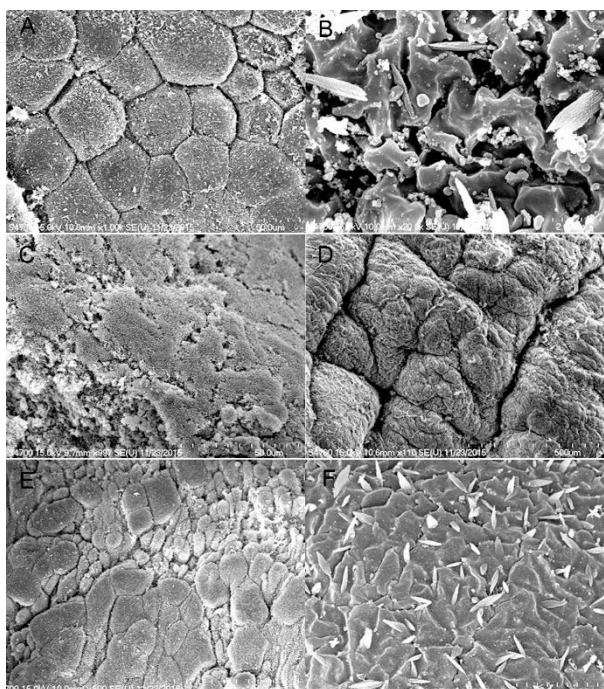


Fig. 2. SEM analysis of urothelium from normal, KC and IC/BPS bladder. A-B urothelium from normal bladder: intact urothelium with uniform umbrella cells and deep folding of cell membrane. C-D urothelium from KC bladder: revealed lack of umbrella cells and exposed submucosa collagen. E-F urothelium from IC/BPS bladder: Surface cells size were not inconsistent, and the folding of cell membrane was also decreased.

Interpretation of results

Our TEM and SEM findings revealed some specific characteristics in KC and IC/BPS urothelium. The urothelium of KC had been almost totally destroyed, and the submucosal tissue were exposed. Collagen tissue was increased even in submucosa. The urothelium of IC/BPS were preserved, but the cellular maturation and differentiation seems to be disappeared. The urothelium functions in the IC/BPS were dysregulated. The microvilli in the IC/BPS urothelium also suggested chronic inflammation.

Concluding message

The urothelium ultrastructure of KC and IC/BPS bladder were abnormal. The urothelium of KC was almost totally destroyed, and the submucosa collagen was exposed. The urothelium maturation and differentiation were disappeared in IC/BPS bladder, and it might result urothelial dysfunction in the patients.

Disclosures

Funding: none **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics Committee:** Research Ethics Committee, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation **Helsinki:** Yes **Informed Consent:** Yes