Editorial

Roundup

ERECTOGENIC CONDOM

Condoms prevent sexually transmitted diseases and accidental pregnancies. However, their acceptance has been only 8% of reproductive age group in the USA.[1] Unappealing physical properties such as the touch, taste, or smell of condoms inhibit their use.[2] Due to physical restriction, condoms are not perceived to enhance pleasure, which is the primary motivator of sexual behavior.[3]

The "Viagra condom" (CSD-500) is lined with 1% glyceryl trinitrate gel in the condom teat, which increases blood flow, helps maintain the erection in men, and thus improves sexual pleasure. Five hundred heterosexual, monogamous couples were randomized to receive either the CSD-500 condoms (Intervention arm; n = 248) or normal condoms (Control arm; n = 252).[4] They were counseled for condom use and female participants were evaluated at precondom use, and at 2, 4, and 6 months for measuring the vaginal prostate-specific antigen (PSA) levels as the surrogate of adherence to condom use. Use of condoms is expected to decrease PSA positivity in vaginal fluid.

PSA detection rates were 12% in the intervention arm and 10% in the control arm. Condom adherence improved with CSD-500 and the PSA-positive rate declined from 11% at enrolment to 6.7% at follow-up. Adverse events were more with the CSD-500 condoms (28% vs. 2%), the most common being headache (10%–17% of females and 4%–7% of males). The higher side effects could be because of the "nocebo effect," i.e., they perceived nonspecific, negative side effects because they were primed during preintervention counseling to expect them. Although the improved adherence reported by the use of erectogenic condoms was not statistically significant, future studies with a heterogeneous population and larger sample size could demonstrate the efficacy.

INCIDENCE AND RISK FACTORS OF VENOUS THROMBOEMBOLISM AFTER TRANSURETHRAL RESECTION OF THE PROSTATE

Venous thromboembolism (VTE) after non-oncological urological surgery has a low incidence of 0.5%–1.4%.[5] VTE encompasses superficial vein thrombosis (SVT), deep vein thrombosis (DVT), and pulmonary embolism (PE), with more than 10-fold 30-day mortality when compared to non-VTE patients.[6] Around 30% of PE patients die within 1-year of diagnosis.[7]

Zheng *et al*. retrospectively evaluated the incidence and risk factors of VTE after transurethral resection of the prostate (TURP).[8] The risk of VTE was evaluated by the Caprini score and in patients with intermediate to high risk for VTE, bilateral lower limb ultrasound was done both pre and postoperatively, and mechanical thromboprophylaxis was provided. Of the total 451 patients who underwent TURP, 8% (n = 36) developed VTE, 4.9% (n = 22) with SVT, 2.7% (n = 12) with DVT, and 0.4% (n = 2) with PE. On multivariate logistic regression analysis, prior VTE (adjusted odds ratio [aOR] = 8.60; 95% confidence interval [CI] 1.47–50.35), postoperative bladder clot (aOR = 4.25; 95% CI 1.29–13.97), and d-dimer >1.25 mg/L (aOR = 4.56; 95% CI 1.41–14.70) were determined as independent risk factors of VTE. Multivariate stepwise logistic regression analysis was then performed considering age as the predominant risk factor and revealed prior VTE (aOR = 10.98; 95% CI 2.26–53.22), postoperative bladder clot (aOR = 6.30; 95% CI 2.26–17.53), d-dimer >1.25 mg/L (aOR = 4.40; 95% CI 1.80–10.77), and age >65 (aOR = 3.11; 95% CI 1.08–8.89) as the independent risk factors of VTE. The higher incidence of VTE in this study could be due to the high rate of postoperative screening ultrasound (60%). The incidence of VTE is underestimated in patients undergoing TURP and a risk-based evaluation with early diagnosis is important.

TRANEXAMIC ACID IN PATIENTS WITH COMPLEX STONES UNDERGOING PERCUTANEOUS NEPHROLITHOTOMY: THE TRANEXAMIC ACID TRAIL

Even though the advantage of tranexamic acid (TxAc) in percutaneous nephrolithotomy has been demonstrated,[9-11] a recent systematic review and meta-analysis[12] suggested more randomized controlled trials (RCT) were required to establish the dose and indications for TxAc.

In this randomized, double-blinded, placebo-controlled trial, 192 patients with a complex kidney stone (Guy's Stone Scores III-IV) were prospectively enrolled and randomized (1:1) to receive either one dose of TxAc (1 g) or a placebo at the time of induction of anesthesia.[13] The blood transfusion rates were lower in the TxAc group (2.2% vs. 10.4%; relative risk [RR] = 0.21, 95% CI 0.03–0.76; P = 0.033). The number needed to treat was 12 (95% CI: 6–236). The use of TxAc significantly reduced the risk of intraoperative blood transfusion and reduced the need for

a blood transfusion by five times. The TxAc group needed shorter time to achieve 95% hemoglobin recovery than the placebo group (mean: 21.3 days; 95% CI: 11.5–31.2 vs. 46.8 days; 95% CI: 35.1–58.4; $P = 0.001$), at follow-up.

There was a steep increase in d-dimer levels at 12 h postoperation in the placebo group (1723.6 vs. 788.7; 95% CI for difference 298.7–763.1; $P = 0.001$) and at 24 h, D-dimer levels decreased but still remained higher in the placebo group ($P = 0.03$). No significant difference was found in level of fibrinogen, platelet count, and prothrombin time. TxAc group showed higher immediate and 3-month seizure frequency reduction compared with those in the placebo group (29% vs. 14.7%, odds ratio: 2.37 $P = 0.019$, and 46.2% vs. 28.1%, odds ratio: 2.20; $P = 0.011$, respectively).

PROGNOSTIC VALUE OF PROSTATE VOLUME IN NON-MUSCLE INVASIVE BLADDER CANCER

Evidence is maturing that benign prostatic hyperplasia (BPH) is associated with an increased incidence of bladder cancer (BC) (RR = 2.38)[14] and using 5- Androgen receptor inhibitor (ARI) or androgen deprivation therapy in prostate cancer also reduces recurrence of BC.[15] Moderate-to-severe lower urinary tract symptoms were associated with a poor prognosis of non-muscle invasive bladder cancer (NMIBC) and the International Prostate Symptom Score is a significant predictor of recurrence of NMIBC.[16] Hence, this study by Ham *et al.*[17] focused on prostate volume (PV) as a prognostic marker of NMIBC.

Medical records of men who underwent TURBT for NMIBC were retrospectively reviewed and based on PV (measured by computed tomography) were grouped (Group 1: 264 patients with ≤30 mL; group 2: 124 patients with >30 mL). Propensity score matching analysis was used to adjust selection bias and assessed for recurrence-free survival (RFS) and progression-free survival (PFS).

At a median follow-up duration of 52 months, group 1 showed higher 5-year RFS and PFS (69.3% vs. 47.0%, $P = 0.001$; 96.7% vs. 87.7%, $P = 0.002$). Multivariable cox analysis showed that a greater PV was associated with worse RFS and PFS. The hypothesis for the cause of these results is that the prognosis of BC is related to androgen receptor (AR) signaling. AR is likely to be relatively suppressed in small prostates, thereby suppressing the recurrence and progression of BC. AR plays an important role in enhancing cell growth in both stromal and epithelial cells, and it promotes the development of BPH.[18] Another possible explanation is that 5-ARI reduces PV by the activity of androgen-regulated growth factor, which is responsible for angiogenesis and expression of vascular endothelial growth factor was reduced in the prostate of patients with huge prostate using 5-ARI.[19]

SEXUAL DYSFUNCTION AND PENILE COMPLICATION AFTER TRANSECTING EXCISION AND PRIMARY ANASTOMOSIS OR BUCCAL MUCOSA GRAFTING FOR SHORT BULBAR URETHRAL STRICTURE: THE FIRST RANDOMIZED CONTROLLED TRIAL

Sexual dysfunction such as penile shortening and impaired erection is more common after anastomotic urethroplasty compared to the augmentation techniques.[20] Augmentation (without transection) of the spongiosal tissue is beneficial as it preserves the blood flow and limits the penile or sexual dysfunction. However, this hypothesis was not supported by any high-level evidence, and only prospective nonrandomized studies were reported to date.[21,22]

In the first multicenter RCT between two different bulbar urethroplasty techniques, Nilsen *et al.*[23] randomized (1:1) men with bulbar urethral stricture of < 2 cm to either transecting excision and primary anastomosis (tEPA) ($n = 75$) or buccal mucosa grafting (BMG) ($n = 76$). At a 12-month follow-up, the tEPA group reported more penile complications ($P = 0.02$), especially reduced glans filling ($P = 0.03$) and shortening of penis ($P = 0.001$). The risk of reporting penile complications was greater in the tEPA group for all questions (Q) in the penile complications questionnaire; Q1 (ejaculation), Q2 (glans filling), Q3 (glans sensation), Q4 (penile length), and Q5 (penile direction), at 3 months and sustained at 12 months for Q2 and Q4. However, there was no significant difference in postoperative IIEF-5 total score between the groups.

Penile complications, especially reduced glans filling and penile shortening, are more common after tEPA than BMG urethroplasty. Differences were observed in glans filling, but not in sensation, supports the hypothesis that reduced blood supply due to transection of the corpus spongiosum is the cause.

SAFETY OF NOT WITHHOLDING CLOPIDOGREL BEFORE TRANSURETHRAL RESECTION OF THE PROSTATE

Current guidelines recommend withholding clopidogrel 5–7 days before elective TURP[24] but its discontinuation can lead to ischemic events in patients with ischemic cardiac disease or with cardiac stents. The prothrombotic tendency of surgery also increases the risk. In this retrospective study, Abdulhamid *et al.* assessed the safety of continuing clopidogrel during TURP.[25]

Men with a prostate size of 55–65 mL underwent monopolar TURP; group 1 continued clopidogrel (CTC; $n = 165$) and the other never used any drug (NCTC; $n = 164$). Intraoperative blood loss was measured by calorimetry

and classified as mild (<200 mL), moderate (200–300 mL), or severe (>300 mL).

There was no statistically significant difference between the CTC and NCTC groups with regards to mild (93% and 95%) or moderate (7% and 5%) blood loss, respectively. Duration of the surgeries (between 65 and 80 min in 90% and 92%), preoperative hematocrit (normal in 94% and 97%), and transfusion rates (3% and 2%) were also similar between the CTC and NCTC groups.

The authors concluded that continuation of clopidogrel during TURP was not associated with a higher probability of hemorrhage, PRBC transfusion, secondary hemorrhage, or clot retention.

A PROSPECTIVE STUDY OF SINGLE-PORT VERSUS MULTI-PORT PATIENT-REPORTED SURGICAL OUTCOMES WITH DA VINCI SINGLE-PORT ROBOTIC SYSTEM

Morgantini *et al.*[26] compared cosmetic and psychometric outcomes of the da Vinci Single Port robotic system (SP) which uses a single 25-mm incision versus the multiport system (MP), which used multiple 5- to 22-mm incisions for uro-oncological surgery.

In this prospective study, including SP (n = 53) and MP (n = 24), patients completed a patient scar assessment questionnaire at 20 days (n = 77) and 90 days (n = 37) following surgery, which had five subscales: appearance, symptoms, consciousness, contentment with appearance, and satisfaction with symptoms.

The number of individuals receiving pain medication (50% vs. 21%, P = 0.009), appearance (17% vs. 14%; P = 0.001), symptoms (10% vs. 8%; P =.012), and consciousness (11% vs. 9%; P =.001) were all significantly better at 20 days and only appearance (14% vs. 12%; P =.016) at 90 days with the SP.

INTERIM ANALYSIS OF PADRES (PRIOR AXITINIB AS A DETERMINANT OF OUTCOME OF RENAL SURGERY-NCT03438708) CLINICAL TRIAL

In this single-arm phase II clinical study of neoadjuvant Axitinib[27] in patients with biopsy-proven clear cell complex RCC with indications for partial nephrectomy (PN), and in whom radical nephrectomy may result in dialysis were recruited. Axitinib 5 mg was taken twice a day for 8 weeks before to surgery.

A total of 26 patients, with a median age of 69 years, were followed up for 12 months. Before treatment, 19 patients (73.1%) had clinical T3a tumors. After treatment, 17 (65.4%) patients had T3a tumors, while 8/26 (31%) of patients had down-staged on imaging. Axitinib reduced median tumor size (19%, 7.7 vs. 6.3 cm, P = 0.001) and RENAL score (11 vs. 10, P = 0.001); 21/26 (80.9%) had partial response (PR), and 5/26 (19.2%) had stable disease (RECIST criteria). PN was conducted in 20/26 (76.9%) cases, with a median ischemia duration of 34 min and negative margins in 25/26 (96.8%). On final pathology, all radical nephrectomy patients were T3a. At the final follow-up, 1/26 (3.8%) of the patients died from progression, and 2/26 (7.7%) experienced recurrence.

In this cohort of extremely complex renal masses, neoadjuvant Axitinib resulted in considerable tumor size and complexity reductions, allowing PN with acceptable safety and functional preservation. Accrual in this study is still going on to attain the goal of 50 patients.

DOSTARLIMAB; IS IT TOO EARLY TO SAY THAT SEARCH FOR A DRUG TO CURE CANCER HAS ENDED?

Dostarlimab (Jemperli; GlaxoSmithKline) is a monoclonal anti-PD1 antibody reported as the most effective treatment for patients with locally advanced rectal adenocarcinoma in a recent phase two research. The drug's effectiveness was previously proven in a multicenter phase one study (GARNET), which enrolled 290 patients with advanced endometrial cancer. An objective response rate of 43.5% was reported, with 36 patients having PR, and 11 showing complete responses (CR).[28]

Dostarlimab blocks the checkpoint receptor (PD-1) in mismatch repair-deficient locally progressed rectal cancer, exposing the tumor cells to the immune system. In this study, 16 patients were administered dostarlimab for 6 months in the neoadjuvant setting (500 mg once every 3 weeks).[29] The medicine was given to 12 patients for a total of 6 months, while the other four patients received one dosage. The average length of follow-up was 12 months (range - 6–25 months). Symptomatic improvement was seen in just 9 weeks after starting therapy. Digital rectal examination, colonoscopy, and magnetic resonance imaging (MRI) were used to evaluate the response. All 12 patients demonstrated a clinical CR. The most commonly reported adverse effects were dermatitis (31%) and pruritus (25%). During the trial period, no adverse events of grade 3 or higher were reported. There were no recurrences in the study population.

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