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1. Introduction

Since their introduction in the treatment of erectile dysfunction (ED), phosphodiesterase type 5 (PDE-5) inhibitors have achieved widespread acceptance. Today PDE-5 inhibitors are considered as first-line oral pharmacotherapy in the management of ED (Hatzimouratidis et al., 2010). However, penile implants are still a popular choice, especially in patients who have failed to achieve erections by chemical enhancement, who prefer a permanent solution to their condition or in those who have considerable scar tissue in the penis resulting in erection deformalities (Mulcahy 1999). Despite its invasiveness, penile prostheses provide high satisfaction rates (Montague & Angermeier 2001).

The types of prosthesis most commonly implanted are the two-piece and the three-piece inflatable device, and the soft and malleable prosthesis. In the last few years the three-piece inflatable device has been used for preference, as it improves the erection with the most acceptable functional and cosmetical results (Minervini et al., 2006; Bettocchi et al., 2008). Engineering changes and designs revisions have reduced the mechanical malfunctions associated with inflatable penis prostheses to less than 5 % (Carson et al., 2000; Carson 2004). As penile prostheses are now expected to function for an average of 8-12 years post implantation, infection has become a more significant problem. The incidence of infection has been reported to range from 0.5 to 17.7% (Quesada & Light, 1993; Wilson & Delk, 1995) usually about 1-3 % in case of primary implantation, and about 10-13 % in case of revision or reimplantation (Abouassaly et al., 2004).

The traditional treatment of penile prosthesis infection is systematic and local antibiotics application with the complete removal of the device followed by reinsertion within 2–12 months. However, removal of the device can lead to corporeal fibrosis, making dilation of the corporeal bodies difficult and reinsertion of a new device more complicated (Brant et al., 1996; Mulcahy, 1999).

To reduce the risk of device associated infections and to avoid the difficulties associated with late reinsertions many modifications have been developed such as antibiotic or hydrophilic coated devices and immediate replacement of the infected prosthesis (salvage techniques).
The aim of this chapter is to summarize the different methods of prevention and treatment of penile prosthesis infections.

2. Pathogenesis/epidemiology

*Staphylococcus* species, especially *Staphylococcus epidermidis* are the most common infecting pathogens, isolated from 35 to 56% of infected penile prostheses patients (Carson, 2003). Gram-negative enteric bacteria including *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Serratia marcescens* may also be pathogens, accounting for 20% of infections (Abouassaly et al., 2004). Gram-negative bacteria can combine with anaerobic organisms in severe infections, such as *Bacteroides* species, and lead to gangrene of the penis. Fungi, mycobacteria and *Neisseria gonorrhoea* have also been reported as etiological agents in penile prosthesis infections (Carson, 1989; Abouassaly et al., 2004).

Penile prostheses get infected predominantly secondary to bacterial seeding at the time of surgery. Prosthetic materials attract bacteria and support subsequent biofilm formation. In a multicenter study culture positive bacteria were found in 70% of patients with clinically uninfected penile prostheses during revision surgery for mechanical malfunction. *Staphylococcus* species were cultured in 90% of the cases (Henry et al., 2004), which have an enhanced ability to produce glycocalyx biofilm.

Penile prosthesis infections can be divided into clinically apparent and subclinical infections. Clinical infections present with penile pain, induration, erythema, fever, purulent drainage from the wound and extrusion. Subclinical infections most often manifest by chronic prosthesis-associated pain.

3. Risk factors

Known risk factors for penile prosthesis infection include urinary tract infection, infections elsewhere in the body and hematogenous spread (Carson & Robertson, 1988; Little & Rhodus, 1992). There is an increased incidence of infection among patients undergoing primary implantation with penile reconstruction or secondary prosthesis revision compared to primary implantation alone, probably due to the increased duration of surgery (Quesada & Light, 1993; Jarow, 1996). The role of diabetes mellitus and spinal chord injury, as risk factors of penile prosthesis infection are contradictory (Jarow, 1996; Cakan et al., 2003).

4. Prevention

4.1 General aspects

Because in most cases bacterial contamination occurs at the time of surgery, it is essential to use appropriate preoperative preparations. Short preoperative hospital stays have been documented to maintain low virulence (Carson, 2003). It is important to eliminate skin infections and to have sterile urine prior to surgery. Washing the genital region with strong soap in the days before the procedure, preoperative shaving and an aggressive scrub of the operating area is recommended to decrease the risk of infection (Mulcahy, 1999; Gomelsky & Dmochowski, 2003).
During surgery adequate sterile technique, short operating time, minimal tissue devitalization along with effective wound closure can all decrease the rate of perioperative infections (Scott, 1987).

4.2 Perioperative antibiotic prophylaxis

Although the effectiveness of prophylactic perioperative antibiotics for implantation of penile prosthesis has never been proven by prospective studies, their use has become established and favored by most urologists. Antibiotics should be administered 1-2 hours prior to surgery and continued for 36-48 hours postoperatively. Most common pathogenic organisms most likely to produce infections must be targeted when choosing prophylactic antibiotics. Therefore traditional prophylaxis include a parenteral aminoglycoside for Gram-negative and a first- or second generation cephalosporin or vancomycin for Gram-positive organisms coverage (Schwartz et al., 1996; Naber et al., 2001). Schwarz et al found in a randomized prospective trial of 20 patients that oral fluoroquinolone (ofloxacin) administered 2 hours before surgery achieved significantly higher intracavernosal levels and was more cost-effective than the combination of gentamicin and cefazolin (Schwartz et al., 1996). To estimate the safety and efficacy of this prophylaxis modality, further studies with similar settings, but bigger sample size should be performed.

4.3 Antibiotic impregnation

Early efforts in device impregnation focused on coating catheters with antibiotics. In 1995 Raad et al reported that in in vitro studies catheters coated with a combination of rifampin and minocycline provided significantly better inhibitory activities against S. epidermidis, S. aureus and E. faecalis than catheters coated with either drug alone or vancomycin (Raad et al., 1995). After additional in vitro and in vivo studies in 2001 the US Food and Drug Administration approved the use of penile prosthesis coated with a combination of rifampin and minocycline called InhibiZone. The concentrations of the antibiotics, while adequate for decreasing colonization, provided only minimal serum levels of the agents. Coated inflatable penile prostheses are implanted in a fashion similar to those without antibiotic treatment except that the devices are not soaked prior to implantation (Carson, 2004).

In a retrospective study Carson et al reported 61.7% decrease in perioperative infection with InhibiZone compared to controls at 1 year post infection (Carson, 2004). The same group recently published their long-term clinical outcomes of almost 40,000 implants. There were significantly less revisions due to infections in the impregnated compared to the non-impregnated group at up to 7.7 years of follow-up (1.1% vs 2.5%, respectively)(Carson et al., 2011). In a subset of diabetic patients in the same series, the rate of infection-related revisions was significantly lower in the impregnated group compared to the controls at 7 years (1.62 % vs 4.24 %)(Mulcahy & Carson, 2011). In 2007 Wilson et al. began a prospective randomized study comparing the infection rate of rifampin and minocycline coated implants with implants without impregnation (Wilson et al., 2007). After it became evident that the infection rate was less with the impregnated group they abandoned the other arm because of ethical considerations and compared they results with the previously published series of the same surgical team with noncoated implants (Wilson & Delk, 1995; Wilson et al. 1998). The use of antibiotic coated inflatable
penile prosthesis resulted in a statistically significant reduction in the infection rates compared with the historical data in nondiabetic virgin implant patients \( (p=0.0024) \), diabetic virgin implant patients \( (p=0.0141) \) and in revision patients in whom washout with antiseptic solutions was used \( (p=0.0095) \). Revision without washout had the same infection rate \( (10\%) \) as with noncoated implants.

4.4 Hydrophilic coating
In 2002 a hydrophilic penile prosthesis coating was developed which has been shown to decrease bacterial adherence \( \text{in vitro} \) and in animal models (Rajpurkar et al., 2004). This coating absorbs surgeon chosen intraoperative antibiotics that can elute into surrounding tissues over 24-72 h to further decrease infection (Hellstrom et al., 2003). Mansouri and colleagues compared the spectrum and durability, both \( \text{in vitro} \) and \( \text{in vivo} \) of the hydrophilic coated prosthesis dipped in vancomycin and the InhibiZone implants, and found that the antibiotic pre-impregnated prosthesis had a broader spectrum \( \text{in vitro} \) and a more durable antimicrobial activity \( \text{in vitro} \) and \( \text{in an animal model} \) than implants dipped in vancomycin (Mansouri et al. 2009).

Clinical data on the hydrophilic coated inflatable penile prosthesis is limited. Wolter et al. presented their one-year experience with the device (Titan, Mentor Corporation, Santa Barbara, CA) (Wolter & Hellstrom 2004), the infection rate for 2357 coated penile prostheses was 1.06 % compared to 2.07 % in 482 uncoated penile prostheses implanted over the same time period. Although preliminary data using this device shows promise, long-term follow-up and prospective studies are not yet available.

5. Treatment
Subclinical infections may be more common than clinically apparent infections. These infections are difficult to diagnose and even more challenging to treat. Parsons \textit{et al.} recommend initial trial of oral antibiotic therapy using long-term antibiotics (ciprofloxacin 500mg twice daily) (Parsons et al., 1993). Following initiation of antibiotics, pain suppression should suggest continuing antibiotics for 10–12 weeks. The authors reported a 60% success rate with conservative treatment of subclinical penile prosthesis infections. The use of oral cephalosporins (cefalexin and cephradine) has also been suggested for 10-12 weeks, although success rates are lower at 25-30% (Choong & Whitfield, 2000; Carson, 2003). If pain fails to resolve or rapidly returns after antibiotics, however, surgical intervention is appropriate. Parsons \textit{et al.} have reported 90% success rate in treating these prostheses with an exchange protocol including systemic antibiotics for 24–48 h using vancomycin. The suspected infected prosthesis is then removed and a combination of vancomycin and protamine was used for antibiotic irrigation prior to reimplantation of a new prostheses. Patients are maintained on vancomycin and parenteral antibiotics for 1 week (Parsons et al., 1993; Carson, 2003).

In case of clinically apparent infection surgical intervention along with antibiotics is of critical importance. The traditional treatment consists of the immediate removal of all the components followed by delayed reimplantation 2-12 months later (Gomelsky & Dmochowski, 2003; Mulcahy, 2003). The advantage of this solution is that the new implant is scheduled only when the infection has completely cleared. However, removal of the
device along with inflammation from the infectious process leads to corporeal fibrosis and scarring, which almost always results in penile shortening and may make dilatation of the corporeal bodies very difficult, resulting reinsertion of a new device more complicated and sometimes impossible (Brant et al., 1996; Mulcahy, 1999).

A salvage protocol was instituted in 1991 to avoid difficult reinsertion and maintain as much penile length as possible. The salvage procedure involves removing all parts of the infected prosthesis, washing the wound, and replacing the device at the same procedure. Mulcahy et al. recommend a sequence of irrigating solutions including kanamycin and bacitracin in normal saline followed by half-strength hydrogen peroxide, half-strength povidone-iodine solution, pressurized normal saline containing vancomycin and gentamicin, half-strength povidone-iodine, half-strength hydrogen peroxide, and finally another kanamycin/bacitracin solution (Mulcahy et al., 1995). Gloves, instruments, gowns, and drapes are changed and a new inflatable penile prosthesis is immediately implanted. Postoperatively, patients are treated with antibiotics (2x500 mg ciprofloxacin) for 4-6 weeks. Antibiotics can be modified based on culture and sensitivity results. The reported success rate of the salvage procedure is 84-91% (Brant et al., 1996; Mulcahy, 2003). To avoid complications of late reinsertion the salvage protocol is a treatment alternative of traditional delayed reimplantation, although in patients with life-threatening systemic conditions such as septicemia, or diabetic ketoacidosis, or in whom necrotizing infections with death of penile skin is occurring salvage procedure is not recommended (Brant et al., 1996; Mulcahy, 1999).

The delayed salvage procedure consists of placement of a drainage tube after removal of the prosthesis; antibiotic solution is irrigated through the drain and a new prosthesis is placed about 3 days later. However, Knoll et al could not find a statistically significant difference between immediate and delayed salvage procedure (Knoll, 1998), while there are the additional cost of the second surgical procedure.

6. Further research

Prospective studies and long-term follow up are needed to make stronger recommendations about the different methods in the prevention or treatment of penile prostheses infections, especially about the hydrophilic coated penile prosthesis.

7. Conclusion

The efforts to apply more effective methods of prevention and the new developments of prosthesis coatings resulted a significant reduction of the infectious complications of penile prosthesis implantation. Further improvements of surgical procedures and prosthesis materials and coatings can lead to further decrease of the infection rates in the future.

8. References


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Complicated urinary tract infections (cUTIs) are a major cause of hospital admissions and are associated with significant morbidity and health care costs. Knowledge of baseline risk of urinary tract infection can help clinicians make informed diagnostic and therapeutic decisions. Prevalence rates of UTI vary by age, gender, race, and other predisposing risk factors. In this regard, this book provides comprehensive information on etiology, epidemiology, immunology, pathology, pathogenic mechanisms, symptomatology, investigation and management of urinary tract infection. Chapters cover common problems in urinary tract infection and put emphasis on the importance of making a correct clinical decision and choosing the appropriate therapeutic approach. Topics are organized to address all of the major complicated conditions frequently seen in urinary tract infection. The authors have paid particular attention to urological problems like the outcome of patients with vesicoureteric reflux, the factors affecting renal scarring, obstructive uropathy, voiding dysfunction and catheter associated problems. This book will be indispensable for all professionals involved in the medical care of patients with urinary tract infection.

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