An Update in the Use of JJ Stents

Actualización en el uso de catéteres JJ

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Abstract

Introduction Ureteral stents are widely used tools in the daily practice of the urologist due to the fact that they solve the endo- and extraluminal ureteral obstructions, enabling an adequate urine flow. They are the preferred tool because they are easy to insert and versatile, and are used to treat various urologic pathologies; nonetheless, they are not exempt from complications.

Objectives To present an update in the use of JJ stents, describing their main associated symptoms and complications, indications and newest developments.

Materials and Methods We performed a literature review in the Embase, Pubmed and Google Scholar databases, with the following terms and cross-references: ureteral stent; diagnosis; treatment; and urology, restricting the search to the past 7 years. A total of 428 articles were found, and 49 were used in the revision.

Results We described the symptoms and complications associated with the use of JJ stents and their prevention, their use in the treatment of lithiasis and oncologic diseases, the utility of metallic stents, and new designs and improvements in their development.

Conclusions JJ stents remain a very useful tool in the daily practice of the urologist, but are not exempt from having adverse effects and complications. There have been advances that decrease the adverse effects associated with their use, mainly infection, symptoms associated to the insertion, and risk of incrustation.

Keywords ▶ catheters ▶ ureteral stent ▶ infection ▶ ureteral obstruction ▶ vesico-ureteral reflux ▶ urolithiasis

Resumen

Introducción Los catéteres ureterales son una herramienta ampliamente usada en la práctica diaria del urólogo, dado a que alivian la obstrucción endo y extraluminal ureteral, permitiendo así el adecuado flujo de orina. Se prefieren por encima de otros métodos por su facilidad de inserción y su versatilidad de uso dentro de las distintas patologías urológicas; sin embargo, no están exentos de complicaciones.

Objetivos Presentar una actualización en el uso de catéteres JJ que incluya información acerca de los síntomas y complicaciones, sus indicaciones de uso y novedades.

Materiales y Métodos Realizamos una revisión narrativa de la literatura en las bases de datos Embase, Pubmed y Google Scholar, con los siguientes términos y sus
Introduction

Ureteral stents (USs) are common tools employed in Urology that enable urine drainage from the kidney to the bladder. Zimskind first described them in 1967; Gibbons introduced the auto retention US in 1976; and, subsequently, Finney described in 1978 the US known as “double J”. They are frequently used in the ureteroscopic management of lithiasis, trauma, oncologic and reconstructive surgery.

Despite their wide use, they present multiple secondary effects due to the fact that they are strange bodies that induce inflammation on the urothelium. Among these effects are pain, a sensation of discomfort, urinary urgency, hematuria, associated infection and incrustation. There is no clear etiology for the inflammatory reaction that the US causes on the urothelium. As of today, different types of US and different biomaterials have been developed in order to decrease these adverse effects.

The ideal US should be easy to insert, relieve the endo- or extraluminal obstruction, enable an adequate urinary flow, be resistant to incrustation and infections, be chemically inert, and should not produce associated symptoms. Therefore, it should have high tensile force, low friction coefficient, and should be self-holding. Unfortunately, we currently do not have an “ideal urinary stent.”

The first designed USs were made of silicone and had an open tip, but were not self-holding. As their use increased, new forms were developed, until the development of the now used double J (JJ), which is self-holding, thus preventing distal and proximal migration, and decreasing the urinary symptoms. The associated complications can be divided into early ones (which occur less than 4 weeks after the insertion), such as dysuria, abdominal pain and hematuria, and late ones (which occur more than 4 weeks after the insertion), such as migration, obstruction, calcification, and urinary tract infection (UTI).

The present article reviews the indications for the use of USs, describing their main associated symptoms, complications and their prevention, and the novelties regarding innovation in this field.

Materials and Methods

We performed a literature review in the Embase, Pubmed and Google Scholar databases, with the following terms and cross-references: ureteral stent; diagnosis; treatment; and urology, restricting the search to the past 7 years. A total of 428 articles were found, and 49 were selected for this peer literary review for being the most relevant and with more novelties.

Review

Symptoms

The associated symptoms with the use of USs are of great importance in the patient’s quality of life. The most frequent are: dysuria, hematuria, urinary urgency, urinary frequency, bladder tenesmus, sexual dysfunction and abdominal pain. Scarneciu et al3 applied the Flanagan quality of life scale to 2,200 patients with USs, and found that their quality of life was affected as early as 7 days after the insertion.

The pathophysiology behind this symptomatology has not been fully understood; it is believed that it is related to the irritation of the bladder mucosa that is in contact with the distal portion of the US, as well as to urine reflux, and smooth muscle spasms.

Due to the high frequency of the associated symptoms, multiple strategies have been developed with different drugs to prevent these adverse effects, such as analgesics, alpha adrenergic blockers and anticholinergics.

Alpha adrenergic blockers are the most used, mainly tamsulosin, which relaxes the ureter and increases urinary drainage. Kwon et al,7 in a systematic review and meta-analysis, compared the use of alfuzosin against tamsulosin and placebo, and found that the symptoms were less severe in the group of patients managed with alpha blockers. In a meta-analysis by He et al8 of 16 controlled and randomized studies, the researchers found that alpha blockers generate an improvement in the symptoms associated with the insertion of a US, and that there is more evidence in favor of alfuzosin and terazosin than in favor of tamsulosin.
Anticolinérgicos son ampliamente utilizados para prevenir síntomas, y hay meta-analisis que justifiquen su uso. Se incluyen en las guías de manejo de la American Urological Association (AUA) para el manejo del US, y sus beneficios han sido extrapolados de pacientes con hiperesplenismo benigno prostatico.2,4,9

Lee et al.8 en un estudio aleatorizado randomizado, doble ciego, y controlado, comparó el uso de estirpes intraretinal de belladonna supositorias contra el uso de placebo, con inserción de US en 71 pacientes;应用于美国尿路协会（AUASS）量表之前，该流程为尿道的，尿路双称症状问卷（USSQ），以及AUASS量表。第一和第三组分别为一和组组使用非丙烯酸盐的支架（对照组）和另一组使用丙烯酸盐的支架（Triumph, Boston Scientific Corp. Inc., Natick, MA, US）短期，使用了尿道支架，使用了尿道支架，使用了静脉移植和代谢或先天性疾病。

Patient education regarding the symptoms associated with the insertion of a US is important; nonetheless, it is not a usual practice. Abt et al.13 recommend high quality education for patients with a US, in order to help them understand their symptoms.

Infection

Bacterial colonization is inherent to the use of USs. The incidence of US colonization has been reported to be between 44 and 48%.14 García-Aparicio et al.14 in a retrospective study with 67 pediatric patients with 73 US, reported a US colonization incidence of 58.9%, and a 5.9% incidence of UTI. Pseudomonas aeruginosa was the most frequent pathogen associated both to the US colonization and to the UTI. In patients with permanent use of US, bacterial colonization reaches an incidence of 100%.1 Antibiotic prophylaxis is not recommended, and the antibiotic treatment is only indicated in patients with symptomatic UTI.1 Hashimoto et al.15 performed two retrospective studies using antibiotic prophylaxis to prevent febrile episodes in patients with history of urinary derivation or reconstruction with JJ stents: in the first study, they compared the incidence of febrile episodes in 39 patients who received prophylaxis and 31 patients who did not (the chosen antimicrobial agent depended on the doctor’s preferences); the incidence of febrile events was significantly lower in patients with prophylaxis (26% versus 51.6%). In the second study, they gave prophylaxis to 75 patients before removing the stent, and they were divided into two groups: the first one was composed of 48 patients who received an oral fluoroquinolone (200 mg of norfloxacin or 200 mg of levofloxacin), and the other group was composed of 27 patients who were given an intramuscular aminoglycoside (200 mg of isepamicin sulfate). The incidence of febrile episodes was similar in both groups (13% for those with fluoroquinolone and 15% for the aminoglycoside group). Nevo et al.16 determined the association between a positive urine culture and a positive US culture in 509 patients, finding positive urine cultures in 17.8% of the sample, and positive US cultures in 20.4%; in 9.4% of the cases, both the urine and the US had positive cultures, but only 50% of these had the same pathogen isolated. The most frequent isolated pathogens were Escherichia coli and enterococci (38.5% and 18.4% respectively); 4.9% of the patients presented urinary sepsis, of which 84% had positive US cultures, and 59% had positive urine cultures. They concluded that the risk of urinary sepsis is greater in female patients and in patients with a positive US culture.

Keheila et al.17 performed a retrospective study with 150 patients to determine the fungal colonization of the US; the patients were divided into 3 groups according to the time of use of the US: the first group had been using the US from 0 to 20 days; the second, from 21 to 30 days; and the third, for more than 30 days. In group one, 70% of the patients presented a positive urine culture, and the main pathogen isolated was diptheroid (31%). In group 2, 64% had a positive urine culture, and the main pathogen was P. aeruginosa (30%). In the last group, 58% had a positive urine culture, and the main pathogen isolated was candida (55%). They concluded that the longer the use of a US, the greater the risk of fungi infection. Cirioni et al.18 performed a study to determine the intravitro sensibility of azithromycin and ceftazidime to prevent the infection of the stent with P. aeruginosa, comparing its use with a monotherapy; they found that the combination of these two antibiotics prevented the formation of the biofilm. Kawahara et al.19 in a study with 29 patients with discolored stents, found that these patients have a greater risk of presenting a positive urine culture, and higher urine pH. The reason why stents lose color is unknown to this date.

Incrustation

The incrustation of the stent is considered a severe complication that requires a multimodal approach. It is mainly associated with a forgotten or retained US.20 The most important risk factor for a US to incrust is a long indwelling time (in general, longer than 6 months). According to el-Faqih et al.21 the rate of incrustation varies from 9.2 to 76.3% depending on the time of use of the stent (6 weeks and more than 12 weeks respectively).

Other associated factors are urinary sepsis, history of lithiasis, chemotherapy, pregnancy, chronic renal disease, and metabolic or congenital diseases.20,22 The best way to prevent a US from incrustation, is to remove it as soon as it is no longer necessary, and to change the US every two to four months if the patient requires permanent use.20

The treatment for incrustation is endourological, but requires experience because there is no consensus or an algorithm to manage this complication. Ahalal et al.20 consider...
that the best management for a small percentage of incrusted USs, in patients with good renal function, is the extracorporeal lithotripsy (EL), which enables the spontaneous release of small fragments. Adanur et al., in a case series of 44 patients with incrusted USs, initiated the management with EL in 18 of them: in 5 of the patients the US removal could be easily performed via direct cystoscopy; the rest of them required other endourological procedures for the extraction of the US. Five cases required cystolithotripsy due to the incrustation of the distal part of the US.

Arenas et al. described the kidney, ureter, bladder (KUB) scale based on the level of incrustation of the stent in the kidney, ureter and bladder, which enables the urologist to identify the complexity of the surgery to remove the stent.

**Migration**

Even though the US must be self-holding, there is a chance of proximal or distal migration. The proximal migration towards the ureter has an incidence of 1 to 8%, and it could be due to the selection of a very large stent. Ureteral stents have an intravesical distal cord that enables an easier endoscopic retrieval of the stent, but this cord is associated with the migration of the catheter. Althaus et al. in a retrospective study with 512 patients taken into ureteroscopy, found that in 15% of the patients with a US the distal cord migrated, especially in female patients.

**Forgotten US**

A forgotten US has a multifactorial etiology: forgetfulness of the patient, lack of follow-up due to problems in the health care system, or lack of communication between the urologist and the patient. It is estimated that up to 12% of USs are forgotten.

Abandoning a US is an important health issue that is associated with an increase in costs, due to the necessary procedures that the diagnosis requires, such as the retrieval of the stent, and the management of the associated complications (UTI, urinary sepsis, incrustation, loss of renal function, among others). Pais et al. performed a systematic review and meta-analysis of 17 papers, and found that the metallic US had higher rates of duration, and the necessity of insertion of a US after performing a laparoscopic ureterolithotomy, and that it was not necessary due to the fact that, in the majority of the cases, there is no urinary leak or ureteral strictures after the surgery.

**Utility of US in cancer and Resonance Metallic Ureteral Stent**

The symptoms associated with the decrease in the ureteral lumen due to malignancy are a clear indication for the insertion of a US. Nonetheless, this is a very controversial topic. Chow et al. studied 42 patients with malignant ureteral obstruction, in whom a polymeric US was initially inserted, and later on was replaced with a Resonance Metallic Ureteral Stent (Cook Medical LLC, Bloomington, IN, US). They found that the metallic US had higher rates of duration, and should be considered as a first treatment option in these patients. However, it has been demonstrated that up to 35% of these metallic stents fail, mainly in patients with wall-invading prostate cancer; the most common signs of failure are hydronephrosis and an increase in creatinine levels. Radiologic findings enable the clinician to predict the risk of failure of a US. Chow et al. inserted Resonance Metallic Ureteral Stents in 74 patients with urinary tract obstruction, and found that the obstruction of the abdominal ureter and lymphatic metastasis are independent risk factors for the failure of the US. Wang et al. studied 164 patients, and found that the Eastern Cooperative Oncology Group performance status (ECOG-PS) grade, the hydronephrosis grade, and the invasion of the bladder are independent factors for the failure of the US; thus, the ambulatory retrograde insertion of the US is not suggested in patients with hydronephrosis > 30 mm, ECOG PS > 2, or in patients with vesical invasion identified by computed tomography (CT) or magnetic resonance imaging (MRI) scans.

Why do USs fail in cases of cancer? In a person with no medical history, the urine flows because of muscular coordination; when a US is inserted, the peristaltic activity decreases,
increasing the intrapelvic pressure, and enabling the production of mucus, which can obstruct the US. Nonetheless, the urine can continue to flow outside the lumen of the US. When malignancy exists, this extra luminal flow of urine is limited by the extrinsic compression caused by the tumor.\textsuperscript{38,39} Metallic USs have greater strength, tensile force, and resistance to exterior compression when compared with non-metallic stents, thus being more durable.\textsuperscript{39,40} The durability of a metallic US is greater in patients with non-malignant obstructions, and metallic USs have been reported by Wang et al\textsuperscript{41} to last up to nine months, and up to five years by Kadlec et al.\textsuperscript{42} Insertion of a metallic US is recommended in patients that have a greater risk of failure, such as those with malignant obstructions.\textsuperscript{43}

Despite the durability of the metallic USs, they can present complications in up to half of the patients, especially in patients with advanced stages of cancer. The complications include: abdominal pain, persistent hematuria, severe dysuria, and insufficient drainage.\textsuperscript{44} Nonetheless, other studies report that the level of failure is the same both for the benign and malignant etiologies of the ureteral obstruction.\textsuperscript{45}

There are different types of metallic USs. Lee and Kim\textsuperscript{46} compared two types of metallic stents: one with a spiral form that expanded with heat (Memokath 051, PNN Medical, Kvistgaard, Denmark), and one self-expandable stent (UVENTA, Taewoong Medical, Gimpan-si, Gyeonggi-do, South Korea); they noted that the UVENTA stent had greater rates of success, and could be used for both benign and malignant pathologies. The rate of complications of both stents is the same.

**Novelties in the use of ureteral stents**

Multiple studies have been conducted with the goal of improving the quality of USs, and despite the fact that most of them are experimental, they give the urological community a hint of the future of USs. Huynh et al\textsuperscript{47} proposed a US that illuminates, enabling an easier identification of the ureter during colonic surgery, thus avoiding a possible injury to the ureter. Soria et al\textsuperscript{48} developed and tested an anti-reflux US in healthy pigs with ultrasonography and excretory urography before inserting a 3 Fr US, and, after removing it, they found that the US had effectively decreased the vesicoureteral reflux.

One of the most studied and controversial topics is the development of biodegradable USs. Li et al\textsuperscript{49} proposed a biodegradable model using poli-L-lactic acid and poli-DL-lactic acid in dogs, and they had good results. Barros et al\textsuperscript{50} developed a model of US based on jelly, which started to degrade after 3 days of its insertion; it was radio-opaque (even when wet), and non-cytotoxic. They developed a totally functioning model, but it was not tested in humans. The same author, in a subsequent study, developed a biodegradable US capable of instilling drugs, with emphasis on paclitaxel, epirubicin, doxorubicin and gemcitabine; this US was exposed to a line of cancer cells in vitro, and the researchers were able to identify a significant decrease in the number of cancer cells.\textsuperscript{51}

It is assumed that preventing the formation of biofilm in the stent could decrease the risk of associated infections, thus enabling the avoidance of the use of prophylactic antibiotics. Rosman et al\textsuperscript{52} invented a US based on resistant biofilm jelly, achieving a decrease in the number of bacteria.

**Discussion**

Advances in the use of JJ stents were accomplished in recent years, which is why we believe it is pertinent to review this topic. We focused our revision in the management and prevention of the symptoms and complications associated with the use of JJ stents.

The main symptoms associated are dysuria, hematuria, urinary frequency, sexual dysfunction and abdominal pain, with a high negative impact on the quality of life. There are multiple studies that have tried to use alpha antagonists for the management of these symptoms, because of the fact that these drugs decrease urine reflux.\textsuperscript{1,7,8} These symptoms are worsened when the distal part of the US crosses the middle line of the bladder.\textsuperscript{1} Anticholinergics are recommended in the AUA guidelines to decrease the symptomatology, but there is no strong evidence for their use.\textsuperscript{4}

The incidence of US colonization has been reported range from 44 to 48%, and *P. aeruginosa* is the most prevalent pathogen reported;\textsuperscript{14} this colonization directly relates to the risk of urinary sepsis. Patients that use stents for longer than 30 days are at a greater risk of infection by candida.\textsuperscript{17}

A strict follow-up of the patients with USs must be performed: up to 12% of stents are forgotten,\textsuperscript{25} and, as a consequence, the patient could end up being submitted to a nephrectomy or with an incrusted US.\textsuperscript{22} This can be prevented by changing the stent every 2 to 4 months,\textsuperscript{1,20} and by performing a strict follow-up of these patients; there are various studies that propose methods to achieve this.

Regarding the use of US in lithiasis, using them after a non-complicated episode of lithiasis is not recommended.\textsuperscript{30–32} Metallic USs have greater strength, tensile force and resistance to external compression when compared with regular ones;\textsuperscript{39} they are cost-effective and useful in both benign and malignant obstructions.\textsuperscript{41} Their complications are more common in patients diagnosed with cancer;\textsuperscript{38,39} nevertheless, they are still preferred to manage malignant obstructions;\textsuperscript{34} there is a risk of failure of up to 35%,\textsuperscript{35} especially in patients with obstruction of the wall of the abdominal ureter, lymphatic metastasis, high ECOG-PS grades, and severe preoperative hydrenephrosis.\textsuperscript{36–38}

There is a great number of studies that intend to improve USs. The most promising ones are those of biodegradables USs, which start to degrade after 3 days, are radio-opaque and non-cytotoxic.\textsuperscript{50} Other novelties are USs that are lumino-sus, anti-reflux, and biofilm-resistant.\textsuperscript{52} They could also be used to instill chemotherapy for the management of upper tract urothelial cancer.\textsuperscript{51}

**Conclusions**

JJ stents remain very useful tools in the daily urologic practice, and they are widely used in the management of ureteral obstruction (both benign and malignant). Nonetheless, they are not exempt from having secondary effects associated with their insertion, such as infection, irritative symptoms, and the risk of incrustation. Even though we still do not have the ideal US, there have been many important
developments that help decrease the associated risks caused by their use.

**Funding**

The authors have none to declare.

**Conflict of Interests**

The authors have none to declare.

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Actualización en el uso de catéteres JJ  
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