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# Urinary Tract Infections in Psychiatric Patients

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## 1. Introduction

Urinary tract infections (UTIs) are widely extended among ambulatory and hospitalized patients under psychiatric treatment in all around the world in developed and developing countries. There are few reports about UTIs in this special type of patients, most of them are hospital inpatients and stay for very long periods of time, while others are hospitalized and discharged several times during years of treatment as their illness evolves. Several factors associated to UTIs including age, gender, type of psychiatric disease, use of invasive devices such as catheter, and recently genetic background has been considered. Despite innate mechanical safeguards against microbial infection of the intact human urinary tract, specific organisms are capable of colonizing and persisting in this environmental niche. Most infections in the urinary tract are caused by Gram negative including uropathogenic *Escherichia coli* (UPEC) and *Proteus mirabilis*, and Gram positive bacteria such as *Staphylococcus aureus* carrying a wide array of virulence factors. A main concern of the frequent antibiotic treatment prescribed for the therapy to combat UTIs is the growing generation of bacterial resistance. Application of antimicrobial agents for treatment of UTIs produces clinically relevant adverse reaction because of their interactions with psychotropic drugs prescribed to psychiatric patients. The pharmaceutical surveillance for tracking adverse reactions represents the main goal in the prevention and control of UTIs in psychiatric patients.

In spite of pathogenic protozoa like *Trichomonas vaginalis* and yeasts such as *Candida albicans* are usually associated to UTIs this chapter is focused on the bacterial pathogens. Therefore this work reviews the UTIs associated to bacteria in psychiatric patients, a group scarcely analyzed in spite of their clinical relevance. The scope of this study is to contribute on the understanding of the treatment for UTIs to prevent their spreading among patients and the medical care workers, due to their special conditions.

## 2. Distribution of UTIs in psychiatric patients

Surveillance of infections in psychiatric hospitals has faced operational difficulties owing to require of strategies based on available standard criteria to the unique needs of these patient population (Loving et al., 1992). Some epidemiologic studies of infections in hospitals reported that the urinary tract infections (UTIs) are the most frequent infections in

psychiatric inpatients (Haenen et al., 1997; Hoving et al., 1981; Reilly et al., 2008; Muller et al., 1997). The results from a survey to estimate the prevalence of health care associated infections (HAI) indicated that UTIs were the most common type of HAI in acute and non-acute hospital inpatients; moreover, in non-acute hospital, 5% of psychiatric inpatients was affected by a HAI (Reilly et al., 2008). According to a prevalence survey done in Norway of infections among hospitalized patients, the psychiatry ward presented the lowest rate of hospital infections and the UTIs were the most common infections among inpatients (Hoving et al., 1981). In a cross sectional study performed to assess the prevalence of infections in psychiatric institutes in Belgium, reported that the UTIs were the most common infections moreover, a statistically significant association with infection prevalence were found with the psychiatric diagnosis and duration of hospitalization (Haenen et al., 1997).

In spite of epidemiologic assessment of UTIs has been difficult because are not reportable diseases (Foxman, 2002), reports of their incidence have been recorded in subpopulations that are at increased risk. At present, a special attention has been devoted to the study of nosocomial infections in long term care facilities (Nicolle, 2000) which include chronic diseases hospitals, rehabilitation centers, psychiatric hospitals, institutions for the mentally retarded and nursing homes.

Nursing homes are a type of geriatric clinic that provide varying levels care (including psychiatric) for aged people, who for personal, social, health or other reasons, can not longer live alone or with their families (Chen et al., 2008) regrettably in some places, these clinics are not equipped with facilities and qualified personal as found in health institutions (Alameida & Pedroso, 1999). In fact, most of research on UTIs among the elderly has done on patients who are institutionalized in nursing homes (Chen et al., 2008; Nicolle, 2002) and hospitals (Foxmann, 2002). In elderly persons, the UTIs are usually asymptomatic i.e. the isolation of bacteria from urine in significant quantities is consistent with the infection, but without the local or systemic genitourinary signs or symptoms. Unlike the symptomatic patients with UTIs, in asymptomatic patients a positive urine culture does not confirm a diagnosis of UTI among this population. Further in geriatric patients, UTIs can be either uncomplicated infections that can occur in a normal genitourinary tract (Nicolle, 2000) or complicated infections characterized by structural or functional abnormalities by instrumentation such as indwelling urinary catheters (Hazeleltt et al., 2006).

The prevalence surveys in nursing homes of different countries report that the frequency of asymptomatic bacteruria is 15-30% of men and 25-50% of women and symptomatic episodes contributed to morbidity in this population (Nicolle, 2000). The high frequency is favored by chronic comorbid conditions including mental deterioration, incontinence of bladder and bowel. The latter can associated to degenerative mental disorders such as Parkinson's and Alzheimer diseases which impaired bladder empty and uretric reflux which favored to the high frequency of bacteriuria (Nicolle, 2000).

Urinary tract infections are commonly present in several psychiatric disorders in elderly people such as depression, psychosis (Woo et al., 2003), Huntington's disease (Dubinsky, 2005), Parkinson's disease (Woodford & Walker, 2005) and dementia (Hewer & Stark, 2010; Manepalli et al., 1990). Urinary tract infections have been the most frequent unrecognized medical disorder in geriatric patients with depression and psychosis (Woo et al., 2003) and also they have been commonly associated to hospital admission of patients with Huntington's disease (Dubinsky, 2005) and idiopathic Parkinson's disease (Woodford & Walker, 2005). They are associated to falls in geriatric women with mental disturbances

(Ericksson et al., 2009) and medical interventions in geriatric inpatients with dementia (Hewer & Stark, 2010).

In a study in hospitalized geriatric patients, UTIs were found as a risk factor associated to delirium (Khurana et al., 2002). A retrospective analysis involving 407 patients discharged over a 2 year period from a psycho-geriatric unit found that 83 (20.4%) had UTIs and 54 (13.3%) had delirium diagnoses at admission. Of the 54 with delirium, 14 (25.9%) had UTIs from which only 14 (42.8%) showed symptoms of UTIs. In this study was concluded that UTIs can precipitate delirium especially in geriatric patients with pre-existing cognitive impairment (Manepalli et al., 1990).

The efficacy of routine admission urine analysis in psychiatric hospitals has been questioned by its little impact on the care of psychiatric patients (Berber & McFeely, 1991) therefore, in the clinical practice the diagnosis of UTIs in geriatric patients in most cases depends on the judgment of signs and symptoms of infection (Nicolle, 2002; Anderson, 1981). A contributing medical practice which affects the reported cases of UTIs is that in some cases the UTIs are not recognized in patients with psychiatric illness because doctors may be more likely to ascribe symptoms to psychiatric cause (Mulder & de Reus, 2001). So this problem deserves attention for doctors to take in account somatic diseases which usually affect psychiatric patients such UTIs by analyzing clinical presentation, urinalysis and bacteriological culture of urine to get an accurate diagnosis (Foxman, 2002).

The infants represent a population at high risk of susceptibility of UTIs whose incidence is approximately 3% and 1% of pre-puberal girls and boys, respectively. The risk of UTIs increases with the age in girls but decreases with the age in boys. In pediatric girls, UTIs are associated with high morbidity and long-term consequences including impaired renal function, hypertension, and complications of pregnancy in adulthood. Pediatric girls are highly vulnerable to recurrent UTIs which may increase their progression to pyelonephritis and subsequent risk of renal scarring (Shortliffe & McCue, 2002). The risk of UTIs is also high in psychiatric children with behavior dysfunctions. The incidence of UTIs in patients of pediatric population has been documented in psychiatric conditions related with diurnal and night miction (Berg et al., 1977), urinary incontinence (Lettgen et al., 2002; von Gontard et al., 2004), urinary retention (Lettgen et al., 2002; Wan et al., 2010) and encopresis (von Gontard et al., 2004). A clinical study found that either boys or girls who wet both during the day and at night are more in risk of suffering psychiatric disturbances. No urinary infections were found in boys and girls who wet at bedtime. Only one case of urinary infection was reported in boys with day and night wetting in contrast, bacteriuria occurred in a 50% of girls who wet at day and night. The occurrence of UTIs in girls was associated to the persistent wet of perineum which favored bacterial proliferation (Berg et al., 1977). A study focused to analyze the behavioral and somatic symptoms in children suffering of enuresis (bedwetting), urinary incontinence (daytime wetting with or without bedwetting) and encopresis (habitual inability to defecate in the appropriate place) found that the more common behavioral disturbances were hyperkinetic syndromes, emotional and conduct disorders but the rates of previous UTIs were higher although not significant (von Gontard et al., 2004). Other reports indicated that children with urge incontinence are in higher risk of suffering UTIs than children with void postponement however, the latter present a wide variety of behavioral symptoms such as aggressivity, delinquent, withdrawn and attention problems (Lettgen et al., 2002). Urinary tract infection was also associated with psychogenic urinary retention as it was indicated in a case report on a 6 year old girl (Wan et al., 2010).

According to the above described, in children with behavior disturbances, the accurate psychiatric evaluation and supportive psychoteraphy along with studies of imaging, ultrasound, uroflowmetry and a reliable bacteriologic diagnosis of UTIs are required for their fully rehabilitation.

Urinary tract infections are very common in female population in fact, approximately, 50% of women have suffered a symptomatic UTI during their lifetime and many have recurrent episodes. About 33% of women with acute uncomplicated UTI have recurrent episodes; during pregnancy asymptomatic or symptomatic UTIs often progress to pielonephritis and increase the risk of premature delivery, fetal mortality or pregnancy induced hypertension (Stamm, 2002). In the particular case of psychiatric morbidity in pregnant women, UTIs have been associated to abortion, preterm delivery and perinatal mortality moreover; psychiatric pathologies contribute as risk factors (Ovalle et al., 1989). On other hand, UTIs have been commonly found in disorders like disuria (painful or difficult of urination) and nocturia (frequent urination during the night) in women (18-55 age) under high levels of distress (Sumners et al., 1992). Although, psychological factors may be involved in clinic symptoms of UTIs, studies in female patients (21-84 age) with recurrent UTIs found that, the associated symptoms such as urinary urgency and frequency and chronic urethral and or pelvic pain decreased with doxycycline treatment and psychiatric or psychological treatment was skipped (Burkhard et al., 2004). Urinary tract infections are the most common bacterial infections in women of all ages but the incidence increases with older age (Foxman, 2002; Shortliffe & McCue, 2002). In very old women UTIs have been associated with delirium (Eriksson et al., 2011) and they seem to be independently associated with low morale (Eriksson et al., 2010b) and multi-infarct dementia (Eriksson et al., 2010a) which might indicate that they are not harmless diseases. Prevention, diagnosis and treatment of UTIs may help for wellbeing in the old women population.

### **3. Risk factors associated to UTIs in psychiatric patients**

Specific subpopulations at increased risk of UTI include infants, pregnant women, the elderly, patients with spinal cord injuries and/or catheters, patients with diabetes or multiple sclerosis, patients with acquired immunodeficiency disease syndrome/human immunodeficiency virus, and patients with underlying urologic abnormalities. However, there has been found some factors related with the mental status of the patients (Juthani-Mehta et al., 2009; Rees & Farhoumand, 1977; Sumners et al., 1992; Wood et al., 2009)

A wide range of risk factors have been identified that can increase susceptibility to UTI, which can be grouped into genetic, biological, and modifiable behavioral factors.

#### **3.1 Genetic factors**

Within the genetic factors that have been studied are those related with the interactions among the microorganisms and their host, in these cases the influence of blood group on the availability of receptors for attachment of uropathogenic bacteria, where depending on the tape of the blood group there is an enhanced attachment of bacteria to the cells (Lomberg, 1986).

Recently the search of genes among risk populations that could be related to UTIs development was performed. Some relevant founding in particular the heat shock protein (HSPA1B), IL-8 receptor genes (CXCR1 and 2), toll-like receptors (TLRs), and transforming growth factor-beta 1 (TGF- $\beta$ 1) genes seem to be associated with an alteration of the host response to UTIs at various levels.

### 3.1.1 Interleukin-8 (IL-8) and IL-8 receptor genes (CXCR1 and CXCR2)

Several clinical studies have demonstrated IL-8 chemokine in the urine of individuals with acute, symptomatic UTI (Hawn et al., 2009). The CXCR1 and CXCR2 genes encode human chemokines receptors genes for IL-8. CXCR1 is the most important gene that seems to be involved in susceptibility to recurrent UTI. A reduced CXCR1 expression was observed in both children and adults with recurrent UTI (Foxman, 2002). CXCR1 polymorphisms were associated with asymptomatic bacteriuria (ASB) and a CXCR1 variant was associated with urine IL-8 levels (Hawn et al., 2009). This is important for schizophrenic patients were higher levels of constitutively IL-8 were found (Reale et al., 2011), raising the risk among these patients to develop UTIs.

### 3.1.2 Heat shock protein (HSPA1B) gene

HSPA1B gene encodes a 70 kDa heat shock protein (HSP) that is a member of the HSP70 family. Patients with recurrent UTIs showed a high prevalence of the HSPA1B 1267G allele (Foxman, 2002). This is important for psychiatric patients because polymorphism in HSP70 protein gene might be implicated in the development of schizophrenia (Kim et al., 2008; Pae et al., 2009).

### 3.1.3 Toll-like receptors (TLRs) pathway genes

TLRs are a family of germline-encoded receptors that orchestrate the innate immune response and recognize Pathogen-Associated Molecular Patterns (PAMPs) such as bacterial flagellin (TLR5), lipopolysaccharide (LPS) (TLR4), and bacterial lipopeptides (TLR1/2/6). Polymorphisms in TLRs 1, 4, and 5 are associated with altered risks of UTI in adult women (Hawn et al., 2009). The 896/AG genotype and the 896G allele of the TLR4 gene showed a higher prevalence among UTI patients and TLR4 expression was reduced in children with recurrent UTIs (Foxman, 2002). Polymorphism TLR2-G2258A, a variant associated with decreased lipopeptide-induced signaling, was associated with increased ASB risk (Hawn et al., 2009). Differences in the expression of TLR genes have been associated with autism and schizophrenia (Chang et al., 2010; Enstrom et al., 2010).

### 3.1.4 Transforming growth factor-beta 1 (TGF- $\beta$ 1) gene

TGF- $\beta$ 1 gene appears to be a key cytokine involved in the regulation of cell proliferation, differentiation, extracellular matrix formation and immune response. TGF- $\beta$ 1 genes seem to be associated at various levels with an alteration of the host response to the UTI. TGF- $\beta$ 1-509T allele showed a protective role in predisposition to recurrent UTIs because they were less frequent in children with recurrent UTIs (Foxman, 2002). It has been observed that changes in the TGF- $\beta$ 1 gene expression could be related to a major depressive disorder (Kim, 2007).

The main genes involved in UTIs are also related to psychiatric disorders, so it is expected that the risk of UTIs among these patients will be enhanced.

## 3.2 Biological factors

### 3.2.1 Gender

Women are significantly more likely to experience UTI than men (Foxman, 2002; Laupland et al., 2005; Zaffanello et al., 2010). UTIs are extremely common infections in women, affecting an estimated 1 in 3 women before the age of 24 years. Approximately 50% of

women have at least 1 symptomatic UTI during their lifetime, and many have recurrent episodes. Infections in men are uncommon until the age of 50 years, when increasing prostatic hypertrophy may obstruct urinary flow (Stamm, 2002).

### **3.2.2 Age**

Patients at increased risk of urinary tract infection are pediatric and elderly patients (Nicolle, 2009). UTIs are one of the most common infections in pediatric patients, 3% in prepubertal girls and 1% prepubertal boys (Shortliffe & McCue, 2002). In noninstitutionalized elderly populations, UTIs are the second most common form of infection (after respiratory tract infection), accounting for nearly 25% of all infections (Foxman, 2002; Shortliffe & McCue, 2002).

### **3.2.3 Diabetes**

Diabetes increases the risk of UTI and bacteriuria among female but not male patients. Patients with diabetes generally have a 2-fold to 4-fold increased incidence of bacteriuria over patients without diabetes. However diabetes does not appear to increase the risk of ASB among men (Foxman, 2002). Furthermore, diabetic patients with a UTI more often develop severe and rare complications, such as emphysematous cystitis and papillary necrosis (Schneeberger et al., 2008).

HIV/AIDS: The incidence of UTI among both women and men who are seropositive for HIV is greater than among women and men who are HIV seronegative (Foxman, 2002).

### **3.2.4 Urologic abnormalities**

Functional and anatomic predispositions associated with UTI are commonly observed in elderly patients. Changes in prostatic function in men, as well as an increased risk of obstructive uropathy in both men and women, may increase susceptibility to UTI. Anatomic changes related to childbearing and/or reproductive surgery, as well as mucosal and smooth muscle changes related to postmenopausal estrogen deficiency with resultant changes in the vaginal flora, can predispose the postmenopausal woman to UTI. Similarly, postmenopausal women with urinary incontinence, cystocele, postvoiding residual urine, or a history of premenopausal UTI are at increased risk of recurrent UTI (Shortliffe & McCue, 2002).

### **3.2.5 Pregnant patients**

UTIs are the most common bacterial infections during pregnancy, and pyelonephritis is the most common severe bacterial infection complicating pregnancy (Foxman, 2002).

### **3.2.6 Multiple sclerosis**

The risk of UTI and bacteriuria is significantly increased (90% and 74%, respectively) among patients with multiple sclerosis. UTI frequently precedes multiple sclerosis relapse, and recurrent UTI is associated with acute exacerbation and neurologic progression of the disease (Foxman, 2002).

### **3.2.7 Spinal cord injuries**

Patients with spinal cord injuries (SCIs) are predominantly young males. UTIs are very common among patients with SCIs and are always complicated in nature (Foxman, 2002). SCIs could cause psychiatric damages increasing UTIs risk in these patients.

### 3.3 Modifiable behavioral factors

Frequency of sexual intercourse and use of diaphragms, condoms and/or spermicides for contraception, and use of antimicrobials among premenopausal women, increases subsequent susceptibility to UTI (Foxman, 2002; Stamm, 2002).

Catheters: A special mention for the catheters, because catheter-associated UTI is the most common nosocomial infection (Foxman, 2002; Trautner & Darouiche, 2004). The risk of UTI increases with increasing duration of catheterization (Foxman, 2002), the majority of cases of nosocomial UTI are associated with an indwelling urinary catheter (Trautner, 2010). The elderly with indwelling urinary catheters are at especially high risk of acquiring UTIs. It has been suggested that UTIs are caused by organisms in the patient's urethra that contaminate the drainage tube and bag (Kane et al., 1985).

Biofilm forms on the surfaces of indwelling catheters, is central to understanding the pathogenesis of infection of these devices. The first step in formation of catheter-associated biofilm is deposition of a conditioning film on the surface of the device. Urine deposits organic molecules such as Tamm-Horsfall glycoprotein, a slimy protein of renal origin. The host proteins deposited from urine may facilitate attachment to the catheter by uropathogens. Lately catheter became colonized. Attached, or *sessile*, organisms divide to form microcolonies and then begin to secrete the extracellular polysaccharide matrix that forms the architectural structure of the biofilm. Sessile organisms can detach and become free-floating, or *planktonic*. The presence of planktonic organisms in the urine can lead in turn to symptomatic host infection (Trautner & Darouiche, 2004).

### 3.4 Psychiatric status

Clinical assessment of UTIs in nursing home residents usually are associated to mental conditions like changes in level of consciousness, periods of altered perception, disorganized speech, or lethargy (Juthani-Mehta et al., 2009).

Studies of women in urology clinics indicated that the urethral syndrome is not associated with increased psychiatric morbidity. Patients with the urethral syndrome are no more neurotic than those with significant bacteriuria and that both groups require tolerance for the distress generated by their condition (Sumners et al., 1992).

Women particularly suffering anxiety with recurrent cystitis have significantly more psychiatric symptoms than the population as a whole (Rees & Farhoumand, 1977).

Psychological stress can impact on visceral function with pathological consequences, one study found that social stress produces marked changes in bladder structure and function induced bladder disorders (Wood et al., 2009).

It has also been noticed that neurologic and other chronic diseases that cause incontinence and weakness increase the risk of UTI. For example, Alzheimer disease is associated with incontinence, often a form of neurologic dysmotility syndrome that could predispose to UTI and asymptomatic bacteriuria (ASB). Similarly, such drugs as antibiotics, anticholinergics, and psychotropics may have a negative effect on bladder function (Shortliffe & McCue, 2002).

## 4. Common microorganisms causing UTIs in psychiatric patients

Psychiatric patients commonly suffer from a variety of infections and may be, more frequently than other populations, and the prevalence may vary substantially among different countries. It has been reported among acute psychiatric patients the prevalence of

viral infections caused by human immunodeficiency, hepatitis B and hepatitis C viruses, monitored by serological tests (Rosenberg et al., 2001; Fernández-Egea et al., 2002). Borna disease virus infections were also found in psychiatric patients (Fukuda et al., 2001). Intestinal parasitosis was also studied among psychiatric patients in several countries (Haghighi et al., 2002; Cheng et al., 2005; Meza et al., 2005; Alvarado et al., 2008).

Urinary tract infections (UTIs) are widely extended among ambulatory and hospitalized patients under psychiatric treatment in all around the world. After respiratory tract infections UTIs were the most common reported infections (Haenen et al., 1997; Sáinz et al., 2008). UTIs among psychiatric patients may be complicated by comorbidities as well as the baseline presence of asymptomatic bacteriuria and benign urinary symptoms that can complicate diagnosis (Shortliffe & McCue 2002). In addition, the great diversity in psychiatric patients ranging from non dependent ones to the long-term care institutionalized patients, affects the etiology, diagnosis and management of UTIs within these special kinds of patients.

The most frequently isolated bacteria strains in psychiatric patients with UTIs were *Escherichia coli*, *Proteus mirabilis*, *Klebsiella* spp. *Pseudomonas aeruginosa* and *Staphylococcus aureus*, *Morganella morganii*, *Proteus vulgaris* and *Citrobacter freundii* were also found (Gabastou et al., 1995; Sáinz et al., 2008). In a recent study among inpatients of a Psychiatric Hospital in Mexico (Sáinz et al., 2008) in order to investigate *E. coli* serotypes associate to UTIs, it was found that the most frequent serogroups were O75, O1 and O2, being O75:H44 the most common serotype, followed by O1:HNM. All these serotypes belong to the UPEC pathotype as reported by JR Johnson (Johnson, 1991). *Klebsiella pneumoniae* and *Morganella morganii* strains were also isolated.

Among the main virulence factors associated with *E. coli* strains that cause UTIs are: adherence to solid substrates of host structures, in order to avoid being swept along by the normal flow of body fluids like urine (Johnson, 1991), and P fimbriae. In the late 1970s it was recognized for the first time that strains of *E. coli* causing UTIs typically agglutinate human erythrocytes, despite the presence of mannose therefore these strains are known as mannose resistant hemagglutination, (MRHA). The close association observed in individual strains between epithelial-cell adherence and MRHA was explained by the discovery that among most urinary isolates, both properties are mediated by fimbriae. Type 1 and P fimbriae are commonly investigated in *E. coli* UTIs strains (Johnson, 1991).

PCR techniques have been utilized in order to investigate several virulence genes like *papA* and also important autotransporter (SPATE's) toxin genes like *sat* and *pic* present in many *E. coli* UTIs strains (Sáinz et al., 2008). In the study carried out in Mexico in all the UPEC (Uropathogenic *E. coli*) strains the three genes were present and also they were identified in serotypes O134:HNM, O139:H10 (Sáinz et al., 2008). *Proteus mirabilis* was also isolated from urine samples of the psychiatric patients studied in Mexico and a DNA probe designed from a conserved sequence of some SPATEs proteins, identified some genes in these strains.

#### 4.1 Antibacterial therapy and bacterial resistance

First-line treatment of acute uncomplicated UTI has traditionally involved a regimen of trimethoprim-sulfamethoxazole (TMP-SMX) or TMP alone for patients with sulfa allergies (Karpman & Kurzrock, 2004; Nicolle, 2002). Increasing resistance among *Escherichia coli* to TMP-SMX worldwide has led to the reassessment of the most appropriate empiric therapy for these infections. Alternative first-line agents include the fluoroquinolones, nitrofurantoin, cephalothin and fosfomycin (Nicolle, 2002; Gupta, 2002). *Enterobacteriaceae*

are progressively becoming resistant to aminopenicillines, but remain sensitive to third generation cephalosporines. A study of antibiotic susceptibility of strains isolated from five hospitals in Paris reported that at least 30% of the *P. aeruginosa* strains are resistant to ciprofloxacin (Gabastou et al., 1995). In the Mexican study *E. coli* isolated strains showed resistance to TMP-SMX, amoxicillin, piperaciline, ciprofloxacin and norfloxacin (Sáinz et al., 2008). Resistant phenotypes to antibiotics of the strains isolated in patients from psychiatric hospitals are located between those observed in outpatients and in patients from non psychiatric hospitals. However, we noticed a worrying evolution of resistance to those encountered in psychiatric hospitals. Therefore, a multiresistant strains emergence monitoring must be carried out regularly.

### 5. Interaction of antibiotics with drugs used for psychiatric treatment

Surveillance of adverse effects of psychotropic drugs is a major concern of health systems (Aagaard et al., 2010; Lin et al., 2010; Wysowski et al., 2005; Moore et al., 2007) in fact, psychiatric patients mainly elderly represent a high risk population of being affected by drug interactions (Janchawee et al., 2005; Hosia-Randell et al., 2008). Interactions of psychotropic drugs and antibiotics are potentially dangerous because sometimes cause adverse events which result in life threatening to patients. In contrast with patients with acute illness who require short-term therapy with one medication, psychiatric patients suffering chronic illness (for instance, depression) which require prolonged treatment with psychotropic drug and medications for other comorbid symptoms. Therefore, they are more exposed to the consequences of drug interactions (Ereshefsky et al., 2009). In psychiatric patients, treatment of UTIs requires the choice of an accurately selection of antibiotics in order to maximize their effectiveness and minimize collateral interactions with the psychotropic drugs prescribed for them. Therapy for uncomplicated or complicated symptomatic UTIs is based in the application of antibiotics including quinolones, cephalosporines, betalactamics, nitrofurantoin, fosfomycin, trimethoprim (TMP) alone or in combination with sulfamethoxazol (TMP-SMX). Nevertheless antibiotics are invaluable for the control of pathogens causing UTIs (Nicolle, 2002) an intrinsic toxicity is associated to their administration. Toxic effect of antibiotics applied for UTIs therapy including for example, hepatotoxicity (sulphonamides), nephrotoxicity (cephalosporines, sulphonamides, quinolones), hepatotoxicity (fluoroquinolones, sulphonamides), neurotoxicity and cardiotoxicity (fluoroquinolones) (Wawruch et al., 2002). The growing rate of resistance to antibiotics like TMP-SMX, has lead to the use of quinolones mainly those from fluoroquinolone group. In clinical practice, fluoroquinolones most widely use are ciprofloxacin, gatifloxacin and levofloxacin and those of limited use include norfloxacin and ofloxacin (Schaeffer, 2002). At present, fluoroquinolones are used as the first choice for the treatment of complicated UTIs in patients from all ages who cannot tolerate sulphonamides or TMP, those who has risk factors for TMP-SMX resistance or who lives in geographical areas of high spreading of bacterial resistance to TMP/SMX (Schaeffer, 2002). However, adverse effects are commonly reported with fluoroquinolones (Louro et al., 2007; Owens, 2005). Drug interactions with psychotropic drugs focused antibiotics commonly prescribed for UTIs are described next.

Ciprofloxacin is a fluoroquinolone widely prescribed in patients with uncomplicated UTIs, complicated UTIs or acute uncomplicated pyelonephritis (Blondeau, 2004) but some adverse effects have been reported. In psychiatric patients under electroconvulsive therapy (ECT)

ciprofloxacin prolonged the electroconvulsive therapy seizures which are serious adverse effects of ECT as it was reported in cases reports of schizophrenia (Saito et al., 2008) and depression postpartum in a woman with UTIs (Kisa et al., 2005). Moreover ciprofloxacin displays intrinsic toxic such as thrombocytopenia as it was reported in a patient diagnosed with UTIs (Starr et al., 2005). Additionally, use of fluoroquinolones leads to the risks of adverse effects of interactions with psychotropic drugs (Fish, 2001). Ciprofloxacin apparently does not alter the elimination of some tranquilizers drugs like diazepam (Wijnands et al., 1990) however, causes clinically interaction with clozapine (Markowitz et al., 1997), an anti-psychotropic drug usually prescribed for treatment of schizophrenia, bipolar disorder, psychotic refractory depression and Parkinson's disease in psychotic patients (Solanki et al., 2007). As reported in a randomized double blind cross over study in schizophrenic inpatients, ciprofloxacin strongly inhibited clozapine metabolism associated to the increase in serum levels of clozapine and a metabolic derivative, N-desmethylclozapine, (Raaska et al., 2000). In a case report of one patient with urosepsis under clozapin therapy, treatment with ciprofloxacin followed by rhabdomyolysis i.e. destruction of skeletal muscle and subsequent leaking of muscle protein into the urine, was caused by a toxic accumulation of clozapin associated to the inhibition of cytochrome P450 (CYP) enzymes 1A2 and 3A4 (Brouwers et al., 2009). The high serum levels of clozapin caused by ciprofloxacin in patients with symptomatic UTI under clozapin therapy produce some toxic effects including dizziness, somnolence (Sandson et al., 2007) myocarditis (Brownlowe, 2008). On other hand, serotonin syndrome caused by excessive serotonergic activity of neurones is a potential life threatening disorder caused by the interaction of ciprofloxacin with serotonin re-uptake inhibitors drugs used as antidepressant (Montané et al., 2009) such as venlafaxine (Lee, 2009). Levofloxacin is a fluoroquinolone with epileptogenic properties causing of seizures (Bellon et al., 2009) and displays toxic effects in combination with lithium (Takahashi et al., 2000), used to treat the episodes of manic depression. Other fluoroquinolone antibiotic, i.e. gatifloxacin causes exacerbation of psychotic symptoms in patients with schizoaffective disorder when is concurrently administered with quetiapine, an antipsychotic drug, and with setraline, a selective serotonin-reuptake inhibitor commonly prescribed as an anti-depressant and with risperdal used in the treatment of paranoid schizophrenia (Reeves, 2007).

Betalactamic antibiotics used as second choice agents for UTIs antimicrobial treatment (Shortliffe & McCue, 2002) and specially prescribed for pielonephritis (Nicolle, 2002), have been associated to adverse effects. In psychiatric patients under ECT, piperacillin (synthetic penicillin derivative) and cefotiam (a cephalosporine) displayed epileptogenic effects causing of tardive seizure (Saito et al., 2008). Convulsive neurotoxic effect resulting from the interaction of penicillin derivatives in combination with flunitrazepam, a sedative benzodiazepine, has been associated to the affinity of penicillin derivatives with benzodiazepine receptor (Antoniadis et al., 1980). Additionally, a case of serotonin syndrome after single doses of *co-amoxiclav* a trade mark to denote the combination of amoxicillin and clavulanic acid (betalactamic derivatives) was reported in a patient taking venlafaxine as maintenance treatment for depression (Connor, 2003). In a study with patients chronically treated with anticonvulsants or chlorpromazine an antipsychotic drug and hetacillin a betalactamic antibiotic no interaction on the metabolism of these psychotropic drugs was observed (Galanopoulou et al., 1990).

Other antibiotics like trimethoprim, sulfamethoxazol prescribed for uncomplicated UTIs, pielonephritis (Nicolle, 2002) and acute UTIs (Shortliffe & McCue, 2002), have been

associate to the increase of toxic levels of clozapine in a patient with maniac and paranoid syndrome with urosepsis (Jecel et al., 2005). It has also been reported that nitrofurantoin, trimetoprim and sulfamethoxazol could cause adverse reactions including gastrointestinal disturbances, cutaneous reactions, pulmonary toxicity, hepatic and haematological toxicity (Karpman & Kurzrock, 2004).

## 6. Conclusions

UTIs are a common bacterial complication that is associated with morbidity but not mortality in psychiatric patients mainly the elderly. There is a relative paucity of research about the prevalence of UTIs in psychiatric population because UTIs are not always reportable diseases.

The etiology of UTIs is also affected by underlying host factors that complicate UTI, such as age, diabetes, catheterization and psychiatric conditions like lethargy, anxiety and Alzheimer disease. Currently genetic factors that may be involved in UTIs are also present in patients with mental problems, where the same gene is altered enhancing the risk of a UTIs, that is the case for schizophrenic patients with IL-8 or HSPA1B polymorphic genes that are also implicated in the development of these infections.

The microbial etiology of urinary infections has been regarded as well established and reasonably consistent. *Enterobacteriaceae* family members like *Escherichia coli* remain the predominant uropathogen isolated in acute uncomplicated infections. Moreover other genders like *Klebsiella*, *Enterobacter* and *Proteus* species frequently cause complicated UTIs. Other common uropathogens include *Pseudomonas* and *Staphylococcus* spp. The pathogens traditionally associated with UTI are changing many of their features, particularly because of antimicrobial resistance.

The advances in molecular biology may facilitate the identification of new etiologic agents for UTI. A renewed interest in the etiology and management of UTI has surfaced over the past few years. The need for accurate and updated population surveillance data is apparent, particularly in light of concerns regarding antimicrobial resistance.

Antimicrobial treatment of symptomatic UTIs should be carefully prescribed and supported with laboratory diagnostic, in order to ensure the effectiveness of the antibiotic, and to avoid bacterial resistances. Drug surveillance should reduce the possibility of side effects or interactions with the psychotropic drugs that are prescribe in clinical illness that affects the psychiatric patients.

More studies are needed to better define the epidemiology and management of these infections in this special type of patients.

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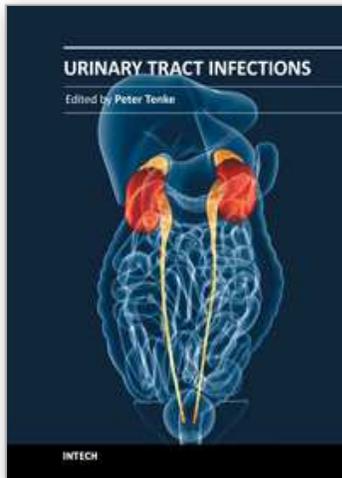
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## **Urinary Tract Infections**

Edited by Dr. Peter Tenke

ISBN 978-953-307-757-4

Hard cover, 360 pages

**Publisher** InTech

**Published online** 30, September, 2011

**Published in print edition** September, 2011

Urinary tract infections (UTIs) are among the most common bacterial infections worldwide, and they are also the leading cause of hospital-acquired infections. Therefore, the appropriate management of UTIs is a major medical and financial issue. This book covers different clinical manifestations of UTI, with special emphasis on some hard-to-treat diseases, and special conditions in respect of treatment; antibiotic resistance and the available alternative strategies for the prevention and treatment of UTIs and it deals with urinary tract infections in children. The aim of this book is to give a summary about the different aspects of the diagnosis, management and prevention of urinary tract infections for all medical disciplines.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Teresita Sáinz Espuñes, Maria Elisa Drago Serrano and Jaime Amadeo Bustos Martínez (2011). Urinary Tract Infections in Psychiatric Patients, Urinary Tract Infections, Dr. Peter Tenke (Ed.), ISBN: 978-953-307-757-4, InTech, Available from: <http://www.intechopen.com/books/urinary-tract-infections/urinary-tract-infections-in-psychiatric-patients>

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