Complicated / Nosocomial UTI and Urosepsis – What Can We Improve?

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Hangzhou, China, 13 September 2008
Complicated/Nosocomial UTI

• **Causes:**
  - complicating factors (e.g. obstruction, stone)
  - urologic interventions
  - catheters or splints

• **Localisations:**
  - lower urinary tract
  - upper urinary tract

• **Complications:**
  - change of pathogen
  - development of resistance
  - biofilm infection
  - urosepsis
Pope John Paul II

died on Saturday, April 2, 2005, from „septic shock“ (urosepsis) and „irreversible cardio-circulatory collapse ...... because of an overwhelming infection“

„Contributing causes:
- Parkinson‘s disease for over a decade;
- episodes of respiratory insufficiency and constriction of the trachea; signs of heart damage;
- and enlarged prostate gland, which made him vulnerable to the kind of urinary tract infection that killed him“
- „He had been admitted twice to the Gemelli hospital clinic since Feb 1, the start of a slow two-month decline toward his death.“

Urosepsis due to catheter associated UTI
NIDEP 1
One Day Prevalence Study

Prevalence Study of NAUTI in Urological Departments (since 2003)

Internet based Study (www.uroweb.org)
sponsored by

European Association of Urology (EAU)

in cooperation with

International Society of Chemotherapy (ISC)
European Society of Clinical Microbiology and Infectious Diseases
Federation of European Societies of Chemotherapy and Infection
Interregional Association of Clinical Microbiology and Antimicrobial Chemotherapy (IACMAC)
Asian Association of UTI and STD (AAUS) (since 2004)
Confederacion Americana de Urologia (CAU) (since 2005)
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Study population

- 6033 patients on study days
- 152 hospitals
  (42 took part in both studies)
- 727 patients with NAUTI
CDC Definitions for NAUTI

1. Symptomatic UTI:
   - symptoms AND bacteriuria
   - two of 7 criteria indicating UTI

2. Asymptomatic Bacteriuria:
   - indwelling urinary catheter present
   - no indwelling urinary catheter present

3. Other infections of the urinary tract:
   - positive culture of fluid (other than urine) or tissue
   - abscess or other evidence of infection
   - two of 5 criteria indicating other infection

Prevalence of NAUTI

- Prevalence in PEP-study: 10%
  322 cases in 3124 hosp. patients

- Prevalence in PEAP-study: 14%
  401 cases in 2909 hosp. patients

- Prevalence in combined analysis: 11%
  528 cases in 4662 hosp. patients
Clinical presentation of NAUTI

- ABU: 33%
- Pyelon: 22%
- Cystitis: 20%
- Urosepsis: 11%
- Other: 14%

% of total
Indications for antibiotics
Average urological patient population

% of total

58% of patients are receiving antibiotics

Prophylaxis: 50%
Proven UTI: 22%
Suspected UTI: 22%
Other: 6%
Characteristics of patients with NAUTI

Risk factors

- Urinary catheter 74%
- Average catheter duration 6-11 days
- Urinary tract obstruction 49%
- Previous UTI 44%
- Antibiotics during previous 3 mo 46%
- Hospitalisation in previous 6 mo 45%
- Urinary stones 20%
Pathogens causing NAUTI

- E coli
- Pseudomonas
- Klebsiella
- Enterococci
- Proteus
- Staphylococci
- Enterobacter
- Candida
- Others

% of total
Use of antibiotics when NAUTI was diagnosed (n=207)

- Aminoglykoside
- Imi-/meropenem
- Ceftazidim
- Cefotax/ceftriaxon
- Am/ampi+BLI
- Cipro-/ofloxacin
- Co-trim/Trim
- Nitrofurantoin

Countries:
- Others
- Germany
- Hungary
- Turkey
- Russia
E. coli – Ciprofloxacin (n=132)

Germany
Hungary
Russia
Turkey
Others

Resistant | Intermediate | Sensitive
There is a clear correlation between Antibiotic Consumption and Antibiotic Resistance.
A

![Graph showing imipenem resistance (%) vs. imipenem consumption (DDDs) for Pseudomonas aeruginosa over the years from July 97 to July 00. The graph includes two lines: one for consumption and another for resistance.](image)

Lepper et al 2002 AAC 46: 2920-5
Antibiotic resistance depends on the environment

- Hygienic factors
- Selective antibiotic pressure

Spontaneous mutations - genetic uptake

Survival and spread of resistant clones

Björn Wullt
Material and Methods

• 12 months 1996/7
• urine isolates from all hospitalised urological patients

• pathogen: identification
• pathogen: susceptibility test
• pathogen: typing

Wagenlehner et al 2002 IJAA 19: 583-91
Results

• 144 patients
  – 250 urine isolates
Clonally related urine isolates cultured from different patients

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<th>Species</th>
<th>N / Isolates</th>
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<td>Gram-negatives</td>
<td>76 / 147</td>
<td>52 %*</td>
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Origine of NAUTI

• NAUTI is mainly catheter related

• Transmission/cross infection plays a major role in pathogenesis of NAUTI

• NAUTI is often a biofilm infection
Experimental Setup of Catheter-associated Infection Model

Scanning Electron Micrograph of *P. aeruginosa* No. 02 Biofilm Formed on a Teflon Catheter in Artificial Urine

Goto et al. 1999 IJAA 11:227-232
Teflon Catheters and Biofilmformation

Pre.  4th  8th day

Time-kill Courses of Piperacillin and Ceftazidime Against Biofilm Cells of *P. aeruginosa* No. 02 in Artificial Urine

Time-kill Courses of Papipenem and Amikacin against Biofilm Cells of *P. aeruginosa* No. 02 in Artificial Urine

Time-kill courses of Ciprofloxacin and Levofloxacin against biofilm cells of *P. aeruginosa* No. 02 in artificial urine

612 episodes of Gram-Negative Bacteremia 1965 - 1974

Natural history of SIRS

Rangel-Frausto MS, JAMA 1995
Treatment of urosepsis

Supportive intensive therapy

As early as possible (first hours)
Treatment of urosepsis

Supportive intensive therapy

Empiric antibiotic therapy

As early as possible (first hours)
Mortality Impact of Inadequate Therapy

Severe sepsis and septic shock

Garnacho-Montero
Harbarth
MacArthur
Dhainaut


F. Scaglione 2007
Empiric antibiotic therapy of bacteremic UTI and clinical success

Treatment of urosepsis

- Supportive intensive therapy
- Empiric antibiotic therapy
- Specific urological therapy

As early as possible (first hours)
Urosepsis

• **Pathogens**
  • *Escherichia coli*
  • other Enterobacteriaceae

• after urological interventions
  multiresistant pathogens:
  • *Pseudomonas* sp.
  • *Proteus* sp.
  • *Serratia* sp.
  • *Enterobacter* sp.

• **Empiric Treatment**
  • Cephalosporine 3a, 3b +
    Aminoglykoside
  • Fluorchinolone*
  • Piperacillin / BLI
  • Carbapeneme

  *with high renal elimination
  BLI = beta-lactamase inhibitor

Duration of therapy: 3-5 days after
defeverescence or elimination of complicating factors

EAU guidelines updated 2007
Urosepsis following ESWL

84 year male patient

Urol. Diagnosis:

- nephrolithiasis both kidneys
- ESWL left kidney one week before (no culture before ESWL !)

Physical exam:

- fever (39.4°C), chills, pain left CVA

Laboratory:

- Leuco 16.6/nl; Creat. 1.76 mg/dl; CRP 23.1 mg/dl

Urinalysis:

- pH 5.0; protein 30 mg/dl; Nitrit: negative; Leuco 70/μl; Ery 80/μl

Urine culture: ?
Hospital St. Elisabeth
Dpt. Radiology
1 week after ESWL
Urosepsis following ESWL

84 year male patient

First step therapy:
- intensive medicine
- piperacillin/tazobactam 3x4.5 g
- JJ-stent left ureter

Patient remains unstable
- no improvement of sepsis

Next step therapy (within 12 hours):
- nephrectomy left kidney
- recovery after several days of intensive care
Urosepsis following ESWL

84 year male patient

Urine culture:

Enterococcus faecalis (10⁶/ml; mono culture)
susceptible to all usual antimicrobials
Urosepsis - Conclusion

- Early diagnosis
- Rapid interdisciplinary approach
  - Early effective antibiotic therapy (dosage!)
  - Early intensive care treatment
  - Early urological treatment
- Prevention of nosocomial UTI
International Society of Chemotherapy for Infection and for Cancer

66 national and regional societies with about 25,000 members

www.ischemo.org

International Congresses of Chemotherapy
Disease Management Symposia
Working Groups
International Journal of Antimicrobial Agents
International Society of Chemotherapy for Infection and for Cancer

Working Groups

- ISC - Cancer Section
- ISC - Virology Section
- ISC - WG Urinary Tract Infections
- ISC - WG Endocarditis
- ISC - WG Pharmacokinetics/Pharmacodynamics
- ISC - WG Catheter related infections
- ISC - WG Infections in Areas with Limited Resources
- ISC - WG Antimicrobials of the Future
- ISC - WG MRSA
- ISC - WG Infections in ICU
Submit your paper online
http://ees.elsevier.com/ijaa/
11th Western Pacific Congress on Chemotherapy and Infectious Diseases
in conjunction with
5th Asian UTI/STD Forum (AAUS 2008)
Taipei International Convention Center, Taiwan
November 29 - December 03, 2008

www.wpccid2008.tw
26th International Congress of Chemotherapy and Infection

“The Changing Climate of Infectious Diseases”

INCORPORATING THE AMMI CANADA – CACMID ANNUAL CONFERENCE 2009

www.icc-09.com