Antibiotics for initial therapy in women with acute pyelonephritis: gentamicin can it be an alternative?

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Background

Acute pyelonephritis (AP) causes considerable morbidity and account for significant healthcare costs particularly in women.

The most common pathogens belong to the Enterobacteriaceae family, and *E. coli* is the causative pathogen in > 80% of cases. There is why, oral fluoroquinolones and third generation cephalosporin are usually recommended for empiric antibiotic therapy of AP.

Unfortunately, antibiotic resistance has increased during recent years. For *E coli*, rates of resistance to fluoroquinolones, have reached 10% to 20%, in various part of the world.

Gentamicin is a potent aminoglycoside antibiotic with bactericidal activity against majority Gram negative bacteria particularly *E. coli,* but has limitations related to nephrotoxicity and ototoxicity.

In our study, we mill try to evaluate the efficacy and safety of treatment with gentamicin as monotherapy in community-acquired AP in women.

Methods and materials

A retrospective study was conducted in Monastir University Hospital, in the department of infectious diseases, from January 2000 to December 2012. Charts were obtained from medical records where the discharge diagnosis was "acute pyelonephritis" as the principle diagnosis.

Inclusion criteria were: women ≥ 15 years old, fever (T ≥ 37.8° C), back pain and/or urinary symptoms, urinary leukocyte count ≥ 10^4/ml and bacteriuria ≥ 10^5 CFU/ml.

Exclusion criteria were: nosocomial infections, pregnancy, initial antibiotherapy with two or more antibiotics and modification of antibiotic regimen before clinical and microbiological successes.

Patients were subdivided in 2 groups.

Group A: patients treated with gentamicin as initial antibiotic regimen (3 mg/kg/d).

Group B: patients treated with another antibiotic.

Efficacy was determined by clinical and microbiological response. Clinical response was determined as cured if complete resolution of original signs and symptoms was obtained. Microbiologic response was judged on urine culture results at 48-72 hours and 6 weeks after the end of treatment.

Safety evaluations were based on the incidence and type of adverse experiences and changes in physical findings from pretreatment to post-treatment examinations.

Results

A total of 265 patients fit the inclusion criteria. Table I resume demographic and clinical variables. *E. coli* was the predominant bacteria, isolated from uroculture in 226 cases (85.3%) (Table II). Blood cultures were positive in 16 cases (6%).

Table I: Table I: epidemiological, clinical and laboratory variables.

Variables	Value
Age, mean (DS)	44 (19.4)
Previous UTI (%)	87 (32.8)
Menopause (%)	80 (30.2)
Acute complicated pyelonephritis (%)	116 (43.8)
Complicated risk factors of AP (%)	
•Age ≥ 65 years old	51 (19.2)
•Diabetes	72 (27.2)
•Chronic renal failure	6 (2.3)
•Catheter associated	3 (1.1)
•Known previous renal calculi	17 (38.6)
Clinical data at presentation	
•Temperature (° C), mean (DS)	38.6 (0.7)
•Back pain (%)	253 (95.5)
•Urinary symptoms (%)	238 (89.8)
Laboratory data at presentation	
•WBC (x10^3/mm^3), mean (DS)	11.5 (5.1)
•CRP (mg/l), mean (DS)	101 (73.15)
•Creatinine (µmol/l), mean (DS)	87.2 (41.7)

Table II: causative microorganisms.

Microorganisms	Number (%)
Escherichia coli	226 (85.3)
Klebsiella pneumoniae	18 (6.8)
Proteus mirabilis	6 (2.3)
Enterobacter cloacae	6 (2.3)
Staphylococcus saprophyticus	3 (1.1)
Staphylococcus aureus	3 (1.1)
Shigella flexneri	1 (0.4)
Acinetobacter spp.	1 (0.4)
Streptococcus spp.	1 (0.4)

Gentamicin was prescribed in 142 cases (53.6%). Group B patients were treated essentially with 3rd cephalosporin generation in 64 cases (24%) and fluroquinolones in 55 (20.8%) (Table III).

Table III: antimicrobial agents used.

Antibiotics	Number (%)
Gentamicin	142 (53.6)
Ampicillin	1 (0.4)
Cefotaxim	64 (24.1)
Imipenem	2 (0.8)
Fluoroquinolones	55 (20.8)
Glycopeptides	1 (0.4)

In group A, patients were younger (35.6 Vs 53.7, $p<0.001$), there were less diabetics (13.4% Vs 43.1%, $p<0.001$), postmenopausal women (12% Vs 51.2%, $p<0.001$), and complicated AP (19% Vs 70%, $p<0.001$). Creatinine baseline was significantly higher in group B ($p = 0.001$).

Side effects were noted in 10 cases (3.9%). Eight were related to gentamicin (5.6%). The most common adverse experience was allergy skin in 5 cases. Other side effects were reversible renal failure in 2 cases and vertigo in one. There were no deaths in this study.

Table IV: efficacy and safety of gentamicin.

	Group A	Group B	*P*
Clinical efficacy			
Fever duration, h	54.8±29	62.4±48	0.13
Disappearance of back pain, d	4.11±1.7	4.7±3.6	0.17
Disappearance of urinary symptoms, d	3.6±1.6	4.2±2.9	0.03
Microbiological efficacy			
Uroculture + at 48-72 hours	4	4	0.82
Uroculture + at the end of treatment	2	0	0.5
Side effects (%)	8 (5.6)	2 (1.6)	0.051

Discussion - Conclusion

This study confirmed the effectiveness of gentamicin as treatment of AP in women. However, some precautions must be taken. Gentamicin should not be prescribed in complicated pyelonephritis essentially in diabetic patients or those with increased creatinine baseline. Gentamicin seems to be safe and no severe adverse effects were noted in our patients except 2 cases of reversible acute renal failure.

Gentamicin concentrates to 85% in the cortex. Unlike the beta-lactam antibiotics, aminoglycosides accumulate higher in infected cortical kidney.

Use a single daily dose allowed optimizing therapeutic effectiveness, decreased hearing and renal toxicity. Indeed, the use of a single dose determines a high serum peak, increasing bactericidal activity and a longer post-antibiotic effect. Moreover, single dose reduce the time of contact with renal binding sites and reduce cochleo-vestibular toxicity.

In conclusion, Gentamicin for treatment of AP in women community is efficacy and safe. Uncomplicated AP in young women can be treated by gentamicin.