

Outcome in acute uncomplicated pyelonephritis after discharge home following initial hospital emergency department treatment

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None

Objective: To determine the clinical course and safety of patients discharged home after hospital emergency department treatment of acute uncomplicated pyelonephritis.

Methods: This prospective, longitudinal, noninterventional, multicenter study enrolled women diagnosed with acute uncomplicated pyelonephritis at 2 hospital emergency services. No patient stayed in the emergency room longer than 24 hours. Medical history, current complaints, test results, and prescribed treatment were recorded for all patients. Between 3 to 5 days after discharge the patient was telephoned to assess clinical course (resolution of fever, lower back pain, and urinary tract symptoms). If symptoms persisted, the patient was called again between 7 and 10 days after discharge. The caller asked if the patient had consulted another doctor and if that consultation led to changes in treatment and/or hospitalization was required.

Results: Seventy-one patients were enrolled; 83% experienced complete resolution within 10 days of discharge. The survival curves of cures were practically identical for the 2 emergency services (no significant difference). Lower back pain was the symptom that took the longest to resolve ($P < .01$, with respect to both fever and urinary tract symptoms). Twelve patients (16.9%) consulted a doctor again and only 2 (2.8% of the entire cohort) had to be hospitalized. Although certain factors were associated with longer duration of certain symptoms, no particular factor was found to correlate with early resolution.

Conclusions: Most patients diagnosed with acute pyelonephritis are cured without requiring hospitalization. Discharge home from the emergency department is therefore justified after an observation period in which a first parenteral antibiotic dose is administered and an appropriate oral antibiotic is chosen. The patient should be warned of the possibility of the persistence of some symptoms and referred for appropriate outpatient follow-up. [Emergencias 2009;21:325-332]

Key words: Acute uncomplicated pyelonephritis. Emergency health services. Treatment. Outpatients.

Introduction

Acute pyelonephritis (APN) is a common infection in our setting that affects mainly children and healthy, sexually active women. It represents about 3% of urological visits to the emergency department (ED), affecting 250,000 patients each year in USA^{1,2}. It affects the pelvis and the renal parenchyma and manifests primarily as fever, back pain and voiding syndrome³. This upper urinary

tract involvement, until recently, carried with it a connotation of severity and potential complications and, probably therefore, many of these patients were referred to the ED to confirm the diagnosis, initiate intravenous therapy and/or monitor evolution. However, the course of the APN in the vast majority of cases is uncomplicated. APN is considered uncomplicated when it involves a woman who is not pregnant, without urinary tract abnormalities or immunosuppression. In

these patients infection is caused by a predictable group of germs so that, after an initial dose of intravenous antibiotic and a short period of observation, one may consider discharge home from the ED with empirical oral antibiotic therapy and outpatient monitoring⁴. Studies performed in recent years, and the emergence of third generation cephalosporins with high oral bioavailability, indicate this new management of patients is safe and associated with a low incidence of return visits⁵⁻⁸. Thus, the study by Sanchez et al demonstrated that a single dose of ceftriaxone followed by oral cefixime is effective and safe for outpatient treatment of women with uncomplicated APN⁹. However, some of the cardinal symptoms of APN can persist for some days, so if the patient is not adequately informed of this, she may well consult her GP or return to the ED. Symptom duration has not been specifically defined, nor have the factors associated with greater persistence been established. With these considerations in mind, we performed the present study of APN patients discharged directly from ED. The main objectives were to determine the chronological pattern of these symptoms, factors associated with faster symptom resolution, and the rate of revisits and admission of these patients.

Method

This was a prospective, longitudinal, non-interventional, multicenter study that included patients diagnosed with ANP in two hospital EDs: one belonging to the Hospital Clinic of Barcelona (HCB), an urban teaching hospital providing tertiary care coverage to 500,000 inhabitants, and the other belonging to the Hospital General de Granollers (HGG), a district university hospital serving 390,000 inhabitants.

Clinical diagnosis of APN was accepted when the patient presented back pain and at least two of the following three conditions: voiding syndrome, fever over 38°C and pathological urine sediment (more than 10 leukocytes per field). The following criteria for inclusion in the study were established: female patients without complicated APN, discharged after an ED stay (of less than or equal to 24 hours in an observation room provided it was fully managed by emergency physicians). No male patients were included since, by definition, APN in the male is considered complicated. Once the patient was informed about the study protocol, we requested a telephone contact number and permission during the days following

discharge. This contact was made within 4 days after discharge, and in the case of any of the symptoms persisting, a further phone call was made within 10 days.

The study did not include any intervention. The attending physicians had complete freedom regarding diagnostic-therapeutic management of each case and the decision to discharge or admit the patient. Only if the patient was to be discharged directly from ED did a member of the research team approach her to solicit inclusion and was then responsible for data collection and follow up. For this reason, the Ethics Committee approval was not considered necessary. Patient recruitment was performed continuously for a period of four months.

As independent variables of the study, we collected demographic and clinical patient data (age, sex, relevant diseases, existence of alterations in the urinary tract, usual drug treatment and previous episodes of urinary tract infection (UTI or APN), the current episode of APN (evolution time, in hours, of the back pain, fever and voiding syndrome, the presence of chills, any prior consultations with other physicians before attending the ED and prior antibiotic and/or anti-inflammatory non-NSAID treatment), physical examination in the ED (blood pressure, heart rate, temperature), complementary examinations (WBC, CRP, creatinine, urine sediment, abdominal ultrasound and its result, urine culture, blood cultures and results), the ED treatment administered and that prescribed at discharge, and time elapsed between their arrival to the ED and the administration of the first dose of antibiotic.

The dependent variables of the study corresponded to follow up data, which were obtained during the telephone interview in which we asked the patient about the presence of low back pain, voiding syndrome and fever, and the time elapsed from their ED visit until the disappearance of each symptom when this was the case. Furthermore, we considered that the patient was clinically cured (dependent variable) when these three symptoms had disappeared, then recorded the time taken for this to occur. We investigated whether any of the independent variables were associated with faster disappearance of individual symptoms (voiding, fever and pain) or faster resolution, for which these independent variables were dichotomized, when appropriate.

We also recorded any related GP consultation or return visits to ED for the same reason, new treatment or changes (if any) and whether the patient had required hospitalization, so as to cal-

culate the rates of re-consultation and hospital admission after ED discharge.

Qualitative variables were expressed as absolute values and percentages, and quantitative variables as mean ± standard deviation. APN symptom persistence (lower back pain, voiding syndrome and fever) was estimated using mortality tables and Kaplan-Meier survival curves. To assess the relationship of the independent variables with the dependent variable "duration of the symptom" we performed a univariate study using the log rank statistic. We used the same analysis for the dependent variable "cure". A p value of less than 0.05 was considered statistically significant.

Results

A total of 71 women were included (55 from HCB, 16 from HGG), with a mean age of 39 ± 17 years. Of these, 2 (2.8%) had diabetes mellitus, 1 (1.4%) HIV infection, 1 (1.4%) was receiving steroids and 11 (15.5%) were known to have some abnormality or previous disease of the urinary tract (renal stones in 5 cases, cystocele in 1, neurogenic bladder in 1, bilateral pyelocalyceal ectasia in 1, pyelocalyceal syndrome in 1, renal cysts in 1, and ureteral catheter in 1). None of them was receiving immunosuppressive (chemotherapy) and none had active malignancy. Twenty women (28.8%) reported previous episodes of UTI, and 10 (14.1%) this involved APN.

The main ED clinical findings of the current episode of APN are shown in Table 1.

Of the 20 patients (28.2%) who had previously consulted a physician for the current symptoms, 9 were diagnosed with UTI, 1 APN and 10 other pathologies not related to the urinary tract. In 12 of these cases, antibiotic therapy was started (ciprofloxacin in 5 cases, amoxicillin-clavulanate in 3 and cefuroxime, fosfomicin, norfloxacin and espiromicina in 1 case each). Urine sediment was pathological in 91.5% of cases, urine culture was positive in 74.6% of cases and blood cultures were positive in 12.9%. The most frequently isolated causal agent was *Escherichia coli* in both types of culture.

Patient data on evolution after diagnosis is presented in Table 2. Notably, 12 patients (16.9%) made non-programmed visits to a physician for a problem related to the episode of APN, but only 2 (2.8% of the total series) required hospitalization. At 10 days, after completing the interviews,

Table 1. Major clinical features of acute pyelonephritis at the time of diagnosis in the emergency department

Clinical data	
Lower back pain [n (%)]	71 (100%)
Evolution time of back pain (hours, mean ± SD)	56 ± 87
Location of back pain [n (%)]	
– Right	47 (66.2%)
– Left	22 (31.0%)
– Bilateral	1 (1.4%)
Voiding symptoms [n (%)]	49 (69.0%)
Evolution time of voiding syndrome (hours, mean ± SD)	94±96
Fever [n (%)]	58 (81.7%)
Evolution time of fever (hours, mean ± SD)	55±40
Chills [n (%)]	33 (46.5%)
Medical consultation before ED visit [n (%)]	20 (28.2%)
Previous antibiotic therapy [n (%)]	12 (16.9%)
Previous anti-inflammatory treatment [n (%)]	21 (29.6%)
Data from physical examination	
Systolic blood pressure <100 mmHg [n (%)]	11 (15.5%)
Heart rate >100 per minute [n (%)]	21 (29.6%)
Fever (above 38°C) in the ED [n (%)]	20 (28.2%)
Immediate results of complementary ED tests	
Leukocytosis >10,000 elements µl [n (%)]	43 (60.6%)
C-reactive protein >10 mg/dL [n (%)]	12 (37.5%)
Creatinine >1.5 mg/dL [n (%)]	0 (0%)
Pathological urine sediment (>10 leukocytes per field) [n (%)]	65 (91.5%)
ED ultrasound performed [n (%)]	10 (14.1%)
Ultrasound found [n (% of the 10 performed)]	
– Normal	6 (60%)
– Slight pyelocalyceal ectasia	2 (20%)
– Microlithiasis	1 (10%)
– Ureteral dilatation without visible obstruction	1 (10%)
Deferred results of complementary ED examinations	
Blood cultures performed [n (%)]	31 (43.7%)
Positive blood cultures [n (% of those performed)]	4 (12.9%)
Pathogens identified in blood cultures [n (% positive)]	
– <i>Escherichia coli</i>	4 (100%)
Urine culture performed [n (%)]	59 (83.1%)
Positive urine culture [n (% respecto a los cursados)]	44 (74.6%)
Germs identified in the urine culture [n (% positive)]	
– <i>Escherichia coli</i>	38 (86.4%)
– <i>Staphylococcus saprophiticus</i>	3 (6.8%)
– <i>Enterobacter cloacae</i>	1 (2.7%)
– <i>Enterococcus faecalis</i>	1 (2.7%)
– <i>Klebsiella oxytoca</i>	1 (2.7%)
Treatment data	
Administration of antibiotics in the ED [n (%)]	69 (97.2%)
Type of antibiotic administered in the ED [n (%)]	
– Ceftriaxone	48 (69.6%)
– Amoxicillin-clavulanate	11 (15.9%)
– Cefotaxime	5 (7.2%)
– Ciprofloxaciono	3 (4.3%)
– Levofloxacin	1 (1.4%)
– Cefuroxime	1 (1.4%)
Administration of antibiotic at ED discharge [n (%)]	71 (100%)
Type of antibiotic administered at ED discharge [n (%)]	
– Ceftibuten	30 (42.3%)
– Amoxicillin-clavulanate	15 (21.1%)
– Cefixima	13 (18.3%)
– Cefixime	8 (11.3%)
– Cefuroxime	3 (4.2%)
– Ciprofloxacin	2 (2.8%)
Time between arrival at ED and antibiotic administration (minutes, mean ± SD)	79 ± 49

Table 2. Main developmental features of acute pyelonephritis after discharge from emergency

	N (%)
Unscheduled revisits	12 (16.9%)
Place revisited*	
– Primary Care Centre	7 (58.3%)
– Hospital Emergency Department	5 (41.7%)
Main reason for the revisit*	
– Persistent fever	6 (50.0%)
– Persistent back pain	4 (33.3%)
– Persistent voiding syndrome	2 (16.7%)
Change of treatment after revisit*	4 (33.3%)
Admission to hospital after revisit*	2 (16.7%)

*Percentages with respect to total revisits.

complete cure was found in 83% of the cases (Figure 1). Analysis of cardinal symptom evolution showed that back pain required significantly more time to resolve (Figure 2). The specific percentage of patients with persisting symptoms at days 1, 2, 3, 4 and 5 after ED discharge are presented in Table 3.

We found no factors associated with earlier cure. Cure time curves were virtually the same for the two hospitals and only showed a trend toward earlier cure in patients with a temperature of $\leq 38^{\circ}\text{C}$ compared to the others ($p = 0.06$) and for those with leucocytosis ($p = 0.09$) (Figure 3). When this analysis was applied to each of the three cardinal symptoms of APN, the following was observed: fever took longer to disappear in patients with a history of UTI ($p < 0.01$) and in those not presenting chills ($p < 0.05$); lumbar pain took longer to disappear in patients with a higher temperature $> 38^{\circ}\text{C}$ in the ED compared to the others ($p = 0.01$); and voiding syndrome took longer to disappear in patients who had no

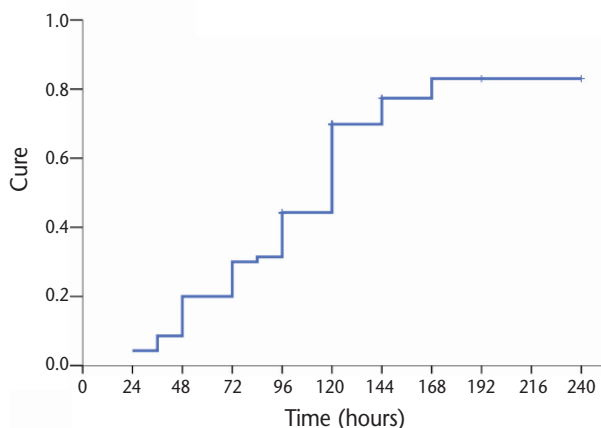


Figure 1. Survival curve with respect to complete clinical cure of pyelonephritis after ED diagnosis.

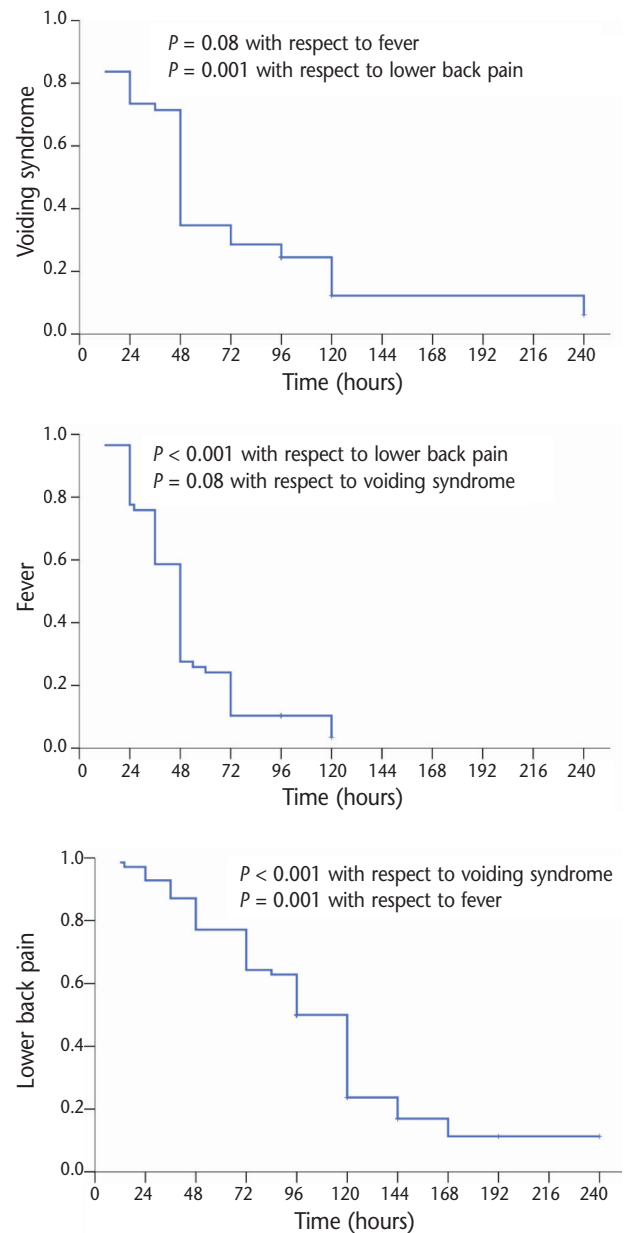


Figure 2. Survival curves for the persistence of the different symptoms of acute pyelonephritis. The P value was calculated using the log rank statistic and compares the evolution of the different symptoms.

tachycardia ($p < 0.01$) and in those with a history of UTI ($p < 0.05$) (Figure 4).

Discussion

The aim of this study was to show that patients diagnosed with uncomplicated ANP can be safely discharged from the ED in less than 24 hours. Of all the findings of this study, we would mainly emphasize three. First, these patients pre-

Table 3. Persistence of symptoms of pyelonephritis during 5 days after the ED visit

	Voiding syndrome	Fever	Lower back pain
After 24 hours	73.5 ± 6.3%	77.6 ± 5.5%	92.9 ± 3.1%
After 48 hours	34.7 ± 6.8%	27.6 ± 5.9%	77.1 ± 5.0%
After 72 hours	28.6 ± 6.5%	10.3 ± 4.0%	64.3 ± 5.7%
At 96 hours	24.5 ± 6.1%	n.a.	50.0 ± 6.0%
At 120 hours	12.2 ± 5.9%	3.4 ± 3.1%	23.7 ± 6.4%

n.a.: Not available from analysis of survival curves.

sented good evolution with low rates of revisits and hospital admission. Second, certain symptoms of APN may resolve slowly after discharge, especially back pain which usually takes longer to disappear. And third, we identified few factors that correlate with symptom persistence (the only one that might be related with greater persistence is a history of previous UTI) and none that predict slower cure time.

Most of the patients studied here were young (age 39 ± 14 years) with little underlying disease, which implies low susceptibility to present poor outcome. In fact, after 72 hours most of them had improved significantly, and only 10% had fever and 28% voiding syndrome. This “defervescence” is the most striking finding, and important, since it signifies that the critical period of infection is over. Re-visit rate was low and only 2 patients were hospitalized (2.8% of the series). These results are consistent with previous reports, showing that outpatient treatment of these patients is safe, given the good clinical outcome observed.

Sanchez et al performed a prospective, randomized study of hospitalized patients diagnosed with uncomplicated APN. They compared the short-term effectiveness of administering single-dose intravenous ceftriaxone followed by oral cefixime versus intravenous cefixime. They found no significant differences in terms of clinical cure of the two groups of patients⁹. Elkharrat et al, 10 years ago, developed an algorithm to predict those patients with uncomplicated APN, and found that up to 85% of pyelonephritis cases meet these criteria. After an initial dose of perflaxacin, 90% showed favourable evolution after direct discharge from the ED, which rose to 98% in those previously kept in an observation unit¹⁰.

Both studies show that, with the right choice of antibiotic, patients show good evolution without requiring hospital admission.

The antibiogram of *E. coli*, which is the most frequently isolated agent in the urine culture of these patients, has undergone changes in recent years^{11,12}, with regional variability. Therefore, the

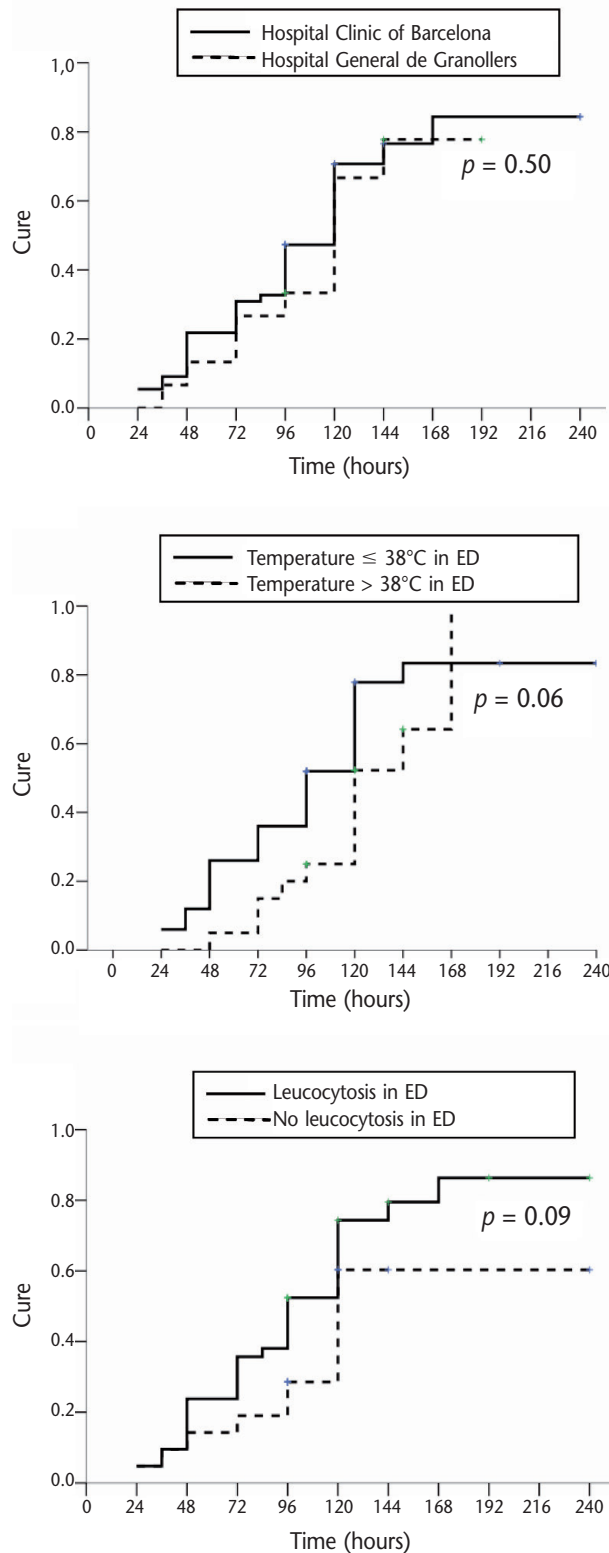


Figure 3. Survival curves for symptom resolution (cure) in relation to some of the factors studied (according to: the hospital providing treatment, upper graph; ED temperature, middle graph; and WBC count, lower graph). The P value was calculated using the log rank statistic.

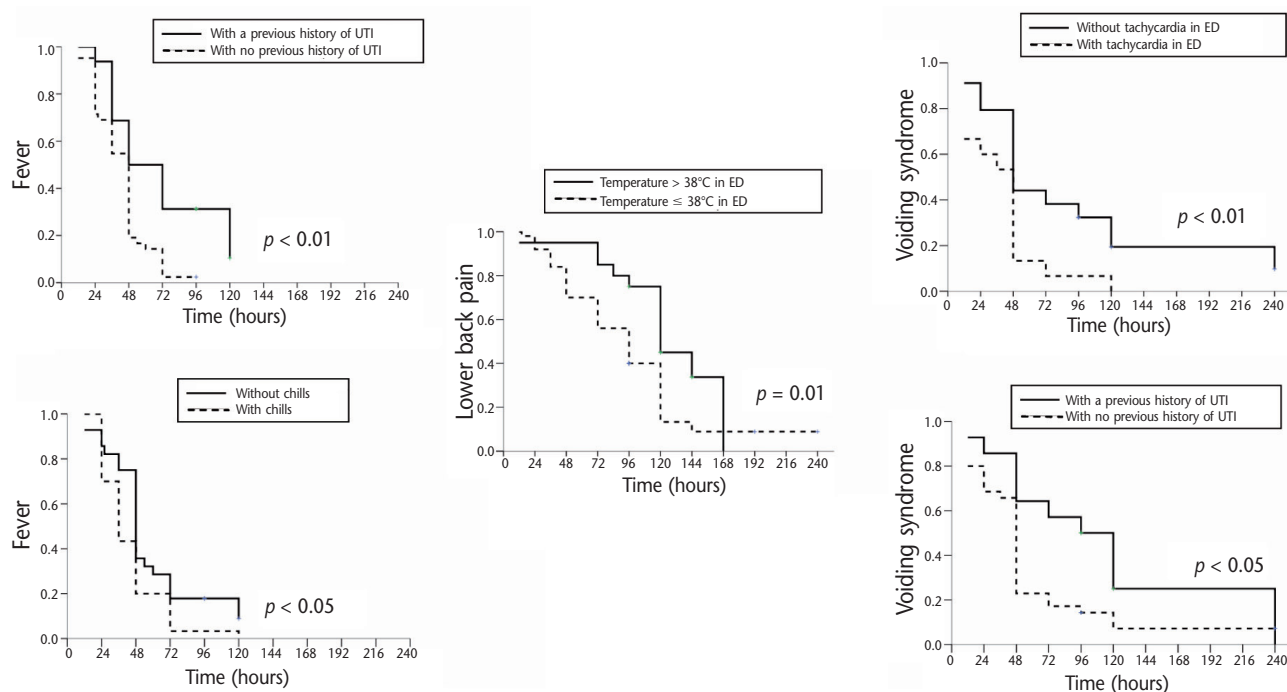


Figure 4. Survival curves for each of the three main symptoms of pyelonephritis (fever, left; lower back pain, centre; and voiding syndrome, right) depending on the presence or absence of certain factors that significantly influence its evolution. UTI: urinary tract infection.

choice of antibiotic treatment should be made according to local microbial sensitivity studies. The strains of microorganisms isolated in U.S.A. and Europe have different patterns of resistance and sensitivity. Without going so far in our study, we found remarkable differences between the antibiotics prescribed at each of the two hospitals. In the HGG area, there was a higher rate of *E. coli* ESBL (extended spectrum beta-lactamase) than in the HCB area, so that clinical guidelines of the HGG recommend the administration of cefuroxime-axetil or amoxicillin-clavulanate at discharge and those of the HCB recommend cefixime or ceftibuten. Anyway, we have at our disposal an arsenal of oral antibiotics with good bioavailability allowing easy, effective treatment regimes to improve patient quality of life and reduce costs¹³.

One issue that arises in this study is the need for blood cultures. In patients with complicated APN, there is no doubt. But in uncomplicated APN (our case) this is less clear, since in general positivity rarely reaches 20%, as in our study which was 12.9%. The fact that blood cultures were positive had no effect on treatment or on patient evolution. Neither did they serve to indicate slower clinical cure. Velasco et al performed a study along these lines and reached the same conclusion¹⁴. In contrast, urine culture is clearly necessary given its large proportion of positivity

and its utility for adjusting antibiotic treatment if necessary.

Lower back pain was found to persist during more days than any other symptom. At 120 hours (5 days), less than 4% of the patients still presented fever, around 10% still had voiding symptoms and almost 25% still reported lower back pain. The latter finding coincides with that noted by Sanchez et al⁹. Lower back pain persisted longer in those patients who presented higher temperatures on ED visit, and this could be a predictor of slower resolution, since it implies greater clinical involvement in the infectious process.

We found few factors predictive of faster or slower symptom resolution. We observed a trend towards earlier cure in patients with a temperature exceeding 38°C. To date, no conclusive studies have been published in this regard. Studies have been performed to determine the risk factors of developing APN, such as that by Scholes et al which concluded that patients with APN were at more risk if there was a personal or maternal history of UTI, and certain sexual habits (new partners, spermicide use and intercourse itself)¹⁵. The fact that in our study consultation with a physician the previous week also had no influence on evolution is somewhat surprising, as half of patients were not diagnosed with UTI or PNA, and did not receive antibiotic therapy: the majority

were diagnosed with lower back pain and started treatment with NSAIDs. This is an example of the variability of ANP clinical presentation and that there really is no order of symptom appearance.

The role of diabetes mellitus (DM) in the development of APN deserves attention. It is generally considered that physicians should be more cautious in the management of infection in diabetic patients, so they are often admitted without any other compelling reason. Our study only included 2 diabetic patients, so we could not analyze whether DM was associated with a worse outcome in APN and/or required different diagnostic or therapeutic measures with respect to the non-diabetic patients. Meiland et al studied this point in depth and found no difference between the course of the disease in diabetic and non-diabetics diagnosed with APN¹⁶. Finally, in this study we found no factor that clearly influenced slower symptom resolution except previous UTI, associated with greater delay in the disappearance of fever and voiding symptom.

Regarding limitations of the study, the moderate number of cases included must be mentioned. A greater number of patients would probably have reinforced some of the conclusions that are only suggested here. In addition, there were a number of cases (exceeding 10%) with persistent cardinal symptoms of APN when the second telephone contact was made and therefore not closed. However, the results of this study together with those of previous studies in recent years allow us to conclude that once a patient is diagnosed with uncomplicated APN in the ED, she can be discharged from the ED within 24 hours of observation. This conclusion is further supported by the fact that in two different settings (HGG and HCP), the healing curves were practically the same. Basically, the following have to be taken into consideration: parenteral dose of antibiotic should be administered, a good oral antibiotic should be prescribed according to the antibiogram corresponding to the area, the patient should be warned about the possible course of infection, especially that back pain that can persist for several days, and we must ensure subsequent ambulatory follow up (in primary care, day hospital or outpatient consultation). With certain patients with more involvement of the general state, home hospitalization may be considered as an al-

ternative, as shown by Regalado et al¹⁷. Since there is still much variability in EDs approach to the management of patients diagnosed with APN¹⁸, it is necessary to develop clinical guidelines from the EDs themselves. This will help optimize the resources available, unify the diagnostic and therapeutic approach in these patients and limit hospital admission to cases of complicated APN¹⁹.

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Evolución de las pacientes con pielonefritis aguda no complicada tras su atención inicial y alta directa desde un servicio de urgencias hospitalario

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Objetivos: Investigar la evolución clínica de los síntomas y comprobar la seguridad del alta directa desde el servicio de urgencias hospitalario (SUH) en mujeres afectadas de pielonefritis aguda (PNA) no complicada.

Método: Estudio prospectivo, longitudinal, no intervencionista y multicéntrico de pacientes procedentes de 2 SUH diferentes con PNA no complicada cuya permanencia en el SUH fuese inferior o igual a 24 horas. Se recogieron antecedentes, datos de la enfermedad actual, exploraciones complementarias y tratamiento prescrito. A los 3-5 días del alta se contactó telefónicamente para valorar su curación clínica (resolución de la fiebre, el dolor lumbar y el síndrome miccional) y, en caso de persistir algún síntoma, se contactó de nuevo a los 7-10 días. Se registraron las reconsultas y si ello había comportado cambios en el tratamiento y/o había requerido hospitalización.

Resultados: Se incluyeron 71 mujeres, el 83% presentaba curación completa a los 10 días del alta del SUH. Las curvas de curación resultaron casi superponibles en ambos SUH ($p = NS$). El dolor lumbar fue el síntoma que más tardó en desaparecer ($p < 0,01$ respecto a la fiebre y el síndrome miccional). Reconsultaron 12 pacientes (16,9%) y sólo 2 de ellas (2,8%) tuvieron que ser hospitalizadas. Algún factor se relacionó con la mayor persistencia de algún síntoma en concreto, pero ninguno con una curación más precoz.

Conclusiones: La mayoría de las pacientes diagnosticadas de PNA no complicada alcanzan la curación clínica sin necesidad de hospitalización, por lo que es seguro proceder al alta directa desde el SUH tras un periodo de observación que permita administrar la primera dosis de antibiótico parenteral, elegir un antibiótico oral adecuado, advertir a la paciente de la posible duración prolongada de algunos síntomas y remitirla a un control ambulatorio adecuado. [Emergencias 2009;21:325-332]

Palabras clave: Pielonefritis aguda no complicada. Servicio de Urgencias. Tratamiento. Paciente ambulatorio.