Uncomplicated urinary tract infections in general practice
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CHAPTER 6

WOMEN WITH SYMPTOMS OF UNCOMPLICATED URINARY TRACT INFECTION ARE OFTEN WILLING TO DELAY ANTIBIOTIC TREATMENT: A PROSPECTIVE COHORT STUDY

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Submitted for publication
Abstract

Background
Women presenting with symptoms of acute uncomplicated urinary tract infection (UTI) are often prescribed antibiotics. However, in 25 to 50% of symptomatic women not taking antibiotics, symptoms recover spontaneously within one week. It is not known how many women are prepared to delay antibiotic treatment. We investigated how many women presenting with UTI symptoms are willing to delay antibiotic treatment when asked by their general practitioner (GP).

Methods
Healthy, non-pregnant women who contacted their GP with painful and/or frequent micturition for no longer than seven days registered their symptoms and collected urine for urinalysis and culture. GPs were requested to ask all patients if they were willing to delay antibiotic treatment, without knowing the result of the culture at that moment. After seven days, patients reported whether their symptoms had improved and whether they had used any antibiotics.

Results
Of 176 women, 137 were asked by their GP to delay antibiotic treatment, of whom 37% (51/137) were willing to delay. After one week, 55% (28/51) of delaying women had not used antibiotics, of whom 71% (20/28) reported clinical improvement or cure. None of the participating women developed pyelonephritis.

Conclusions
More than a third of women with UTI symptoms are willing to delay antibiotic treatment when asked by their GP. The majority of delaying women report spontaneous symptom improvement after one week.
Background

Acute uncomplicated urinary tract infections (UTIs) are infections of the lower urinary tract in otherwise healthy, non-pregnant, adult women without known anatomical or functional abnormalities of the urinary tract. The symptoms are bothersome and have a negative impact on quality of life. Although empiric antibiotic treatment of all women with urinary symptoms has been reported to be cost-effective, bacterial resistance is rising and strategies to reduce antibiotic use are needed.

Placebo arms of randomized trials have shown that 25 to 50% of women presenting with UTI symptoms will have recovered in one week without using antibiotics. Moreover, qualitative research has suggested that these women often want to avoid taking antibiotics and may prefer delayed antibiotic treatment. Therefore, antibiotic use might be reduced if all women with UTI were asked to delay treatment.

We investigated how many women with UTI symptoms are willing to delay antibiotic treatment when asked by their general practitioner (GP). In addition, we explored how many of these women reported not to have used antibiotics after one week and whether their symptoms had improved.

Materials and Methods

Design and setting

From 18 April 2006 until 8 October 2008, in a prospective cohort study, patients were recruited in 20 GP practices in and around Amsterdam, the Netherlands, as part of the Amsterdam Cystitis / Urinary Tract Infection Study (ACUTIS).

Participants

Eligible were female patients over 12 years of age, contacting their GP with painful and/or frequent micturition. The symptoms had to be present for no longer than seven days.

Exclusion criteria were: pregnancy, lactation, signs of pyelonephritis, having used antibiotics or having undergone a urological procedure in the past two weeks, known anatomical or functional abnormalities of the urogenital tract, and being immunocompromised (with the exception of diabetes mellitus).

Assessments

Included patients filled in a questionnaire to record presence and severity of signs and symptoms on a 4-point scale, and collected a urine sample for urinalysis and culture according to pre-specified criteria. In line with the national guideline of the Dutch College of General Practitioners, no instructions for the urine collection method were given, since these have been reported to have no consequences for the extent of contamination.
After performance of clinical history and urinalysis, GPs were requested to ask all patients whether they were willing to delay antibiotic treatment as long as possible. During this period, participating patients could still change to antibiotic treatment at any time. Patients were asked to report after one week whether their symptoms had either improved or were cured, and if they had used any antibiotics. The result of the baseline culture became known after the follow-up period of one week, \( \geq 10^3 \) colony-forming units (CFU) of a single uropathogen per milliliter (mL) being defined as a positive culture according to international guidelines.20

**Analysis**

Key characteristics from history and urinalysis were compared between patients who were asked by their GP to delay antibiotic treatment and patients who were not. For patients who were asked to delay, we determined how many were willing to do so and how many were not. We crosstabulated the data on clinical cure and baseline culture in women who were willing to delay antibiotic treatment and had not used any antibiotics during the following week. If no follow-up data on antibiotic use were available, patients were analyzed as having used antibiotics. Analyses were performed in Stata/SE, version 10.1.

**Ethics and informed consent**

The study procedure was approved of by the Medical Research Ethics Committee of the Academic Medical Center in Amsterdam. Participating women received a letter with information about the study and provided written informed consent. For patients under the age of 18, written parental authorization was obtained.

**Results**

In total 205 women were eligible, of whom 29 were excluded (Figure 1). For principal reasons, GPs participating in one of the 20 GP practices did not ask any of their 25 patients to delay antibiotic treatment. No differences in main patient characteristics (age, socioeconomic status, number of diagnosed UTIs in the past) were present between patients of this non-participating practice and those of the other practices. For four patients, GPs did not report whether they had been asked to delay.

Of the remaining 176 patients, 137 were asked by their GP to delay antibiotic treatment and 39 were not. Table 6.1 shows the main characteristics of these two groups. Overall UTI prevalence was 59% (103/176). Women who reported at least considerable pain and women who thought they had a UTI were more likely to be asked to delay antibiotic treatment.
Table 6.1  Patient characteristics: asked to delay vs. not asked to delay

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Asked by GP</th>
<th>Not asked by GP</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>missing (n)</td>
<td>n (%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>137 (100)</td>
<td>39 (100)</td>
<td></td>
</tr>
<tr>
<td><strong>History</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age in years (range)</td>
<td>43 (16-89)</td>
<td>3</td>
<td>38 (16-71)</td>
</tr>
<tr>
<td>At least considerable frequency</td>
<td>86 (63)</td>
<td>3</td>
<td>19 (49)</td>
</tr>
<tr>
<td>At least considerable pain</td>
<td>66 (48)</td>
<td>3</td>
<td>11 (28)</td>
</tr>
<tr>
<td>Any vaginal irritation</td>
<td>57 (42)</td>
<td>3</td>
<td>15 (38)</td>
</tr>
<tr>
<td>At least 1 UTI ever diagnosed</td>
<td>106 (77)</td>
<td>4</td>
<td>27 (69)</td>
</tr>
<tr>
<td>Patient thinks she has a UTI</td>
<td>122 (89)</td>
<td>3</td>
<td>23 (59)</td>
</tr>
<tr>
<td><strong>Stick</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrite positive</td>
<td>47 (34)</td>
<td>1</td>
<td>12 (31)</td>
</tr>
<tr>
<td>Blood ≥ 1+</td>
<td>85 (62)</td>
<td>1</td>
<td>27 (69)</td>
</tr>
<tr>
<td>Leucocytes ≥ trace</td>
<td>114 (83)</td>
<td>1</td>
<td>27 (69)</td>
</tr>
<tr>
<td><strong>Culture</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture positive</td>
<td>84 (61)</td>
<td>6</td>
<td>19 (49)</td>
</tr>
</tbody>
</table>

Of the 176 included patients, 137 were asked by their GP to delay antibiotic treatment and 39 were not. Women who reported at least considerable pain and women who thought they had a UTI were more likely to be asked to delay antibiotic treatment.

Of those asked, 37% (51/137) were willing to delay (Figure 6.1). After one week, 55% (28/51) of women who were willing to delay reported not to have used antibiotics and 71% (20/28) of these women reported clinical improvement or cure (Table 6.2). Of these patients, 35% (7/20) had a positive baseline culture. Of the eight women not reporting clinical improvement or cure after one week, two turned out to have had a positive culture at baseline.
In total, 205 women were eligible. For principal reasons, one participating GP surgery did not ask any of their 25 patients to delay antibiotic treatment. For four patients, the GP did not report whether they were asked to delay.

Of the remaining 176 patients, 137 were asked by their GP to delay antibiotic treatment. Of these patients, 37% (51/137) were willing to delay, of whom 55% (28/51) did not use any antibiotics during the following week.

The table shows the association between clinical cure and baseline culture in women who were willing to delay antibiotic treatment and did not use any antibiotics during the following week. The result of the baseline culture was known only after the follow-up period of one week.

In total, 28 delaying women did not use any antibiotics. Of these women, 20 (71%) reported clinical cure or improvement. Of the eight women who did not report cure or improvement, two turned out to have had a positive baseline culture.
Of the 51 women willing to delay, 15 (29%) had used an antibiotic after one week, all of whom reported clinical improvement or cure and 13 had a positive baseline culture. 8 of the 51 women (16%) did not report on their antibiotic use.

Of women who had been asked by their GP to delay treatment, 25% (34/137) reported not to have used antibiotics after one week, against 15% (6/39) of women who had not been asked, yielding a difference of 10% (95% CI -6 to 21%). Of the 137 women who were asked to delay, 30 did not report on antibiotic use after one week (Figure 1), 22 of whom belonged to the group not willing to delay at baseline. Of the 39 women who were not asked to delay, one did not report on antibiotic use.

The result of the baseline culture was known only after the follow-up period of one week. It turned out to be positive for 51% (26/51) of the delaying women and for 67% (58/86) of the non-delaying women (risk difference 16% (95% CI 0-33%)). No patients developed pyelonephritis during the follow-up period of one week.

**Discussion**

Our results suggest that more than a third of women with UTI symptoms are willing to delay antibiotic treatment when asked by their GP. More than half of these women will not have used antibiotics after one week, of whom more than 70% will have improvement of their symptoms. The majority of non-improving women in our sample (6/8) turned out to have had a negative baseline culture, suggesting that their symptoms might not have improved had they used an antibiotic.

The proportion of women reporting the use of antibiotics was 10% lower in the group that had been asked to delay as compared to those who had not been asked. The true reduction may be somewhat higher, since in the group asked to delay 30 patients were analyzed as having used antibiotics because no follow-up data were available. However, it should be taken into account that not all baseline characteristics were similar between these two groups (in the group asked to delay, more women reported at least considerable pain and/or thought they had a UTI).

As far as we know, this is the first study that describes the proportion of women with UTI symptoms that are willing to delay antibiotic treatment. Our findings are consistent with the results from a qualitative study by Leydon et al, which revealed that patients do not always want to use antibiotics, although clinicians often assume that they do.14 This misinterpretation by clinicians might be illustrated by the fact that not all eligible patients in our study were asked to delay antibiotic treatment by their GP.

In addition to the 28 women willing to delay treatment, 6 women not willing to delay had not used antibiotics after one week. Although being asked to delay might have stimulated these 6 women in changing their minds to not using antibiotics, we did not obtain information on their motives.

We had no further information on reasons for GPs not to enquire after their
patients’ willingness to delay, which may be seen as the main limitation of our study. However, patients who were excluded by their GP did not have worse baseline characteristics than those who were included. On the contrary: women who reported at least considerable pain and women who thought they had a UTI were more likely to be included. This suggests that the GPs’ decisions whether to ask patients to delay or not may be based more on their personal attitude towards antibiotic prescriptions than on patient characteristics, which is in line with the previously mentioned findings of the study by Leydon et al.\(^\text{14}\)

In addition, patient attitudes (e.g. demanding personality) and previous experiences (e.g. problematic UTI history) might influence the GPs’ decisions.

Another limitation is the large number of missing data in the group of patients who were not willing to delay antibiotic treatment. More than a third of these patients did not report on antibiotic use and symptom improvement after one week. We consider it likely that most of these patients were cured and therefore did not feel inclined to report on follow-up results.

Due to cultural differences, our results might not be completely generalisable to other countries, where women may be less willing to delay antibiotic treatment than in the Netherlands. However, similar patient attitudes towards antibiotic prescriptions have been reported for the United Kingdom and Hong Kong.\(^\text{14,21,22}\)

An uncommon but severe complication of UTIs is pyelonephritis, which may be a reason to treat all women with a suspected UTI. However, placebo arms of randomized trials suggest that cystitis seldom progresses to pyelonephritis.\(^\text{11-13}\)

Similarly, no women developed pyelonephritis in our study population.

Since in clinical practice the result of the urine culture is not available at the moment that a treatment decision is taken, we included all patients with symptoms, independent of the result of their urine culture. We consider this a more pragmatic approach than including only patients with microbiologically proven UTI.

Our findings imply that antibiotic use might be considerably reduced by simply asking women with UTI symptoms whether they are willing to delay antibiotic treatment. Besides, most of delaying women will have symptom improvement after one week. This is in line with results from a randomized trial by Little et al., in which a treatment strategy of delayed prescription reduced antibiotic use by 20% while yielding the same symptom control when compared to a strategy of immediate antibiotics.\(^\text{23}\)

A potentially promising strategy being currently under investigation is initial treatment with pain medication instead of immediate antibiotics.\(^\text{24,25}\)

In conclusion, our results support previous findings that women with UTI symptoms may be more receptive to delayed antibiotic prescriptions than is assumed by many clinicians. If all of these women were asked to delay antibiotic treatment, antibiotic use might be substantially reduced without negatively impacting clinical recovery.
References


