Natural history of urinary tract infection in a primary care environment in Canada

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Objective: *To characterize the natural history of uncomplicated urinary tract infection (uUTI) in a Canadian primary care environment from the patient's perspective.*

Materials and methods: *Female patients (n = 2323) with symptoms of uUTI were recruited by 581 family physicians who collected baseline demographic and clinical data and prescribed 500 mg/day extended release ciprofloxacin (Cipro® XL™). Follow-up data were collected 4 and 10 days later by patient telephone interview assessing uUTI symptoms, medication compliance, time to symptom resolution, impact on usual activities and overall satisfaction.*

Results: *Patients (mean age 40) had on average 3.56 uUTI symptoms at baseline, the most common of which was frequency (94% of patients). The mean duration of symptoms was 4.9 days. Sixty-three percent of patients reported an impact of uUTI on usual activities prior to antibiotic therapy with a mean impact score of 4.33 {scale 0 to 10 (maximum)}. At day 4, uUTI symptoms had decreased to 0.74/patient, 71.5% of patients reported symptom resolution, while medication compliance was 97%. By day 10, uUTI symptoms had decreased further to 0.42/patient, 84.3% of patients had symptom resolution and only 13% reported a residual impact on usual activities (mean impact score, 0.76). Patients showed high levels of satisfaction (> 80%) with all aspects of therapy.*

Conclusions: *Patients wait almost 5 days before seeking medical attention for uUTI and by that time symptoms can significantly impact normal activities. This assessment of symptoms and outcomes of uUTI provides physicians with a better view of the impact of infection on patient's lives.*

Key Words: uncomplicated urinary tract infection, Canadian family practitioners, urinary tract infection, patient impact

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Introduction

Uncomplicated urinary tract infections (uUTI) are very common bacterial infections. Approximately one third of women will have a uUTI requiring antibacterial therapy before the age of 24 while as many as 50% will experience at least one infection in their lifetime.[1,2] The majority of uUTIs are treated in a primary care setting and account for a significant number of physician visits each year.[3,4] However, despite the frequency of the condition and the guidelines

designed to direct uUTI care, management strategies based on case presentation, treatment and expected outcomes can be inconsistent at the family practice level[2,5-7] where empiric antibiotic treatment without urine culture is the usual recommended strategy.[8] One of the principal factors governing diagnosis and management of uUTI under these circumstances during a family physician consultation is the physician's interpretation of the patient's symptoms, and their perception of the pain and symptom severity associated with the infection.[2,9] These diagnostic parameters are often underappreciated by the physician, possibly contributing to inadequate therapeutic intervention resulting in clinical failure and uUTI recurrence with a negative impact on patient quality of life (QoL).[2,9,10] This suggests that family physicians may lack information on the broader impact of uUTI, particularly as the infection relates to the impact on patient functioning and quality of life (QoL). One of the few studies assessing QoL in uUTI patients has shown a substantial effect on physical and emotional functioning during the acute phase of the infection suggesting that this impact, and the duration of the impact, might be an additional factor in the overall assessment of patient management.[11] However, this aspect of patient care has not been studied in a family physician setting and indeed few studies have assessed uUTI from a patient perspective.

The present study was designed to characterize the natural history of uUTI in the Canadian primary care environment, by defining the type of uUTI symptoms found in presenting patients, the impact of symptoms on patient functioning, how rapidly symptoms resolve after antibiotic therapy from a patient perspective, and patient satisfaction with the care received. The objective of the study was to provide family physicians with a broader view of the impact of uUTI symptoms on patients and to aid in the prediction of outcomes of antibiotic therapy given specific presentation symptom scenarios.

Methods

Study design and recruitment

This was an observational, open-label, phase IV survey designed to collect data from patients who presented with uUTI symptoms at family physician offices across Canada and who were prescribed extended-release ciprofloxacin (Cipro® XL™) to treat their uUTI. Family physicians were recruited for the study through an initial fax out which described the study objectives and a follow-up phone call. Based on this contact process, 581 physicians agreed to participate in the study and each participant was asked to recruit up to 10 patients. Patient inclusion criteria included non-pregnant female patients 18 to 65 years of age with a clinical diagnosis of uUTI (acute cystitis). Exclusion criteria included patients with confirmed complicated UTIs, patients whose current uUTI episode had been unsuccessfully treated with another anti-microbial agent (i.e., treatment failures), patients who had been on antibiotics (for any indication) within 10 days prior to diagnosis of uUTI, and patients with allergies/contraindications to ciprofloxacin. All patients who agreed to participate signed an informed consent document and the study protocol was reviewed and approved by a central Investigational Review Board. Recruitment at each site continued in a consecutive manner until the target number of patients was reached. Physicians prescribed urine culture tests or reagent strip tests based on their normal clinical practice, and all patients who participated in the study were prescribed 500 mg extended-release ciprofloxacin once a day for 3 days at the baseline visit.

Data collection

Patients were assessed at three points during the study; baseline assessment; day 4 assessment (4 days after initiation of antibiotic therapy), and day 10 assessment (10 days after initiation of antibiotic therapy). Apart from the baseline assessment, which was completed by the physician, all subsequent data were collected through telephone interviews. Initial calls were made on day 4 and day 10, but if a patient was unavailable, follow-up calls continued until contact was made and the questionnaires administered.

At the baseline assessment the physician completed a patient registration form which included information on presenting symptoms and their duration and uUTI history. The day 4 and day 10 surveys were designed to assess patient status before and after ciprofloxacin therapy, respectively, and were accomplished using a questionnaire administered by telephone. The questionnaire assessed compliance with medication, time in hours to symptom improvement/resolution, and remaining uUTI symptoms. Questions relating to remaining uUTI symptoms at the day 4 and 10 assessments asked if patients were suffering from pain, burning during urination, frequent urination, urgent need to urinate, pain in bladder area, or blood in urine. These descriptions were assumed to correspond to uUTI symptoms of dysuria, frequency, urgency, suprapubic pain and visible hematuria, respectively.

In addition, impact of the uUTI before starting antibiotic therapy on usual activities (0-10 scale where 0 means no impact) and patient work, functioning, personal life, social life and sexual relations, based on the number of days affected, were also assessed during the day 4 survey. Impact on usual activities and patient functioning after taking antibiotic for the prescribed period was determined using the same questionnaire at the day 10 survey. In addition, the day 10 survey contained a number of questions dealing with an assessment of patient satisfaction with therapy in terms of symptom improvement, symptom resolution and return to normal activities and overall satisfaction. A second series of satisfaction questions, relating specifically to antibiotic therapy, were administered only to patients who had reported previous uUTIs. All satisfaction surveys were quantified using a 1-5 scale (1, very satisfied/strongly agree; 5, very dissatisfied/strongly disagree). Compliance with medication was quantified at both day 4 and day 10 surveys by asking patients how many tablets they had taken.

Data analysis

The analysis on uUTI symptoms and patient functioning before and after therapy was carried out only on the per protocol population, defined as those patients who met the inclusion criteria and for whom there was both baseline and day 4 survey data. Per protocol patients who also participated in the day 10 survey, and therefore provided data at all three assessment points, were also included in the study as a follow-up population. The primary clinical parameter assessed was the percent of patients reporting symptom improvement/symptom resolution at the day 4 survey and the approximate timing of both events. Secondary analyses included the impact of uUTI before and after antibiotic therapy on usual activities, expressed as a mean score, and the impact on patient functioning parameters in terms

TABLE 1. **Demographic and baseline clinical characteristics of the intent-to-treat and per protocol populations**

Variable	Intent-to-treat population (n=3285)	Per protocol population (n= 2323)
Mean patient age (years)	42 ± 12	40 ± 13
Age distribution (percent of patients)		
< 40 years of age	46.3%	52%
> 40 years of age	53.7%	47.4%
UTI history		
Patients with prior uUTI infections (%) (over last 12 months)	45.3%	46.8%
None	52.2%	53.2%
1	22.0%	21.9%
2-3	18.5%	17.9%
>3	7.2%	7%
Baseline symptoms		
Mean number of uUTI symptoms	3.57 ± 0.98	3.56 ± 0.98
Type of symptom (% of patients)		
Dysuria	86.9%	85.9%
Frequency	93.4%	93.6%
Urgency	83.4%	83.2%
Suprapubic pain	70.5%	69.7%
Visible hematuria	24.9%	24.4%
Duration of symptoms (days)		
Median	3	3
Mean	4.61 ± 6.93	4.9 ± 10.0
Patients with a urine culture test (%)	53.7%	45.4%
Patients with positive test (%)*	68.3%	90.2%

*Percent of patients tested

of the percent of patients reporting an impact and the number of days affected. Compliance was expressed as the percent of patients reporting that all three doses of medication had been taken at the day 4 survey.

Additional statistical analyses examined correlations between baseline and day 4 symptoms and patient reported impact on usual activities using Pearson Correlation coefficient analysis. Relationships between patient satisfaction and number of uUTI symptoms were investigated using Kendall's tau correlation coefficient or Spearman's rho correlation coefficient.

Safety data were expressed in terms of the intent-to-treat population defined as all patients who were registered for the study at baseline and who received at least one dose of medication.

Results

Over the recruitment period 3285 patients were registered at 581 sites in Canada forming the intent-to-treat population. Baseline data were obtained for these patients and all were prescribed a 3 day course of extended release ciprofloxacin. The per protocol population at day 4 consisted of 2323 patients, while 2141 patients had assessments at baseline, day 4 and day 10. The most common reason for exclusion from the per protocol population defined at day 4 was the inability to contact patients, accounting for 80% of the exclusions. The demographic and baseline clinical characteristics of both the intent-to-treat and per protocol populations are shown in Table 1. Both

TABLE 2. **Impact of uUTI on usual activities before and after antibiotic treatment**

Activity	Prior to antibiotic therapy*	After antibiotic therapy*	Percent change
Overall impact			
Mean impact score (± SD)‡	4.33 ± 3.81	0.76 ± 0.47	
Min-max	0 – 10	0 – 10	
Percent of patients reporting an impact	62.9%	13.0%	-79.3%
Impact on work			
Percent of patients reporting an impact	35.9%	10.2%	-71.6%
Mean number of days†	3.06 ± 2.7	3.72 ± 0.2	
Impact on functioning at work/school/home			
Percent of patients reporting an impact	49.5%	12.3%	-75.2%
Mean number of days†	3.25 ± 2.6	3.58 ± 0.2	
Impact on personal life			
Percent of patients reporting an impact	46.7%	11.9%	-74.5%
Mean number of days†	3.6 ± 2.6	3.74 ± 0.2	
Impact on social life			
Percent of patients reporting an impact	39.3%	11.0%	-72.0%
Mean number of days†	3.66 ± 2.7	3.7 ± 0.2	
Impact on sexual relations			
Percent of patients reporting an impact	40.3%	10.9%	-73.0%
Mean number of days†	3.98 ± 2.6	3.89 ± 0.2	

*Questionnaire assessed impact of UTI prior to antibiotic therapy (retrospectively at the day 4 survey) and post antibiotic therapy at the day 10 assessment.
‡Mean impact score based on the total patient population at each assessment.
†Reflects the mean number of days affected in those patients reporting an impact, for each parameter.

populations were very similar in terms of patient age, uUTI history and number and type of baseline uUTI symptoms. The only major difference in the two populations was in the results from urine culture testing. Although physicians initiated testing in 53.7% of the intent-to-treat population, only 68.3% of the tests were positive. Many of the patients with negative tests in this patient group may have ceased study participation and as a result, because of the per protocol population selection process, the number of patients with a positive test increased to 90.2% in the per protocol population. Longitudinal data relating to patient response to therapy was analyzed only for the per protocol population. At baseline this population had a mean age of 40 and the majority (53.2%) had no history of previous uUTIs. On presentation, the mean number of uUTI symptoms was 3.56 and the most common symptom was frequency, present in 93.6% of the patients, Table 1, while visible hematuria was present in 24.4%. The mean and median duration of uUTI symptoms were 4.9 and 3 days, respectively.

The uUTI symptoms had a dramatic impact on patient functioning parameters at baseline, as assessed by the telephone survey 4 days after initiating antibiotic therapy. As shown in Table 2, 62.9% of the per protocol population reported that their usual activities were impacted by the uUTI with a mean impact score, based on the total population, of 4.33. When the analysis was restricted to those individuals indicating an impact, the mean score was 6.89 (out of a maximum score of 10), suggesting a substantial impact of uUTI in some patients. The largest impact in terms of specific parameters was on functioning while at work/school or home; 49.5% of the patients reported that the infection had an impact on this parameter with a mean duration of impact of 3.3 days. In contrast, only 35.9% of patients reported a specific impact on work alone, with a mean duration of 3.1 days. Pearson correlation analysis indicated small but significant correlations between the number of days of uUTI symptoms at baseline and the duration of the impact on patient functioning parameters. Similarly, the number of symptoms at baseline was correlated with the percent of patients reporting a subsequent impact on functioning parameters. For the latter, Pearson correlation coefficient values ranged from 0.075 for work impact ($p<0.01$) to 0.119 ($p<0.01$) for the impact on personal life. All symptoms and signs at baseline correlated significantly ($p<0.01$ for dysuria, frequency, urgency and hematuria; $p<0.05$ for suprapubic pain) with the overall impact on usual activities at the day 4 assessment, but because most patients at this point had more than one symptom it was not possible to determine if a specific symptom had a larger impact.

At the day 4 assessment patients were also asked about medication compliance and symptom improvement and resolution. The per protocol population were highly compliant with medication and, based on patient responses, 97% of patients were fully compliant with the once daily dosing for the 3 day period. Eighty percent of the patients reported that their uUTI symptoms had improved within 48 hours of initiating antibiotic therapy and 39% reported complete symptom resolution, Figure 1. The median

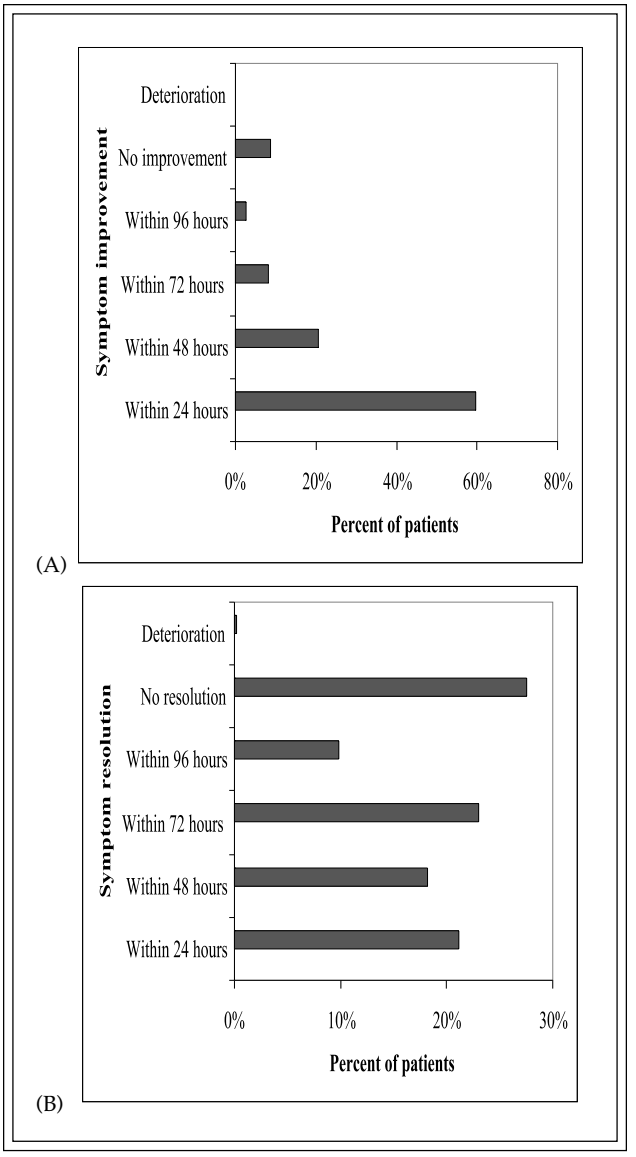

Figure 1. Time to symptom improvement (A) and symptom resolution (B) in the per protocol patient population at the day 4 assessment point.

time to symptom improvement and resolution at the day 4 survey was 24 and 48 hours, respectively. However, 8.8% of the population had no symptom improvement at day 4 and for 27.5%, symptoms had not resolved. On re-assessment 10 days after initiation of antibiotic in the follow-up population, the percentage of patients with continued non-resolution of symptoms had decreased to 14.1% and 1.6% reported symptom deterioration. For those patients with no symptom improvement at day 4 (8.8%) by day 10, 36% now reported improvement while the remainder had continued non-resolution (55%) or deterioration (8.7%) of symptoms (based on responses from 72.5% of this patient group). Therefore, in the per protocol population, 10 days after initiating a 3 day course of antibiotic therapy, 84.3% of patients reported complete symptom resolution while for the remaining 15.7%, symptoms had either not resolved (14.1%) or had deteriorated (1.6%).

The impact of therapy on symptom resolution was also apparent in the number of symptoms present at the day 4 and 10 surveys, Figure 2 and Figure 3. At baseline the majority of patients had multiple uUTI symptoms, Figure 2 and Table 1. However, at days 4 and 10 the percentage of patients reporting no uUTI symptoms increased to 66.8% (versus 0.6% at baseline) and 80.2%, respectively, Figure 2, while mean symptom scores were 0.74 (day 4 score versus 3.56 at baseline) and 0.42. The most persistent symptom was frequency with 19.1% and 12.4% of the patients reporting this symptom at day 4 and 10, respectively, versus 93.6% of the patients at baseline, Table 1. Hematuria was the least persistent sign, reported by only 3.2% of patients at day 10, versus 24.4% at baseline. An identical trend was observed in patients with concomitant symptoms categorized as pain (dysuria and suprapubic pain), irritation (frequency and dysuria) and lower uUTI symptoms (frequency and dysuria), Figure 3. In each case the percentage of patients reporting concomitant symptoms decreased dramatically after initiation of antibiotic, particularly over the first 4 days of therapy. Data summarizing the changes in the incidence of irritation and lower uUTI symptoms are summarized in Figure 3.

Symptom resolution also had a profound effect on patient functioning parameters. At the day 10 survey only 13% of patients reported a residual impact of uUTI on their usual activities (mean impact score for the total per protocol population was 0.76 versus 4.33 at baseline) and all functioning parameters showed a similar decrease in the percent of patients reporting an impact, Table 2. However, for those patients with a continuing impact at day 10, the magnitude of the

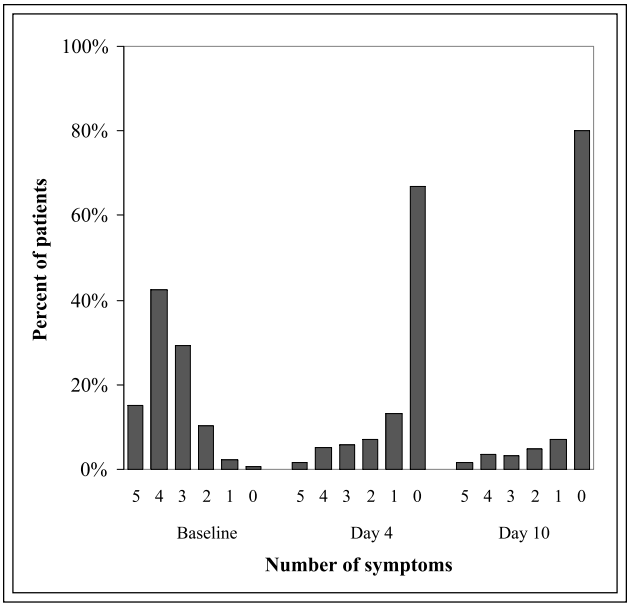

Figure 2. Changes in the number of symptoms over the complete study period.

impact was relatively unchanged from baseline; for these patients mean impact score was 5.8, only marginally lower than the score of 6.89 recorded for patients in the same category at baseline. Similarly, although there was almost an identical decrease in the percent of patients reporting an impact on all functioning parameters (mean decrease of 74%, Table 2) between baseline and day 10, for those affected patients the duration of the impact was

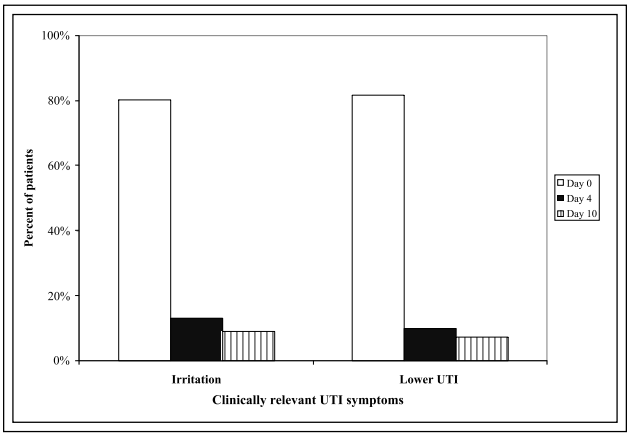

Figure 3. Decrease in the incidence of clinically relevant concomitant uUTI symptoms between baseline and the day 10 assessment. Survey assessed the per protocol population on symptoms of irritation (frequency and urgency) and lower uUTI symptoms (frequency and dysuria).

similar to that recorded prior to antibiotic therapy. As at the day 4 survey, there was a weak but significant correlation between the number of symptoms remaining at day 10 and patients reporting a subsequent impact on functioning parameters, ranging from a correlation coefficient of 0.116 for sexual relations ($p<0.01$) to 0.212 for impact on work ($p<0.01$).

In response to high levels of symptom improvement and resolution, and the subsequent impact on functioning parameters, patients reported high levels of satisfaction with therapy. As shown in Table 3, 84.1% and 85.7% of patients were very or somewhat satisfied with speed of recovery and overall satisfaction, respectively, at the day 10 survey. Mean satisfaction scores for speed of recovery and overall satisfaction were 1.66 and 1.56, respectively, based on a 1 to 5 scale where 1 implies strong agreement and 5 indicates strong disagreement. Similar levels of satisfaction were recorded for survey questions relating to symptom improvement and antibiotic convenience (results not shown). There was a small but significant relationship between the number of uUTI symptoms at baseline and overall patient satisfaction with treatment ($r(tau) = -0.040$, $p<0.05$), with fewer symptoms at baseline associated with higher levels of satisfaction at day 10. However, there was no such relationship between baseline uUTI symptoms and patient satisfaction with either symptom improvement or speed of recovery. Further analysis revealed that overall patient satisfaction scores were significantly ($r(rho)= -0.117$, $p<0.01$) related to the magnitude of the change in usual activities during therapy with higher functional changes associated with higher levels of satisfaction with therapy. In contrast, patients with remaining symptoms at day 10 recorded lower levels of overall satisfaction with therapy than those without symptoms ($r (rho) = 0.419$, $p<0.01$).

As shown in Figure 4, there was also a high level of preference for, and satisfaction with, once a day antibiotic therapy in patients who had previously received antibiotics for the treatment of uUTIs ($n = 1556$). In this group, 69% were very or somewhat satisfied with extended release ciprofloxacin and 70% preferred the once a day regimen to previous antibiotics they had received in the treatment of uUTI.

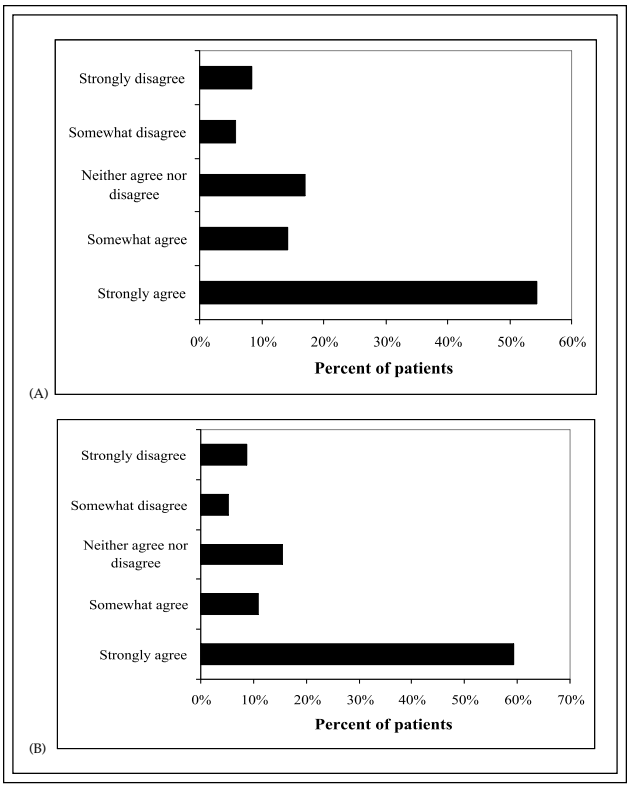

Figure 4. Patient preference (A) and overall satisfaction (B) with antibiotic therapy in subjects who had previously received antibiotics for the treatment of uUTI. Patients were asked to base their assessment in terms of their preference for, or satisfaction with, current antibiotic therapy compared to previously dispensed antibiotics.

TABLE 3. **Patient satisfaction with speed of recovery and overall satisfaction with therapy; per protocol patient population**

Questionnaire response	Speed of recovery (%)	Overall satisfaction (%)
Very satisfied	63.6%	72.6%
Somewhat satisfied	20.5%	13.1%
Neither satisfied nor dissatisfied	6.6%	5.0%
Somewhat dissatisfied	4.5%	3.7%
Very dissatisfied	4.8%	5.6%

There was a very low level of adverse reactions over the treatment period. Only 155 patients (4.7% of the intent-to-treat population) reported a total of 223 after adverse reactions, the most common events being nausea (1.1% of intent-to-treat population), stomach discomfort (1.0%) and headache (0.8%). There was only a single serious adverse event where the patient developed cramping with severe spasms in the bladder area and was hospitalized. Eight patients (0.2%) discontinued medication as a result of an adverse event.

Discussion

Although previous studies have examined treatment of uUTIs in a family physician setting in terms of optimal and cost-effective diagnostic and antibiotic management pathways,[3,5,12,13,16] few studies have assessed the disease from a patient perspective. Given the design of the present study, and the requirements for patient contact on two occasions following the initial physician consultation, the per protocol population was selected for analyses because of the need for longitudinal data to effectively track patient outcomes. The baseline symptoms of this population were similar to those recorded in previous studies, with frequency the most common uUTI symptom and hematuria the least common, and each patient had a mean number of 3.56 symptoms.[8,14,15] This baseline symptom profile had a significant impact on usual activities with 63% of patients indicating that normal activities were curtailed, with a mean impact score of 6.89. The degree of impact showed a weak correlation with the number of baseline uUTI symptoms and all symptoms were similarly correlated to the overall impact of the infection. However, attempts to identify a single symptom, or combination of symptoms, with a strong impact on usual activities were unsuccessful because, at least at baseline, most patients had multiple uUTI symptoms and only 3% of the per protocol patients (n = 70) had $\leq$ one symptom. The duration of impact on each functioning parameter, ranging from a mean period of 3.06 days for work (median 2 days) to 3.98 days for sexual relations (median 3 days), was similar to the mean and median duration of uUTI symptoms at baseline, which were 4.61 and 3 days, respectively. Therefore, at baseline the impact of the uUTI on functioning parameters was only apparent during the acute phase of the infection. This data demonstrates that uUTI is not a benign condition and although for most patients the active infection has a short duration, it nevertheless can have a large impact on usual activities. Using the generic SF-36 QoL instrument, Ellis and Verma[11] in a Canadian study showed a significant impact of uUTI on patient QoL. Compared to a control female population, women with an active uUTI had significant decreases in all SF-36 scales including general health perception, physical functioning, emotional health and social functioning. Similarly Barry et al,[16] in an assessment of the cost-utility of office-based uUTI treatment strategies, assigned a disutility of 0.2894 to a persistent uUTI health state, based on a utility scale where 0 is death and 1 is optimal health. Although the present study did not employ a validated QoL instrument, the questionnaire used nevertheless did confirm that an active uUTI has a substantial impact on patient functioning parameters and that the degree of impact correlates with the number of uUTI symptoms present.

Once a day therapy with an extended release antibiotic formulation led to a dramatic decrease in the number of patient reported symptoms, and to high levels of symptom improvement and resolution. Between baseline and day 4 mean number of symptoms decreased from 3.56 to 0.74, the percent of patients with no uUTI symptoms increased from 0.6% to 66.8%, and 72% of patients had resolution. By day 10 only 15.7% of patients reported that their symptoms had either not resolved or had deteriorated, and 84.3% of the per-protocol population had complete symptom resolution at this point. Although symptom resolution was not confirmed by physicians, from a patient perspective the data provides a clinical cure rate of 84.3% in a family physician outpatient setting, where clinical cure is defined as the disappearance of uUTI symptoms. This patient assessed clinical cure rate compares favorably with protocol driven clinical trial data on the efficacy of extended release ciprofloxacin where, in patients with confirmed uUTI, clinical cure rates were 95% and 89%, 4-11 days and 25-50 days, respectively, after completion of therapy.[2,17]

Symptom resolution was accompanied by dramatic changes in the number of patients reporting an impact on functioning activities. At day 10 only 13% of patients reported a continuing overall impact on usual activities but the magnitude of this impact (impact score was 5.9) was similar to the impact on equivalent patients at baseline. There were almost identical decreases in the number of patients reporting an impact on all functioning activities after antibiotic therapy. However, for those patients with a continuing uUTI impact after therapy, the duration of the impact was similar to that recorded prior to therapy. This provides clear evidence that persistent disease symptoms continue to impact patient functioning

activities and emphasizes the continuing burden of the infection in patients with treatment failure.

All the patients in the present study received extended release ciprofloxacin. This antibiotic was selected because clinical trials have demonstrated the efficacy and tolerability of the drug in treatment of uUTI, and its utilization as a routine antibiotic in the treatment of uUTI has increased considerably, particularly with the emergence of bacterial resistance to conventional first line therapies.[2,17,18] The extended release formulation, and once a day dosing, also has clear benefits for compliance. The compliance advantages of oral antibiotic therapy administered once a day compared to twice or three times daily have been demonstrated[19] and in the present study compliance in the per protocol population was 97%. In addition, 92.5% of the per protocol population reported that they were satisfied with the treatment convenience associated with the extended release formulation.

There were a number of limitations associated with the present study. These include the fact that all aspects of symptom resolution were based on patient responses to a questionnaire and were not confirmed by physician examination or urine culture. In addition, although patients may have been followed up by their physicians after the 10 day survey, this data was not collected in the present study. Hence uUTI recurrence beyond day 10, or the continuing treatment of patients with non-resolution of symptoms at day 10, were not assessed. However, the major objective of the study was to assess uUTI symptoms from a patient perspective and a final assessment at 10 days post initiation of antibiotic therapy reflects the anticipated time course over which a response to extended release ciprofloxacin therapy would be expected to occur.[2,17]

In addition, although data were prospectively collected by telephone interview, patients at the day 4 survey were asked to recall the impact of the uUTI on usual activities prior to initiation of antibiotic therapy. Patients then had to recall a uUTI impact when in many cases the infection itself was already resolved. This may have led to problems with recall in some patients. In addition, the recall issue was compounded by the fact that not all patients were called exactly 4 or 10 days after initiation of antibiotic therapy, due mainly to the inability to reach patients. For some patients these delays may have further complicated accurate recall regarding uUTI symptoms and impact on usual activities.

Finally the questionnaire used in the study was not validated prior to use, nor was the sensitivity of the questionnaire to changes in patient symptoms tested. However, the statistical analyses carried out demonstrate that there was a correlation between the number of patient symptoms and the subsequent impact on all functioning parameters. More symptoms at baseline, and remaining symptoms at day 10, were both correlated, albeit weakly, with a larger functioning impact. Therefore, for the assessment of disease impact, the questionnaire was sensitive to the number of uUTI symptoms and the associated disease burden recorded by the patient. Similarly, data on patient reported decreases in the number of uUTI symptoms correlated with the degree of symptom improvement and resolution, validating the questionnaire in quantifying disease changes with therapy. This internal validation supports the use of the questionnaire in this study.

The data in the present study does present some practical points to assist the practicing physician in the care of patients with uUTI. It is clear that the longer the patient experiences uUTI symptoms prior to therapy, the greater the impact on functioning activities, therefore early treatment is desirable. In addition, when prescribing antibiotic therapy the physician can advise the patient with a uUTI, who is compliant with appropriate therapy, that within 48 hours there is an 80% probability that their symptoms will have improved and a 40% chance of being cured. However, the physician should also be aware that 10 days after initiation of antibiotic therapy, 10% of the patients may show no symptom improvement. These patients should be investigated further (assessment of clinical history, physical examination, urine culture) and if symptoms do not improve and no other etiology is found, then referral to a urologist may be indicated. Finally, approximately 25% of the patients in this study reported gross hematuria, a worrisome symptom for both patients and physicians, and at day 10, 3% of the population continued to report this symptom. Further investigation and follow-up is indicated in uUTI patients who have persistent hematuria after appropriate antibiotic therapy.

Conclusions

Acute symptoms suggestive of a uUTI can have a large impact on normal patient activities. However, this effect is transient and for most patients appropriate antibiotic prescribing relieves symptoms rapidly and restores normal functioning activities. However, for some patients therapy is unsuccessful and symptoms persist with a resulting longer term impact on patient functioning and usual activities. By assessing

outcomes from a patient perspective, the present study provides family physicians with a broader view of uUTI and the potential impact of the disease on some of their patients. The study will allow physicians to more accurately counsel their patients on what to expect over the initial 10 day period once antibiotic treatment has been initiated. □

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