Validity of the urine dipslide under daily practice conditions

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Background. So far, the validity of urine dipslides has been studied only under optimal conditions, which may not reflect the situation in daily practice.

Objective. We studied the validity of the urine dipslide as performed under daily practice conditions and assessed the influence of the incubation period (24 h versus 48 h) on validity.

Methods. Fresh urine samples of patients with signs/symptoms of a possible urinary tract infection (UTI) were examined in general practice via a nitrite test, a urine sediment and a dipslide. A second dipslide was inoculated and sent to the hospital microbiology laboratory for culture. This culture acted as gold standard. We calculated the sensitivity and specificity of the tests performed.

Results. Of the 273 patient episodes included, 62% had a UTI (166 of 268 cultures). The sensitivity of the dipslide performed in daily general practice was 73% and the specificity was 94%.

Conclusion. The validity of the dipslide read under practice conditions is lower than under optimal conditions. Actions to improve performance are needed. Nonetheless, using the dipslide instead of the sediment as a second step after the nitrite test would improve the diagnostic work-up of UTI.

Keywords. External validity, sensitivity, specificity, urine dipslide.

Introduction

Urinary tract infections (UTIs) are common in general practice (annual incidence: ± 40 per 1000 patients).1 The number of patients consulting their GP with signs that may reflect a UTI is probably much higher.

The GP can use various tests to confirm or exclude a UTI, such as the nitrite test, the leukocyte esterase test, the urine sediment and a culture. Through history taking, the pre-test probability of a UTI hardly exceeds 60%.2 If we were to treat patients on the basis of the their history, we would treat ≥40% of patients without a UTI. Therefore, guidelines such as the standard for UTI of the Dutch College of General Practitioners recommend performing urine tests before starting antibiotic treatment.2 The first step is a nitrite test. In the case of a positive result, treatment is indicated (specificity is high). In the case of a negative nitrite test result, the dipslide is recommended, or the sediment test (when performed correctly: the sediment test is laborious and has many sources of error).

The validity of the dipslide seems excellent (sensitivity ± 95%, specificity up to 99%).3,4 However, validity is usually assessed under optimal laboratory conditions rather than under daily practice conditions. This may affect the external validity of the characteristics of urine tests.5 Therefore, data from laboratory studies may not be valid for daily general practice. Several studies concluded that validity was lower when dipslides are read by practice nurses instead of laboratory staff.6,7

Based on the available literature, it is unclear if the dipslide in daily practice is as reliable as in the laboratory. Therefore, we studied the validity of the dipslide under daily practice conditions.

Here we present the results of a study on the validity of the dipslide performed and judged in general practice under routine ‘non-optimal’ conditions.

Methods

The study was performed in five practices (16 GPs) in the region of Maastricht. All patients aged 12 years or more with signs of a UTI (such as painful micturition) with no
UTI within the preceding 3 months were included in the study. Both GPs and practice nurses could enrol patients.

To study the usual care provided as much as possible, we asked GPs and practice nurses to ‘act as usual’ with the only exception that after each consultation the urine sample was not discarded but two dipslides (Uriline by BioMerieux) were inoculated. One dipslide was sent to the microbiological laboratory of the University Hospital in Maastricht for culture and identification of the microorganism. This appeared safe: sending dipslides does not affect the reliability of the results.8 The result of the culture in the laboratory was our gold standard. The second dipslide was cultured and read in general practice. Each practice used its own incubator. We considered dipslides with at least 10^5 colony-forming units (c.f.u.) as positive. This concentration of 10^5 c.f.u. is considered to reflect a UTI. Dipslides containing only skin flora were considered negative.

The nitrite test is positive in the case of a colour change from white to pink or purple. For the sediment, 10 ml of fresh urine was centrifuged and its sediment was examined at 400× magnification. The sediment was considered positive when >20 bacteria or at least five leukocytes per microscopic high power field were found.9 All urine tests in general practice, including the dipslides, were performed and read as usual by the practice nurses.

We calculated the sensitivity and specificity plus the predictive values of the individual tests performed.

When following guidelines for detecting a UTI, the dipslide (or eventually the sediment) is performed on a population with a pre-test probability <60%, due to the preceding nitrite test having a negative test result.

Therefore, apart from validity (sensitivity, specificity) and the predictive values of the individual nitrite test and the dipslide, we also calculated the predictive values of the cascade combination of the nitrite test and the dipslide.

All test characteristics are presented with their 95% confidence intervals (CIs).

Results

We included 232 patients in the study (83% female, 17% male, median age 54 years, range 9–93) with 273 episodes of signs/symptoms. In all 273 cases, a nitrite test and a dipslide were performed. In 112 cases, the results of the urine sediment were not available. The culture results from five urine samples were missing due to transportation errors.

Of the remaining 268 urine samples, 166 (62%) were positive (predominant bacteria: Escherichia coli in 55%, Klebsiella pneumoniae in 9%, Proteus mirabilis in 8% and Enterococcus faecalis in 7%). In 23 cases, more than one bacterial type was isolated. In 51 urine samples (19%), we found contamination with skin flora; four dipslides (1%) contained Candida albicans. Of these contaminated samples, 13 dipslides were read as (false) positive in general practice. Of four dipslides containing Candida albicans, two were read as (false) positive in general practice.

In all practices, the nitrite test was the initial test. We found a sensitivity of 42% (95% CI 34–49%) and a specificity of 95% (CI 89–98%). The positive and negative predictive value were 93% (CI 85–98%) and 50% (CI 42–57%), respectively (Table 1).

The sensitivity of the dipslide read in general practice after 24 h was 73% (CI 66–80%) and specificity was 94% (CI 88–98%). The positive and negative predictive values were 95% (CI 90–98%) and 68% (CI 60–76%), respectively (Table 2).

We also calculated the predictive values of the dipslide and urinary sediment when performed after a negative nitrite test. Since the dipslide is only recommended in the case of a negative nitrite test, predictive values should be calculated for this subgroup with a different pre-test probability.

When performed after a negative nitrite test result, the positive and negative predictive value of the dipslide was 92% (CI 84–98%) and 73% (CI 64–81%), respectively (Table 2).

Discussion

This study shows that under daily practice conditions, the sensitivity in particular, but also the specificity and the predictive values of the dipslide are lower than under optimal laboratory conditions.

An explanation may be that reading a dipslide is more difficult than expected. Reading errors may affect the sensitivity and specificity of the dipslide. Expertise may play a role here. We assume that reading a dipslide seems so simple that readers act and judge rashly. Unfortunately, the low number of practice assistants participating in our study made it impossible to monitor this.

A possible explanation for the lower sensitivity is an incubation temperature lower than 37°C, which increases the risk of false-negative dipslide results. During our study, the dipslide agar melted at room temperature, and therefore the dipslides were stored in refrigerators until

| Table 1 Nitrite test, compared with the laboratory culture (gold standard) |
|------------------|----------|----------|----------|
| Nitrite test                  | Culture >10^5 |
| Positive                           | Negative | Total    |
| Positive                           | 69       | 5        | 74       |
| Negative                           | 97       | 97       | 194      |
| Total                              | 166      | 102      | 268      |
used. This may have affected the initial growth of bacteria. Related to this is the quality of the incubators used in the practices. All practices used their own incubator. Changing the temperature of these incubators was not possible, and it cannot be ruled out that the incubators did not reach the necessary 37°C, possibly leading to false-negative results. We recommend a regular temperature check of incubators.

Besides the cascade ‘nitrite test plus dipslide’, we also evaluated the cascade ‘nitrite plus sediment’. In our study, the predictive value of the test cascade ‘nitrite test first, when negative followed by a sediment’ was considerably lower than that of the cascade with the dipslide (data not presented).

All test characteristics are presented only for the current international standard, namely a cut-off level of $10^4$ bacteria per ml, although we also assessed the validity of all tests for a cut-off level of $10^4$. This latter cut-off level is recommended in the revised standard of the Dutch College of General Practitioners. At a cut-off level of $10^4$ bacteria per ml, sensitivity of the dipslide is slightly higher, but specificity is lower. It is difficult to say which cut-off level is to be preferred, $10^4$ or $10^5$. Given the fact that the nitrite test—recommended as the first test—has a high specificity, perhaps a test with a high sensitivity would be preferred as the second test. In the case of the dipslide as the second test, this would favour a cut-off level of $10^4$ bacteria per ml.

An additional issue in our study was the influence of the incubation time; to date, there is no evidence suggesting an optimal incubation period: is 24 h sufficient or should we wait 48 h until reading dipslides? Even the fact that the nitrite test—recommended as the first test—has a high specificity, perhaps a test with a high sensitivity would be preferred as the second test. In the case of the dipslide as the second test, this would favour a cut-off level of $10^4$ bacteria per ml.

An additional issue in our study was the influence of the incubation time; to date, there is no evidence suggesting an optimal incubation period: is 24 h sufficient or should we wait 48 h until reading dipslides? Even the recommendations and instructions for use provided by the manufacturer give no clear preference for one or the other. In the practices, dipslides were examined after 24 h. In 204 cases, dipslides were also read after 48 h.

The validity of the dipslide read after 24 h was similar to that read after 48 h (data not presented).

Should these findings make us act differently? The nitrite test can still be used as the first step. Although the validity of the dipslide in daily practice is considerably lower than under optimal conditions, the combination of the nitrite test plus dipslide is still sufficient. Of the 20 false-positive dipslides, 13 were contaminated and two were identified as *C.albicans*. Thus, specificity can be improved by instructing the patient well and by using only fresh urine samples. Also, (re)education in inoculating and reading dipslides may be necessary, but this would require an evaluation of performance to find sources of error. From that perspective, efforts to optimize the use of dipslides in daily general practice are welcomed.

Nonetheless, the diagnostic work-up of UTI would benefit from using the dipslide in general practice instead of the sediment or multiple reagent test strips for leukocyte esterase and blood, as the validity of the sediment and such test strips so far seemed disappointing.

<table>
<thead>
<tr>
<th>Dipslide on all samples</th>
<th>Culture $\geq 10^5$ (in the laboratory)</th>
<th>Dipslide after negative nitrite test</th>
<th>Culture $\geq 10^5$ (in the laboratory)</th>
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<tbody>
<tr>
<td></td>
<td>Positive</td>
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References