

Gupta K, Hooton TM, Roberts PL, Stamm WE. Short-course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. *Arch Intern Med.* 2007;167:2207–2212.

Does a short course of nitrofurantoin cure acute uncomplicated cystitis?

Yes. In fact, it is now the preferred treatment in women because of increasing resistance among uropathogens to trimethoprim-sulfamethoxazole (TMP-SMX) and other fluoroquinolones.

In this randomized trial, 338 women 18 to 45 years old who had acute uncomplicated urinary tract infection (UTI) were randomized to open-label treatment with nitrofurantoin (Macrobid), 100 mg twice daily for 5 days, or trimethoprim-sulfamethoxazole, one double-strength tablet twice daily for 3 days. Clinical cure 30 days after therapy was achieved in 84% of the women taking nitrofurantoin and in 79% of women taking trimethoprim-sulfamethoxazole.

zole in the treatment of uncomplicated cystitis. Such replacements are inappropriate for empiric therapy, and indiscriminate use of fluoroquinolones has led to increased resistance among *Staphylococcus aureus* organisms.

Nor has there been proper concern about the way antibiotics alter the endogenous bacteria of the body. Overuse of antibiotics such as the β -lactams (cephalosporin and expanded-spectrum penicillins), fluoroquinolones, and macrolides has added not only to the emergence of resistant bacteria strains but also to an increase in adverse events.

EXPERT COMMENTARY

Sebastian Faro, MD, PhD, Clinical Professor of Obstetrics and Gynecology at the University of Texas, Houston, and Attending Physician at the Woman's Hospital of Texas in Houston.

This study is important because UTI is routinely treated empirically. The usual drugs prescribed for uncomplicated UTI are TMP-SMX, extended-release ciprofloxacin (Cipro), or a first- or second-generation cephalosporin. Empiric use of fluoroquinolones such as ciprofloxacin has replaced trimethoprim-sulfamethoxazole

Resistance to TMP-SMX ranged from 12% to 21%

In this study, the authors isolated and identified bacteria responsible for infection, and the outcome reflects the national bacterial etiology in this age group (18 to 45 years). The number one bacterium isolated in the study was *Escherichia coli* (82%) as the sole uropathogen (TABLE, page 21). These data confirm that *E coli* remains the bacterium most likely to cause acute uncomplicated UTI.

The problem is that *E coli* has developed resistance to the antibiotics most commonly prescribed to treat this condition. In this study, 12% of the *E coli* isolates were resistant to trimethoprim-sulfamethoxazole. Even more alarming, 21% of non-*E coli* strains were resistant to trimethoprim-sulfamethoxazole. In contrast, 99.6% of *E coli* isolates and 90% of non-*E coli* isolates were sensitive to nitrofurantoin.

Adverse effects did not deter use

In the trimethoprim-sulfamethoxazole

FAST TRACK

84% of women taking nitrofurantoin and 79% of those taking TMP-SMX were cured 30 days after therapy

What this evidence means for clinical practice

A 5-day course of nitrofurantoin is highly effective in treating uncomplicated UTI in women. It should be the initial empiric treatment of this infection because it is effective, safe, and well tolerated.

If a 3-day course of trimethoprim-sulfamethoxazole is used, the clinician should be aware that, as *E coli* resistance to this agent increases, its efficacy decreases.

—Sebastian Faro, MD, PhD

TABLE

Bacteria isolated from the study population (n = 338)

BACTERIUM	NUMBER OF ISOLATES
<i>Escherichia coli</i>	276
Non- <i>E coli</i>	61
<i>Staphylococcus aureus</i>	5

Klebsiella species, *Proteus mirabilis*, *Enterobacter* species, and *Streptococcus agalactiae* made up the remainder of the isolates (1% to 3%).

group, 31% of women experienced adverse effects, as did 28% in the nitrofurantoin group. Side effects included those commonly seen with oral antibiotic therapy: nausea, diarrhea, headache, light-headedness, and vaginal itching.

Adherence was good; only 1% of women taking trimethoprim-sulfamethoxazole and 2% of women taking nitrofurantoin discontinued the drug.

An advantage for women taking nitrofurantoin is that it is concentrated in the urine, with little uptake in tissue and other bodily fluids. Therefore, it has very little effect on the endogenous vaginal microflora and little chance of causing vaginitis.

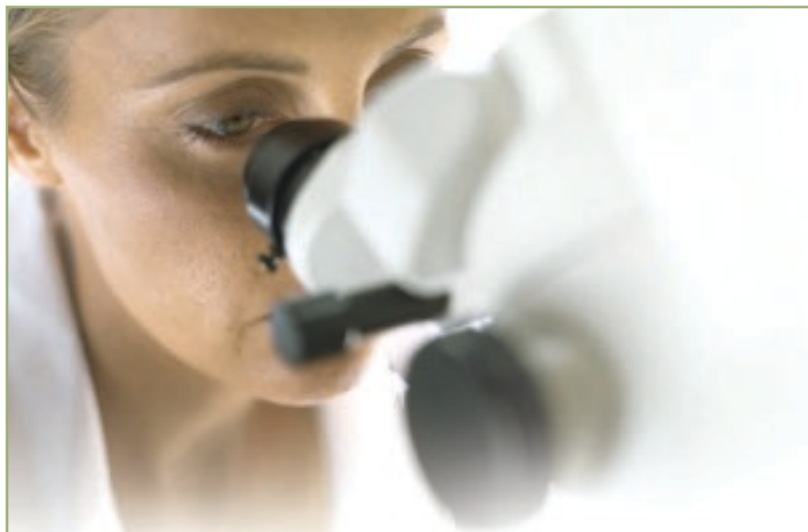
Weaknesses of the study

This study was not blinded; therefore, clinical evaluation may have been biased.

The population involved in the study was rather homogenous—mostly white college students. A mix of races would have been more informative.

Another limitation is that the investigators chose cefotaxime (Claforan) as one of the comparative antibiotics in the microbiologic arm, but gave no reason for this choice. Cefotaxime is administered either intravenously or intramuscularly and therefore has questionable relevance to this study. The other antibiotics chosen in addition to the two study drugs were ciprofloxacin and amoxicillin-clavulanate—both commonly used to treat acute uncomplicated cystitis.

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Holmgren C, Aagaard-Tillery KM, Silver RM, Porter TF, Varner M. Hyperemesis in pregnancy: an evaluation of treatment strategies with maternal and neonatal outcomes. *Am J Obstet Gynecol*. 2008;198:56.e1-56.e4.

Does a PICC line facilitate treatment of hyperemesis gravidarum?

No. In fact, it may be dangerous. In this study, 42 women hospitalized with hyperemesis gravidarum (HEG) were assigned to treatment with medication alone, 33 to a peripherally inserted central catheter (PICC) line, and 19 to a nasogastric (NG) or nasoduodenal (ND) tube. Of those managed with a PICC line, 66.4% ($P < .001$) required treatment for infection, thromboembolism, or both. In addition, neonatal complications including small for gestational age (SGA), admission to neonatal intensive care, termination of pregnancy because of HEG, and fetal loss were increased in the women who had a PICC line.

EXPERT COMMENTARY

T. Murphy Goodwin, MD, Professor and Director of the Division of Maternal-Fetal Medicine and Co-Director of the Institute for Maternal and Fetal Health, University of Southern California, Los Angeles.

This important study expands on the observations of previous authors who have pointed out the numerous complications of PICC line access for parenteral nutrition during pregnancy. The vast majority of such interventions during pregnancy are for the diagnosis of HEG.

That some form of nutritional supplementation is needed for women who experience persistent weight loss with hyperemesis is clear. Although it is rare, maternal mortality still does occur and comes almost exclusively from this group of women. The same is true

for major maternal morbidity such as Wernicke's encephalopathy.

Fetal effects such as growth restriction are limited to women who have HEG who also lose weight. Apart from growth restriction, which can be recognizable at birth, substantial data in both humans and experimental animals suggest adverse consequences later in life as a result of maternal calorie restriction for even a few months of pregnancy.

Interestingly, in this study, there were no SGA infants in either the group treated with medication alone or the group managed with NG/ND tube placement.

Main complications are thrombosis, infection

The major complications of peripheral and central venous access for nutrition in pregnancy are thrombosis and infection, and the prevalence is now well established to be around 50%. Maternal death from complications of line access has also been reported.

A confirmation of case reports and small series

This study is important because it represents the largest report of women who have received total nutritional support via an enteral feeding tube. Previous reports were limited to single cases or small series.

There is little evidence indicating that the better safety record of enteral feeding and greater efficacy compared with parenteral feeding via a PICC line have led to increased usage. In our own survey of 792 women who self-reported hyperemesis gravidarum from 2000 to 2004, 16.7% reported parenteral nutrition, compared with only 2.3% who reported enteral tube feeding. It is hoped that this study will help reverse this ratio. ■

FAST TRACK

66.4% of women managed with a PICC line required treatment for thromboembolism or infection, or both

What this evidence means for clinical practice

Enteral feeding for women with hyperemesis gravidarum is safer than parenteral feeding and is accepted by patients. Obstetricians should make every effort to use enteral feeding for women with hyperemesis gravidarum and persistent weight loss.

—T. Murphy Goodwin, MD