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EDITORIALS

Antibiotics or NSAIDs for uncomplicated urinary tract infection?

Pain relief and a delayed antibiotic prescription is a pragmatic and balanced approach

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Urinary tract infection (UTI) is second only to respiratory tract infection in the use of antibiotics. It is an international priority to rationalise antibiotic use in primary care given the dangers of antibiotic resistance and the evidence that prescribing in primary care is likely to be a key driver of antibiotic resistance.[1] The trial by Kronenberg and colleagues (doi:10.1136/bmj.j4784)[2] provides a welcome addition to the literature, providing a head-to-head comparison of an antibiotic compared with a non-steroidal anti-inflammatory drug (NSAID, diclofenac) and extending the findings of a previous German trial of antibiotics compared with the NSAID ibuprofen.[3]

The results show that an initial prescription for antibiotics is superior to NSAIDs for symptomatic management and inferior in terms of net antibiotic usage. However, the difference in symptom control may not be as stark as the 27% absolute difference in symptom resolution by day 3 would suggest, since the reduction in symptom score by day 3 in the NSAID group was 70% of the effect in the antibiotic group (diclofenac −7.3; norfloxacin −10.3) and quality of life was reasonably well maintained using diclofenac (8.8 *v* 9.4 on the EuroQol health state). NSAIDs may be supporting a useful improvement in symptom control as an alternative to initial use of antibiotics.

Of more concern were the findings that a larger number of women in the NSAID group had prolonged illness (12% more with unresolved symptoms at 7 days) and had more pyelonephritis (5% *v* 0%)—a higher difference than in the previous German study (2% *v* 0.4%).[3] Is a 5% complication rate in the NSAID group what might be expected anyway from no initial antibiotic treatment? The answer is probably not: among previous placebo controlled studies, one reported that 1/38 of the placebo group developed pyelonephritis,[4] whereas another reported 1/288.[5] Combining these suggests a risk somewhere near 0.6% for placebos. Thus the concern is that NSAIDs may not be just neutral in their impact on the progression of infections but actively harmful, presumably by interfering with the inflammatory element of the host's defences.

If the possibility of adverse outcomes with NSAIDs was an isolated finding it could be dismissed as due to chance or the drawbacks of historical comparisons. However, the finding of increased complications when using NSAIDs is supported by evidence from other infections: evidence is emerging from both trials and case-control studies that prolonged illness or the complications of respiratory infections may be more common when NSAIDs are used.[6-9]

Does this mean that to help reduce antibiotic use we should not use NSAIDs at all in managing UTIs? Here we are caught between the short term disadvantage of worse symptom control for women managed without antibiotics and the longer term harms from antibiotic resistance, including poorer symptom control, when using antibiotics routinely. Resistance among urinary tract pathogens is clearly related to an individual's past use of antibiotics, is relatively common for many of the antibiotics used to treat UTI, such as trimethoprim, and results in much more prolonged symptoms.[10 11] So even for symptom management the short term benefits of antibiotics must be balanced against the longer term harms.

Given these dilemmas what can women and their clinicians do in practice? Paracetamol could be used more regularly as the first line analgesic in infections since it seems to be associated with a lower risk of adverse outcomes.[6] When advocating an NSAID clinicians could consider advising women to take ibuprofen rather than diclofenac because in the previous larger study, which used ibuprofen, pyelonephritis occurred less often.[3] NSAIDs could also be used more sparingly: the current study shows that in an efficacy trial where drugs are taken regularly, harm may ensue, but it has not shown that intermittent use, more likely in everyday practice, is necessarily harmful.

Clinicians can also issue a delayed antibiotic prescription—giving women rapid access to antibiotics if symptoms do not improve within 48 hours, or get worse. Delayed prescriptions did not increase the risk of complications in a recent trial.[12] However, the use of a delayed prescription alone for a UTI is only likely to result in a 20-25% reduction in antibiotic use,[12] unlike the larger effect in respiratory tract infections.

Clearly, more evidence to inform best practice is necessary, but in the meantime a pragmatic strategy of using paracetamol regularly, ibuprofen when necessary, and backed up with a

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delayed antibiotic prescription using a drug with a low resistance profile (eg, nitrofurantoin) could potentially balance competing needs to reduce antibiotic consumption, provide reasonable symptom control, and minimise the risk of complications.

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