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Should We Use Antibiotic Prophylaxis for Flexible Cystoscopy? A Systematic Review and Meta-Analysis

Key Words

Antibiotic prophylaxis · Flexible cystoscopy · Urinary tract infection

Abstract

Introduction: The role of antibiotic prophylaxis for routine flexible cystoscopy (FC) is not clear due to the varying practices of individual clinicians. There are no formal guidelines, and this may be due to a lack of formal summary of the data. **Methods:** A systematic review was conducted in April 2014 including all randomised control trials on prophylactic antibiotic use for FC. The main outcome measures were confirmed bacteriuria on mid-stream urine (MSU), asymptomatic bacteriuria and symptomatic bacteriuria. A meta-analysis was conducted with difference between groups expressed as an odds ratio (OR) and control group risk. **Results:** 5,107 patients were included, 2,173 in placebo and 2,934 in the antibiotic group. The OR for all three outcomes favoured the antibiotic group; the risk of developing symptomatic bacteriuria was 0.06 times more likely in the control group (OR 0.34), 0.054 (OR 0.40) for developing asymptomatic bacteriuria and 0.109 for confirming bacteriuria on MSU (OR 0.36). The number needed to treat (NNT) was 15 (13–19) for MSU positive bacteriuria; 32 (27–42) for symptomatic bacteriuria

and 26 (23–33) for asymptomatic bacteriuria. **Conclusions:** Antibiotic prophylaxis did confer a reduction in cases of symptomatic and asymptomatic bacteriuria but the NNT were high. Therefore, the authors cannot advocate the use of antibiotic prophylaxis for routine FC procedures.

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Introduction

The flexible cystoscope was introduced to practice in the early 1980s and since then it has undergone numerous modifications, giving us the sophisticated video scope we use today [1]. The high-definition optics allows excellent visualisation of the lower urinary tract for diagnostic purposes. The relatively small size of the flexible scope compared with its rigid counterpart allows it to be used safely under local anaesthesia making it more acceptable to patients. In addition, a working channel allows interventions such as bladder biopsies and diathermy. It is now routinely used to investigate haematuria, recurrent urinary tract infections, lower urinary tract symptoms and for bladder tumour surveillance [2]. Other uses include insertion and removal of ureteric stents and therapeutic procedures such as botulinum toxin injections [3].

Instrumentation of the urinary tract, however, is not without complication with pain, bleeding and infection being the possible post-instrumentation reasons [4]. Urinary tract infection (UTI) after cystoscopic procedures has a reported incidence ranging from 2.7–35%, of which 10–16% patients can go on to develop septicaemia [4–8]. Given the risk of UTI, the use of prophylactic antibiotics prior to flexible cystoscopy (FC) has been suggested; however, supportive evidence has been inconclusive. Systematic reviews have generally concentrated on the evidence for all transurethral procedures and not specifically for FC [6, 9]. A previous systematic review summarised bacteriuria outcomes for FC among other procedures [10]. However, the review did not include two recent RCTs published after their search date and an additional large RCT that was written in Spanish [11–13]. The lack of a thorough and contemporary systemic review is reflected in the absence of robust guidelines regarding prophylactic antibiotic use. The American Urological Association states that patients should receive prophylactic antibiotics in FC only if they have significant risk factors affecting their response to surgical infections [14]. The European Urological Association does not recommend antibiotic use in standard FC, but does recommend considering antibiotics prophylaxis in high-risk patients [15].

This timely systematic review, therefore, aims to highlight the current evidence for the use of prophylactic antibiotics for FC to allow clinicians to make an informed decision regarding prophylactic antibiotic use in patients undergoing FC.

Evidence Acquisition

Search Strategy and Study Selection

The systematic review was performed according to the Cochrane guidelines. Relevant trials were obtained from the following sources: MEDLINE (1966–April 2014), EMBASE (1980–April 2014), Cochrane Central Register of Controlled Trials – CENTRAL (in The Cochrane Library – Issue 1, 2014), CINAHL (1872–April 2014), ClinicalTrials.gov and Google Scholar.

Search terms used were: cystoscopy, flexible cystoscopy, antibiotics, antimicrobials, antibiotic prophylaxis, and randomised controlled trials. MeSH terms used were (('Cystoscopy'[Mesh]) AND 'Antibiotic Prophylaxis'[Mesh]), (('Cystoscopy'[Mesh]) AND 'Antibiotic Prophylaxis'[Mesh]) AND 'Randomized Controlled Trial', (('Cystoscopy'[Mesh]) AND ('Anti-Bacterial Agents'[Mesh])).

The references of all identified studies were scrutinised to identify any further trials for inclusion. In addition, a manual search was also performed.

Randomised controlled trials comparing antibiotic prophylaxis to either a placebo or a no-antibiotic administration in order to prevent the risk of infection after FC were considered for inclusion with subsequent assessment of full papers (of the titles and abstracts). Studies in all languages were included if the data could be extracted either directly from the article or by contacting the author.

Three assessors (M.M.C., A.Z. and O.M.A.) reviewed articles independently. Data extraction was carried out using data extraction forms. Corresponding authors for the respective studies were contacted for any additional information required or missing data. Any disagreement about papers for inclusion was discussed and a consensus reached. Comparable data from each study was combined in a meta-analysis where possible.

Data Extraction and Analysis

The primary outcome was to determine whether antibiotic prophylaxis should be initiated prior to FC in the outpatient population by comparing the infection rate between the two groups: the prophylactic antibiotic administered or placebo/no antibiotic administered. The outcomes were divided into microbiologically confirmed infection, asymptomatic bacteriuria, and symptomatic bacteriuria. Bacteriuria was defined as bacteria present on microscopic examination with symptomatic bacteriuria producing symptoms of cystitis, such as dysuria and increase urinary frequency. Secondary outcomes were to identify the most common organism causing post cystoscopy infections, determination of the most effective antibiotic regime and finally the rate of hospital admissions or primary care consultations for symptoms post FC.

The data of each study were grouped into a meta-analysis. Only similar results that were pooled from the included studies were meta-analysed. For continuous data, a Mantel-Haenszel Chi-square test was used and expressed as the mean difference with 95% confidence interval (CI) and for dichotomous data. An inverse variance was used and expressed as risk ratio with 95% CI. In both cases $p < 0.05$ was considered significant.

Heterogeneity was analysed using a χ^2 test on $N - 1$ degrees of freedom, with an alpha of 0.05 used for statistical significance with the I^2 test [13]. I^2 values of 25, 50 and 75% correspond to low, medium and high levels of heterogeneity. A fixed-effect model was used unless statistically significant high heterogeneity ($I^2 > 75\%$ was considered significantly high heterogeneity) existed between

Fig. 1. Flowchart for article selection process of the review.

studies. A random-effects model was employed if heterogeneity existed.

An assessment of the methodological quality of the included studies was conducted in line with the Cochrane Handbook for Systematic Reviews of Interventions [16]. Quality assessment of selection bias, performance bias, detection bias, attrition bias, and reporting bias were assessed in each of the included studies using RevMan v.5.2.

Evidence Synthesis

Literature Search

The literature search yielded 99 studies, of which 72 were excluded due to non-relevance based on titles and 15 excluded due to non-relevance based on the abstracts (fig. 1). Full manuscripts were evaluated in 12 studies, of which 7 were included into the review [7, 11–13, 17–19]. The studies were published between 1971 and 2013, reflecting the time-tested, unanswered question of prophylactic use of antibiotics for FC.

After reading the manuscripts, we excluded 5 studies for various reasons. Lo et al. was not a randomised trial [20]. Herr's study was on the frequency of UTIs in patients with bladder cancer and after BCG treatment [21]. Alsaywid et al. and Wagenlehner et al., produced review articles [22, 23], while Hori and Kennedy's article is a commentary on one of the included studies [24].

Characteristics of Included Studies

Characteristics of each study are depicted in table 1. Seven studies were included [7, 11–13, 17–19]. All studies included participants who were for surveillance or diagnostic cystoscopy with a normal urinary tract. Those currently taking antibiotics were excluded. Six of the studies administered a single dose of antibiotic approximately one hour before FC [7, 11–13, 17, 19]. Five studies for each group reported numbers of confirmed bacteriuria on MSU [7, 11, 12, 17, 18], asymptomatic bacteriuria [11, 13, 17–19] and symptomatic bacteriuria [11–13, 17, 19]. Three studies performed questionnaire follow-up to assess urinary symptoms [11, 12, 19] and one study hospitalised patients for the duration of the study to monitor objective parameters, which was the routine practice at that time [18].

Primary Outcome Meta-Analysis

A meta-analysis was performed looking at three key outcomes; confirmed bacteriuria on MSU, asymptomatic bacteriuria and symptomatic bacteriuria. In studies where there were two treatment groups and one placebo/non-treatment group, these results are dealt with as a separate set [17, 18]. The results confirmed that prophylactic antibiotics do reduce rates of MSU-proven bacteriuria, symptomatic bacteria and asymptomatic bacteriuria in patients undergoing FC (fig. 2).

In the 'confirmed bacteriuria on MSU' group, the control arm were statistically more likely to get a positive

Table 1. Characteristics of the included trials

Author	Population control (controls completed); intervention (interventions completed)	Inclusion criteria	Exclusion criteria	Intervention	Outcome parameter	Outcome	Additional remarks
Mendoza (1971)	60: 30: 0*total 3 groups (2 different antibiotic groups)	Male patients	Severe renal impairment, active severe cystitis, known allergy to drugs used	150 mg stat dose following procedure then 4 times a day for 4 days Demeclocycline Hydrochloride or 1 g stat dose then 0.5 g daily for 3 days Sulfamethoxypyridazine. Both stat doses given after the procedure	Participants hospitalised for study duration and examined on day 1, 3, 4 post cystoscopy	No significant differences with Sulfamethoxypyridazine	In Ddemeclocycline group more cultures remained negative (20 of 22 with drug vs. 11 of 21) in patients who had other positive symptoms
Jiménez Cruz (1993)	1,087 (1,057): 1,197 (1,115)	Patients over age of 16 years with negative urine culture	Unclear	Ceftriaxone 1 g IM	Clinical and microbiological responses at 48–72 h and 4 weeks later	Symptomatic bacteriuria 10.2% in control vs. 2.5% prophylaxis	
Rané (2001)	115 (80): 124 (82)	Patients undergoing follow-up surveillance for superficial TCC	Biopsy at time of cystoscopy, indwelling catheter, specific risk of endocarditis or on antibiotics for other reason	120 mg Gentamicin IM prior to cystoscopy	MSU 5–7 days post cystoscopy ¹	Gentamicin reduced the rate of post-cystoscopy-positive MSUs from 21 to 5%	
Wilson (2005)	122: 112 (no mention of how many completed study for each group)	Patients presenting for diagnostic FC	Patients undergoing therapeutic interventions (e.g. stent removal or biopsy), those already taking antibiotics	400 mg Norfloxacin PO 20–60 min prior to cystoscopy	MSU 3–7 days post cystoscopy and telephone questionnaire to correlate symptoms of UTI	No difference in infection rates between the treatments	Interim analysis performed only due to low recruitment rate and significantly low infection rate (overall infection rate for FC 0.85%)
Johnson (2007)	830 (684): 822 (687) Ciprofloxacin: 829 (712) Trimethoprim	Patients attending for diagnostic or surveillance cystoscopy	Symptoms of a UTI, hypersensitivity to Ciprofloxacin or Trimethoprim, potential interaction with other drugs, specific indication for parenteral prophylaxis (e.g. heart valve replacement), urethral catheter or already on antibiotics	Either Trimethoprim 200 mg or Ciprofloxacin 500 mg given approx 1 h (median time 55 min) prior to cystoscopy	MSU 5 days post cystoscopy ¹	Patients on placebo were 5 times more likely to be infected after FC than before. 2.0 times more likely when on Trimethoprim and 0.46 times on Ciprofloxacin	Ciprofloxacin as a once only dose significantly reduces bacteriuria
Jiménez-Pacheco (2012)	30: 30 (no mention of how many completed the study in each group)	Patients attending for diagnostic cystoscopy aged over 18	Antibiotic administration for any reason in last month, urethral catheter, UTI history during previous month, positive culture, pregnancy, obstructive uropathy, VU reflux, anatomical malformation of the urinary tract, those at risk of endocarditis	3 g Fosfomycin Trometamol 2 h prior to cystoscopy	MSU 10 days post cystoscopy and telephone interview for symptoms UTI 1 month later ²	No statistical differences between groups for bacteria, pyuria, microhematuria	

Table 1. (continued)

Author	Population control (controls completed): intervention (interventions completed)	Inclusion criteria	Exclusion criteria	Intervention	Outcome parameter	Outcome	Additional remarks
García-Perdomo (2013)	144 (138): 141 (138)	Patients over age 18 attending outpatient cystoscopy for non-urgent indication	Allergic to antibiotics, taking other medication that might interact with antibiotic given, taking antibiotics at time of procedure, permanent urinary catheter, immunosuppression or spinal cord injury	500 mg Levofloxacin PO 30–60 min before cystoscopy	MSU at follow-up appointment 3 days post cystoscopy plus questionnaire about UTI symptoms	No significant difference in urinary infection rate	Patients in the antibiotic group had significantly less asymptomatic bacteriuria than those in placebo group

¹ Positive culture more than or equal to 10⁵ organisms/ml and more than 10 white cells/mm³.² Positive culture more than or equal to 10⁵ organisms/ml and more than 5 white cells/mm³.

MSU than the antibiotic group ($p < 0.00001$; OR: 0.36, 95% CI: 0.27–0.48). The calculated number needed to treat to avoid one positive MSU was 15.

With symptomatic bacteriuria, the control group were more likely to have symptomatic bacteriuria post FC than the antibiotic group ($p < 0.00001$; OR: 0.34, 95% CI: 0.25–0.47). The number needed to treat to prevent one episode was 26.

With the asymptomatic bacteriuria group, the control group were more likely to develop asymptomatic bacteriuria than the antibiotic group ($p < 0.00001$; OR: 0.40, 95% CI: 0.29–0.54). The number needed to treat was 32 patients to prevent one asymptomatic bacteriuria episode.

Secondary Outcomes

Antibiotic Choice. Most of the studies administered prophylactic antibiotics approximately one hour before the procedure as a single dose; however, they varied in the type and route. Oral Ciprofloxacin (500 mg), Trimethoprim (200 mg), Levofloxacin (500 mg), Norfloxacin (400 mg), Fosfomycin Trometamol (3 g) were used in different trials and showed similar results. The intramuscular route was used in two trials: Gentamicin [7] and Ceftriaxone [13]. One study administered an extended course of antibiotics, which were either oral Demeclocycline Hydrochloride (150 mg dose 4 times a day for 4 days) or Sulfamethoxypyridazine (initially 1 g, then 500 mg once daily for three days) [18].

Organisms. Organisms causing positive cultures varied in the studies. Rané et al., found *Streptococcus faecalis* to be the most common organism causing a positive culture in both their placebo and antibiotic prophylactic groups, with *Coagulase-negative staphylococcus* and *Escherichia coli* being the second and third most common, respectively. *Proteus* spp caused 1 positive culture in the placebo group [7]. Johnson, Jiménez Cruz, Wilson and García-Perdomo found *Escherichia coli* to be the most common organism, with *Klebsiella pneumonia*, *Enterococcus* and *Streptococcus* being other causes [11, 13, 17, 19]. Jimenez-Pacheco found *Serratia liquefaciens* grown in one control culture [12].

Admission to Hospital. Overall, the admission to hospital rate post FC was low (6 cases across the studies; with 3 in the treatment group and 3 in the control group. The overall rate of admission across studies was 0.12%). These numbers do not include patients from Mendoza's study who admitted all their patients to hospital as routine practice. Three people had sought primary care advice (all in the treatment group of Jiménez-Pacheco et al. study).

Fig. 2. Forest plots demonstrating the meta-analysis. Forest plots of outcomes. **a** Confirmed bacteriuria on MSU post FC; **b** asymptomatic bacteriuria; **c** symptomatic bacteriuria. OR = Odds ratio; NNT = number needed to treat; CI = confidence interval.

Fig. 2. Forest plots demonstrating the meta-analysis. Forest plots of outcomes. **d** Forest plot of subgroup analysis of symptomatic bacteriuria to assess moderate heterogeneity. CI = Confidence interval.

Fig. 2. Forest plots demonstrating the meta-analysis. Forest plots of outcomes. **e** Subgroup analysis of studies with low risk of bias. CI = Confidence interval.

Methodological Quality Assessment

All the studies were randomised controlled trials. Figure 3 depicts the summary of the quality assessment based on the reviewing author's judgement of risks of bias for each included study. There was good quality randomisation, which is described in detail in three studies [11, 13, 17]. Whereas two other studies did not comment on how they randomised their patients [18, 19]. Rané et al. allocated in accordance with consultant practice [7] giving rise to a high risk of selection bias. Two studies used IM administration of Gentamicin [7] and Ceftriaxone [13] in the antibiotic groups with no placebo, that is, no injections to the placebo group, leading to a high risk of performance bias due to unblinding of the participants and personnel. Similarly, Jiménez-Pacheco and colleagues did not give an oral placebo, which could also lead to performance bias [12]. All studies had a low risk of attrition bias; Wilson et al. [19] performed an interim analysis to avoid this form of bias. Similarly, all studies were deemed low risk for reporting bias or identification of any other sources of bias.

Discussion

Flexible cystoscopy is the most common procedure performed in the urology department. It is an essential tool in the management and surveillance of superficial bladder tumours as well as in the investigation of haema-

turia [20]. Despite the widespread use of this technique, there is no consensus regarding the prophylactic use of antibiotics prior to instrumentation [21]. We carried out this systematic review to evaluate the evidence regarding the use of prophylactic antibiotics. The review also aimed to identify the most common organism causing post cystoscopy infections and determine the most effective antibiotic regime.

Primary Outcome

The results of the meta-analysis demonstrated a statistically significant advantage of using prophylactic antibiotics to prevent infection post FC. However, the number needed to treat to prevent one episode of infection is still considerably high (32 for symptomatic UTI and 26 for asymptomatic bacteriuria).

The largest study that we reviewed (Johnson et al. [17]) had a large sample size. The patients were randomised into three arms (placebo, Trimethoprim and Ciprofloxacin). The antibiotics were given in a single oral dose one hour prior to the procedure. The main outcome of this study was to measure the rate of bacteriuria post FC and showed a reduction from 9% in the placebo arm to 5 and 3% in patients receiving Trimethoprim and Ciprofloxacin, respectively. This clearly showed a statistically significant ($p < 0.001$) benefit for giving prophylactic antibiotics to reduce bacteriuria. However, it is noted that up to 73% of the patients with positive bacteriuria were asymptomatic and therefore did not necessarily need treatment.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
García-Perdomo 2013	+	+	+	+	+	+	+
Jiménez Cruz 1993		+	−	+	+	+	
Jiménez-Pacheco 2012	+		−		+	+	+
Johnson 2007	+	+	+	+	+	+	+
Mendoza 1971					+	+	
Rané 2001	−		−	+	+	+	+
Wilson 2005				+	+	+	+

Fig. 3. Quality assessment and risk of bias summary. Review of author's judgements about each risk of bias item for each included study. The following studies are cited: García-Perdomo et al. [11], Jiménez Cruz et al. [13], Jiménez-Pacheco et al. [12], Johnson et al. [17], Mendoza et al. [18], Rané et al. [7], Wilson et al. [19].

Secondary Outcomes

Admissions to Hospital. In the largest study that showed a statistically significant effect of antibiotic prophylaxis by Johnson et al. [17], there were 2 severe infections requiring hospital admission in the Ciprofloxacin group compared to 3 in the placebo group meaning that 687 patients had to be treated to prevent one hospital admission. This clearly has high cost implications.

Across all studies, the admission to hospital for symptomatic infection was low (0.12% of our study population); however, not all studies reported on hospitalisation rates.

Rate of Infection. There is limited high quality literature in the incidence of infection post FC. In the studies analysed here, infection rates varied from 0.85% [19] to

28% [18], with most of the studies recording an incidence of <10%: 1.8% [11], 9% [17]. However, it is pertinent to mention that patients who develop post-cystoscopy infection are likely to be treated by their general practitioner (GP); therefore, the incidence could be much higher than this. This perhaps explains why Mendoza and colleagues document a higher infection rate than the other studies in this review; this was the only study that admitted patients to the ward to monitor for post-FC infection, ensuring no patients were lost to follow-up or reported to another source for urinary infection treatment. Therefore, post FC infection rates could be more accurate in Mendoza's study compared to the others analysed in this review.

Jiménez-Pacheco et al. [12] tried to eliminate this problem by asking patients whether they had consulted their GP in the telephone interview conducted 1 month post FC. They found 3 patients (10%) of their treatment group had attended the GP for UTI symptoms ($p < 0.182$) and none of the participants had attended the GP in the control group. However, similar to hospital admission reporting rates, not all studies looked at GP consultation as an outcome so we cannot conclude GP referral rate post FC.

Due to the nature of FC being performed on outpatients, and therefore the relatively high number of patients lost to follow-up in the studies analysed, it is not possible to conclude whether the infection rates mentioned above are accurate. However, most of the studies suggest an infection rate of <10% showing that infection post FC affects a small minority of patients.

Causative Organisms. *Escherichia coli* was the main organism causing UTIs in 4 studies [11, 12, 17, 19] whereas *Streptococcus faecalis* was found to be the most common cause in one study [7]. This study included patients who had previous endoscopic surgery to treat bladder tumours and were on cystoscopic surveillance. The studies analysed here could not agree on the organism most commonly causing infection post FC.

Antibiotic Choice. Different types of antibiotics were used in the studies, which could relate to the local guidelines or antibiotics efficacy in the area. García-Perdomo conducted a randomised trial using a single dose of Levofloxacin 500 mg without any statistically significant benefit [11]. Intramuscular Gentamicin was used in another study [7] and showed benefit in reducing the rate of positive urine culture following FC. All of the patients in this study were on follow-up surveillance for bladder cancer and the total rate of infection in this study was higher when compared to other studies which could exaggerate the effect of antibiotics. Jiménez-Pacheco et al. used 3 g of

Fosfomycin and did not find it clinically beneficial in a small cohort [12]. Norfloxacin was used in a study with a very low total infection rate (0.85%) [19].

The current EAU guidelines recommend the use of Trimethoprim for high-risk patients undergoing urodynamic or cystoscopy [15]. However, there are no specific criteria set out to place the patient as high risk.

Cost Analysis. None of the studies conducted a cost analysis of the antibiotic use. However, it is safe to ascertain that with the multitude of patients undergoing diagnostic and check flexible cystoscopies monthly and yearly, the cost will no doubt increase.

Resistance. There are concerns that the increased use of prophylactic antibiotics could lead to increased bacterial resistance [6, 15]. The rate of antibiotic resistance varies between different areas with some countries reporting increased resistance to Trimethoprim or Ciprofloxacin [15]. Therefore, the introduction of prophylactic antibiotics before FC should be supported by a significant clinical benefit to justify the risk of developing resistance. The analysis shows that the rate of infection post FC is generally low and the number needed to prevent one symptomatic infection is high. This is similar to the number needed to prevent an infection following any urethral instrumentation including TUR procedures [6]. One could argue that the use of antibiotics before such procedures is routine in most centres. On the other hand, the use of antibiotics for FC, which is a much more common procedure, will have a significant effect on the antibiotics resistance rates as well as cost effectiveness implications.

Overall, the studies included in this review have failed to agree on the most common causative organism for infection post-FC and therefore, it would be difficult to conclude which antibiotic would be the most effective in prophylaxis for FC due to the range of sensitivities with each organism. Taking resistance concerns into account, clinicians are advised to refer to the local protocol, susceptibility patterns and patient choice when making their decision about antibiotic usage.

Side Effects of Antibiotics. García-Perdomo et al. [11] reported side effects to Levofloxacin of nausea (0.7%) and pruritis (0.7%). Most of the other studies did not mention side effects to the antibiotics given and we can assume there were no significant reactions observed. No studies admitted patients to hospital due to an anaphylaxis or severe reaction to any of the antibiotics. It is likely that the side-effect rate is very low across all studies due to the once-only dose of antibiotics given. In Mendoza's study, where an extended course of antibiotics was administered, one patient had an allergy to Sulfamethoxypyridazine [18].

Pre-Procedure Urinalysis. Patients were not stratified into groups according to their indication for FC, as it was considered that all of them are undergoing the same procedure. All studies performed urinalysis on patients prior to FC. However, the rate of patients who had positive urine dipstick or bacteriuria prior to FC was not provided in most of the studies. Most studies did exclude patients with positive cultures prior to FC [7, 11, 12, 13]. Two studies did not exclude patients with a positive MSU prior to FC [18, 19], but they did deal with these patients separately in the analysis. Johnson et al. [17] excluded those with symptoms of a UTI but used discordant pairs to adjust for confirmed bacteriuria pre-FC. This data showed the ratio of 5, 2 and 0.46 in the placebo, Trimethoprim and Ciprofloxacin respectively (ratio being defined as baseline presence of bacteriuria: post-FC bacteriuria presence). This shows that a once-only dose of either antibiotic can reduce some preexisting bacteriuria.

Strengths and Limitations of Review

This review was conducted in accordance with Cochrane guidelines in addition to following the PRISMA statement. Its methodology ensured a high degree of impartiality leading to an unbiased analysis of the results. Nonetheless, it is limited by the fact that three of the studies included had a high risk of bias in their methodology. However, when a subgroup analysis was conducted removing these studies with a high risk of bias, the final outcome was not altered (fig. 2). Furthermore, there was low to moderate heterogeneity throughout the analysis results, which is acceptable. However to ensure robustness of the results, the meta-analysis of the symptomatic bacteriuria group was borderline moderate to high at 70%. Therefore, we conducted a subgroup analysis to identify potential causes. Removing the two studies with a high risk of bias due to unblinding brought down the heterogeneity to 0% (fig. 2). In addition, removing the data of Jiménez-Pacheco et al., reduced the heterogeneity as well. This could be attributed to the fact that they included a low number of patient cohort as compared to the other studies, which is reflective on their final results.

Conclusion

Despite the evidence that prophylactic antibiotics statistically reduces the incidence of UTI post FC, the clinical benefit is less significant reflected by the high numbers to treat to prevent an infection. The incidence of UTI post FC is low and the number need to treat to prevent one

infection is high. There are concerns about resistance to antibiotics in addition to cost effectiveness issues which need to be further looked into. Nonetheless, the routine use of prophylactic antibiotics before FC cannot be justified based on the current evidence provided.

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