

QUESTION

Should prophylactic antibiotics vs. not using prophylactic antibiotics be used for people presenting with recurrent UTI with Friedreich ataxia?

POPULATION:	people presenting with recurrent UTI with Friedreich ataxia
INTERVENTION:	prophylactic antibiotics
COMPARISON:	not using prophylactic antibiotics
MAIN OUTCOMES:	UTI symptoms; Hospitalisations; Accurate diagnosis; Presence of UTI;

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>Lad and colleagues (2017) found that 80% of individuals with Friedreich ataxia over the age of 16 years report lower urinary tract (LUT) symptoms, which can be associated with urinary tract infections (UTIs). Risk factors for UTI, including neurogenic bladder (Lad et al 2017) and diabetes mellitus (Cnop et al 2013), have an increased prevalence in individuals with FRDA compared with the general population.</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of fever, chest infections and UTIs.</p> <p>4/6 indicated that the problem was serious, 1/6 indicated probably not serious, 1/6 indicated they didn't know if serious.</p> <p>4/6 indicated that the problem was urgent, 1/6 indicated probably not urgent, 1/6 indicated they didn't know if urgent.</p> <p>4/6 indicated that the problem was a priority, 1/6 indicated probably a priority, 1/6 indicated they didn't know if a priority. (Aug 2020)</p>

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input checked="" type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>A search of four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 14 December 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	<p>Recurrent infections may lead to residual kidney damage and therefore should be managed.</p> <p>Any consideration of prophylactic antibiotics should only be made after review by urologists with an interest in the field and after additional considerations (see below).</p>

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know 	<p>A search of four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 14 December 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	<p>Due to potential antibiotic resistance and possible gastrointestinal effects, non-antibiotic agents, behavioural and hygiene methods should be recommended first.</p>

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ○ Low ○ Moderate ○ High ● No included studies 	<p>No published research.</p>	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS									
<ul style="list-style-type: none"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability 	<table border="1"> <thead> <tr> <th>Outcomes</th> <th>Importance</th> <th>Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>UTI symptoms - not measured</td> <td>CRITICAL^a</td> <td>-</td> </tr> <tr> <td>Hospitalisations - not measured</td> <td>IMPORTANT^b</td> <td>-</td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	UTI symptoms - not measured	CRITICAL ^a	-	Hospitalisations - not measured	IMPORTANT ^b	-	
Outcomes	Importance	Certainty of the evidence (GRADE)									
UTI symptoms - not measured	CRITICAL ^a	-									
Hospitalisations - not measured	IMPORTANT ^b	-									

	<table border="1"> <tr> <td>Accurate diagnosis - not measured</td> <td>CRITICAL^a</td> <td>-</td> </tr> <tr> <td>Presence of UTI - not measured</td> <td>CRITICAL^a</td> <td>-</td> </tr> </table>	Accurate diagnosis - not measured	CRITICAL ^a	-	Presence of UTI - not measured	CRITICAL ^a	-	
Accurate diagnosis - not measured	CRITICAL ^a	-						
Presence of UTI - not measured	CRITICAL ^a	-						
	<p>a. Identified as critical by expert authors on this topic. b. Identified as important by expert authors on this topic.</p>							

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	No published research.	Management with prophylactic antibiotics for recurrent UTI in individuals with FRDA should be no different to care of individuals without FRDA.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input checked="" type="radio"/> Don't know	No published research.	

SUMMARY OF JUDGEMENTS

JUDGEMENT

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ●	Strong recommendation for the intervention ○
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CONCLUSIONS

Recommendation

We suggest use of non-antibiotic agents, and if unsuccessful, antibiotic prophylactic agents over no antibiotic prophylaxis for the management of recurrent urinary tract infections (UTIs) in individuals with Friedreich ataxia.

Justification

There should be no fundamental difference in the treatment of recurrent UTIs in individuals with FRDA as compared to individuals without FRDA. Recurrent UTIs may lead to residual kidney damage and therefore should be managed. Due to potential for antibiotic resistance, non-antibiotic treatment could be tried first, but if unsuccessful, prophylactic antibiotics are warranted after discussion with expert urologists.

Subgroup considerations

This recommendation is for individuals with Friedreich ataxia and recurrent UTIs. Individuals who are pregnant and presenting with recurrent UTIs should be referred to obstetrics for UTI management.

Research priorities

Future research examining the frequency of presentations of individuals with FRDA with UTIs, alongside its treatment and prevention strategies and outcomes, would strengthen any recommendations.

References

Lad M, Parkinson MH, Rai M, Pandolfo M, Bogdanova-Mihaylova P, Walsh RA, et al. Urinary, bowel and sexual symptoms in a cohort of patients with Friedreich's ataxia. *Orphanet J Rare Dis.* 2017;12(1):158.

Cnop M, Mulder H, Igoillo-Estevé M. Diabetes in Friedreich ataxia. *J Neurochem.* 2013;126 Suppl 1:94-102.