

QUESTION

Should medications vs. conservative therapy be used for optic neuropathy in Friedreich ataxia?	
POPULATION:	optic neuropathy in Friedreich ataxia
INTERVENTION:	medications
COMPARISON:	conservative therapy
MAIN OUTCOMES:	Visual acuity; Side effects;
BACKGROUND:	

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 type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>Reetz et al (2018) reported 90.1% of individuals with FRDA (cohort n=650) present with abnormal eye movements whereas 3.1% develop blindness/low vision.</p> <p>Studies have shown a significant number of people with FRDA have thinning of the retinal nerve fiber layer (Seyer et al, 2013; Fortuna et al, 2009) although this is not always reflected in overt visual dysfunction.</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the topic.</p> <p>2/7 indicated vision disturbance was probably serious, 4/7 indicated vision disturbance was serious, 1/7 indicated didn't know if serious.</p> <p>3/7 indicated vision disturbance was probably urgent, 3/7 indicated probably urgent, 1/7 indicated didn't know if urgent.</p> <p>3/7 indicated vision disturbance was probably a priority, 3/7 indicated priority, 1/7 indicated 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 type="radio"/> Large <input type="radio"/> Varies <input checked="" type="radio"/> Don't know 	<p>A search of three databases (CENTRAL, MEDLINE, EMBASE) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 03 July 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</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 three databases (CENTRAL, MEDLINE, EMBASE) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 03 July 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</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 evidence.</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" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 33%;">Outcomes</th> <th style="width: 33%;">Importance</th> <th style="width: 33%;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Visual acuity - not measured</td> <td>IMPORTANT^a</td> <td style="text-align: center;">-</td> </tr> <tr> <td>Side effects - not measured</td> <td>IMPORTANT^a</td> <td style="text-align: center;">-</td> </tr> </tbody> </table> <p>a. Identified as critical (2/6), important (3/6) and requiring more information</p>	Outcomes	Importance	Certainty of the evidence (GRADE)	Visual acuity - not measured	IMPORTANT ^a	-	Side effects - not measured	IMPORTANT ^a	-	
Outcomes	Importance	Certainty of the evidence (GRADE)									
Visual acuity - not measured	IMPORTANT ^a	-									
Side effects - not measured	IMPORTANT ^a	-									

	(1/6) by people with FA and critical by expert authors on the topic.	
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Balance of effects

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <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 type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input checked="" type="radio"/> Don't know 	No published evidence.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input type="radio"/> Yes <input checked="" type="radio"/> Varies <input type="radio"/> Don't know 	No published evidence.	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were asked if the intervention was acceptable (weighing up the balance between benefits, harms and costs).</p> <p>1/5 indicated medications for optic neuropathy in FA were probably reasonable, 2/5 indicated reasonable, 1/5 indicated more information on benefits and potential harms required, 1/5 indicated didn't know if reasonable. (Aug 2020).</p>

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	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

JUDGEMENT							
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 standard treatments for optic neuropathy be used as appropriate in individuals with Friedreich ataxia. There is insufficient evidence to recommend the use of medications over conservative therapy for optic neuropathy in individuals with Friedreich ataxia.

Justification

There are no published studies supporting the use of medications in the management of optic neuropathy in Friedreich ataxia.

Subgroup considerations

This recommendation is for individuals with Friedreich ataxia with optic neuropathy.

Research priorities

References

Fortuna F, Barboni P, Liguori R, Valentino ML, Savini G, Gellera C, et al. Visual system involvement in patients with Friedreich's ataxia. *Brain*. 2009;132(Pt 1):116-23.

Reetz K, Dogan I, Hohenfeld C, Didszun C, Giunti P, Mariotti C, et al. Nonataxia symptoms in Friedreich Ataxia: Report from the Registry of the European Friedreich's Ataxia Consortium for Translational Studies (EFACTS). *Neurology*. 2018;91(10):e917-e30.

Seyer LA, Galetta K, Wilson J, Sakai R, Perlman S, Mathews K, et al. Analysis of the visual system in Friedreich ataxia. *J Neurol*. 2013;260(9):2362-9.