

QUESTION

Should monitoring at diagnosis vs. monitoring at later stages be used for restrictive lung disease for people with Friedreich ataxia?

POPULATION:	restrictive lung disease for people with Friedreich ataxia
INTERVENTION:	monitoring at diagnosis
COMPARISON:	monitoring at later stages
MAIN OUTCOMES:	Non-restorative sleep; Dyspnea, orthopnea; Quality of night time sleep; Blood gas parameters; Excessive daytime sleepiness, fatigue;

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>There is a single case report (Botez et al, 1997) documenting a patient with severe FA and "arduous" breathing and O2 desaturation together with sleep disordered breathing (SDB) at night. In a study of 21 FA patients with abnormal scores on Epworth Sleepiness Scale (Corben et al, 2013), 17 had obstructive sleep apnea (SDB). Preliminary data collected by one of the authors indicates decline in respiratory volumes in severe FA and also impaired cough mechanisms. Also, in a web-based survey of FA patients presented at IARC (Patterson et al, 2018), 16.5% FA patients reported sleep apnea, correlated with higher age, longer duration and higher functional stage.</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of pulmonary function.</p> <p>6/7 indicated that the problem was serious, 1/7 indicated they didn't know if serious.</p> <p>6/7 indicated that the problem was urgent, 1/7 indicated they didn't know if urgent.</p> <p>6/7 indicated that the problem was a priority, 1/7 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 type="radio"/> Large <input type="radio"/> Varies <input checked="" 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 28 October 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 four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 28 October 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	
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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>	<p>Preliminary data collected by one of the authors indicates decline in respiratory volumes in severe FA and also impaired cough mechanisms.</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="text-align: center;">Outcomes</th> <th style="text-align: center;">Importance</th> <th style="text-align: center;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">Non-restorative sleep - not measured</td> <td style="text-align: center;">IMPORTANT^a</td> <td style="text-align: center;">-</td> </tr> <tr> <td style="text-align: center;">Dyspnea, orthopnea - not measured</td> <td style="text-align: center;">CRITICAL^b</td> <td style="text-align: center;">-</td> </tr> <tr> <td style="text-align: center;">Quality of night time sleep - not measured</td> <td style="text-align: center;">IMPORTANT^c</td> <td style="text-align: center;">-</td> </tr> <tr> <td style="text-align: center;">Blood gas parameters - not measured</td> <td style="text-align: center;">IMPORTANT^d</td> <td style="text-align: center;">-</td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	Non-restorative sleep - not measured	IMPORTANT ^a	-	Dyspnea, orthopnea - not measured	CRITICAL ^b	-	Quality of night time sleep - not measured	IMPORTANT ^c	-	Blood gas parameters - not measured	IMPORTANT ^d	-	
Outcomes	Importance	Certainty of the evidence (GRADE)															
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Quality of night time sleep - not measured	IMPORTANT ^c	-															
Blood gas parameters - not measured	IMPORTANT ^d	-															

	Excessive daytime sleepiness, fatigue - not measured	IMPORTANT ^e	-	
<ul style="list-style-type: none"> a. Identified as critical (2/6) and important (4/6) by people with FA and important by experts on this topic. b. Identified as critical (3/6), important (1/6) and low importance (2/6) by people with FA and critical by experts on this topic. c. Identified as critical (2/5), important (2/5), and low importance (1/5) by people with FA and important by experts on this topic. d. Identified as critical (1/6), important (4/6) and low importance (1/6) by people with FA and critical by experts on this topic. e. Identified as important (4/6) and low importance (2/6) by people with FA 				

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 checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input 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 monitoring in people with restrictive lung disease was acceptable (weighing up the balance between benefits, harms and costs).</p> <p>2/3 indicated the intervention was acceptable, 1/3 indicated probably acceptable. (Aug 2020).</p>

SUMMARY OF JUDGEMENTS

	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 <input type="radio"/>	Conditional recommendation against the intervention <input checked="" type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

We conditionally recommend *against* monitoring for restrictive lung disease and sleep disordered breathing at diagnosis of Friedreich ataxia rather than at later stages of the disease, as there is no evidence that this would be of benefit.

Justification

There are no published data on prevalence of abnormal respiratory muscle function in FRDA. Unpublished data indicates that restrictive lung disease and impaired cough can occur in later stages of the disease. There is no clear evidence of the effect of monitoring for restrictive lung disease/SDB/sleep apnea at diagnosis compared to later in the disease, on abnormal lung volumes; impaired airway clearance; excessive daytime sleepiness, or fatigue in individuals with FRDA. Monitoring could be done in later stages of FRDA.

Subgroup considerations

Individuals who are later in the progression of Friedreich ataxia are more likely to experience restrictive lung disease.

Research priorities

Confirming the incidence and establishing the benefits of monitoring for restrictive lung disease/SDB/sleep apnea at diagnosis in people with FRDA is required.

References

Botez MI, Mayer P, Bellemare F, Couture J. Can we treat respiratory failure in Friedreich ataxia? *Archives of Neurology*. 1997;54(8):1030-3.

Corben LA, Ho M, Copland J, Tai G, Delatycki MB. Increased prevalence of sleep-disordered breathing in Friedreich ataxia. *Neurology*. 2013;81(1):46-51.

Patterson A, Almeida L, Monari E, et al. Sleep and fatigue in Friedreich ataxia. IARC Meeting; Pisa, Italy 2018.