

Online supplementary Table S10b

QUESTION

Can measuring total serum IgE help diagnose asthma in adults with episodic/chronic suggestive symptoms?

POPULATION:	Population of adults (>18 yrs old) with diagnostic uncertainty of asthma
INTERVENTION:	Total serum IgE test
GOLD STANDARD :	1. Peak flow variability > 20% or spontaneous variation in FEV ₁ > 12%- and 200-ml between several clinic visits 2. Bronchodilation > 12% AND > 200 ml improvement 3. Airway hyperresponsiveness: PC20 < 16 mg/ml (or 8 mg/ml) of Methacholine (or Histamine) or PD mannitol < 625 mg or fall in FEV ₁ > 10% after exercise 4. Improvement in FEV ₁ > 12% and 200 ml after a 2-week course of OCS or a 4-week course of ICS

ASSESSMENT

Test accuracy

How accurate is the test?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Very inaccurate <input checked="" type="radio"/> Inaccurate <input type="radio"/> Accurate <input type="radio"/> Very accurate <input type="radio"/> Varies <input type="radio"/> Don't know	Low test sensitivity (ranging from 0.33 to 0.51) Greater specificity (ranging from 0.72 to 0.85) One study (Nekoe et al) provided the 95% specificity at 584 Ku/L	Two large studies (one prospective from primary care and one retrospective from secondary care) providing similar AUC. AUC around 0,6. Thresholds ranging from 90 to 132 Ku/L (Tilemann et al ; Nekoe et al)

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input type="radio"/> Small <input checked="" type="radio"/> Moderate	Total serum IgE might be useful to endotype asthma and establish eligibility to biological treatment in severe forms of the disease.	

<ul style="list-style-type: none"> ○ Large ○ Varies ○ Don't know 	An elevated level should prompt detailed investigation towards specific allergy	
---	---	--

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large ○ Moderate ○ Small X Trivial ○ Varies ○ Don't know 	No major undesirable effects. Pain and concerns related to venepuncture. Potential impact of other allergic comorbidities on test results.	

Certainty of the evidence of test accuracy

What is the overall certainty of the evidence of test accuracy?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low X Low ○ Moderate ○ High ○ No included studies 	Few observational studies. No RCT	

Certainty of the evidence of management's effects

What is the overall certainty of the evidence of effects of the management that is guided by the test results?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low X Low ○ Moderate ○ High ○ No included studies 	High total serum IgE suggests but not proves atopy, a condition often associated with asthma. The presence of atopy may drive some aspect of the treatment (allergen avoidance, immunotherapy, anti-IgE)	

Certainty of the evidence of test result/management

How certain is the link between test results and management decisions?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Very low<input checked="" type="radio"/> Low<input type="radio"/> Moderate<input type="radio"/> High<input type="radio"/> No included studies		

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 checked="" 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 type="radio"/> Don't know	<p>Serum IgE has an insufficient sensitivity to diagnose asthma</p> <p>As a marker of airway inflammation FeNO offers a better alternative allowing for immediate results and, overall, slightly greater statistical performance</p> <p>Bronchial challenge tests show better PPV and NPV</p>	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"><input type="radio"/> Large costs<input type="radio"/> Moderate costs<input checked="" type="radio"/> Negligible costs and savings<input type="radio"/> Moderate savings<input type="radio"/> Large savings<input type="radio"/> Varies<input type="radio"/> Don't know	<p>Non-expensive and easy to perform and to read test</p>	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Reduced <input type="radio"/> Probably reduced <input checked="" type="radio"/> Probably no impact <input type="radio"/> Probably increased <input type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know		
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<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		
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<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	Non-expensive and easy to perform and to read test	

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention ●	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"/>
---	--	---	--	---

CONCLUSIONS

Recommendation

The TF suggests not measuring total serum IgE for asthma diagnosis (Conditional recommendation, low quality of evidence)

Total serum IgE does not define asthma but rather contributes to phenotyping

Justification

Total serum IgE should not be used for the diagnosis of asthma because of consistently poor sensitivities across the studies, reaching at best 51%. This is in line with the existence of a significant proportion of non IgE-mediated asthma, also called “intrinsic” asthma. Measuring total serum IgE does not provide immediate results at the time of the consultation. If specificity is better than sensitivity it remains limited at the cut-offs provided by the ROC curves, ranging from 39% to 85%. The value of measuring IgE may vary according to the population of patients investigated, the seasonal manifestations of the symptoms, the coexistence of allergic rhinitis and is likely to be more valid in young patients as IgE levels decline with age.