Statin Intolerance Panel

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Charles Peirce (1839-1914)
Founder of Pragmatism
(1) Does statin intolerance exist?

ANSWER: Yes.

STRENGTH OF RECOMMENDATION: A (Strong)

QUALITY OF EVIDENCE: Moderate
In the individual case, statin intolerance is defined as adverse symptoms or objective findings attributed by the patient (or provider) to the statin and in most cases perceived by the patient to interfere unacceptably with activities of daily living, leading to a decision to stop or reduce statin therapy.
Statin Intolerance – 2\textsuperscript{nd} definition

For an aggregate population, statin intolerance is defined as clinical or laboratory adverse experiences linked to statin treatment by validated clinical evidence and presenting with pain, impairment, or risk, which justifies statin cessation or dose reduction.
(2) Are statins generally well tolerated and safe?

ANSWER: Yes.

STRENGTH OF RECOMMENDATION: A (Strong)
QUALITY OF EVIDENCE: High

From clinical trials (27 RCTS, 175,000 patients) and observational data, the benefit from statins in appropriate patient groups is to avoid several hundred to perhaps more than a thousand deaths from ASCVD for every death from statin-associated rhabdomyolysis.
(3) Do large randomized trials provide reliable estimates of statin intolerance? 

ANSWER: No. 

STRENGTH OF RECOMMENDATION: E (Expert Opinion) 

QUALITY OF EVIDENCE: Low
Statin Intolerance in Randomized Trials

• In HPS, no significant difference in muscle symptoms.
• This has been interpreted to mean that muscle adverse effects were “undetectable.”
• The only RCT showing a difference – STOMP 2013.
• In observational data, PRIMO 10.5%, USAGE 29%.
• Problems in RCTs prior to STOMP
  – Avoidance of participation by certain patients.
  – Dropout during run-in phase.
  – Lack of active monitoring.
(4) Is statin intolerance best defined in the context of patient-centered medicine?

ANSWER: Yes.

STRENGTH OF RECOMMENDATION: E (Expert Opinion)

QUALITY OF EVIDENCE: Not Applicable
Patient-centered medicine – 2 parallel agendas

Figure 1 The patient-centred clinical method
(5) Should the clinician sometimes advise patients to continue statin therapy even when some degree of statin intolerance is present?

ANSWER: Yes.

STRENGTH OF RECOMMENDATION: B
(Moderate)
QUALITY OF EVIDENCE: Low
Tolerance versus Diagnosis

The decision for or against continuing to take a statin can be simplified by casting it as a question of tolerance (i.e., how bothersome are the symptoms?) rather than a question of diagnosis (i.e., are the symptoms really due to the statin?).
(6) Are recommendations for widespread use of statins to prevent atherosclerotic cardio-vascular disease appropriate, given the emerging evidence with regard to statin intolerance?

ANSWER: Yes.

STRENGTH OF RECOMMENDATION: A (Strong)

QUALITY OF EVIDENCE: High
27 randomized controlled trials

175,000 patients in RCTs
(7) Are there clinical trial designs that may reliably address questions of statin intolerance?

ANSWER: Yes.

STRENGTH OF RECOMMENDATION: E (Expert Opinion)

QUALITY OF EVIDENCE: Not Applicable
Parallel Group design

Time
Crossover design

Patient #1
Patient #2
Patient #3
Patient #4
Patient #5
Patient #6
Crossover design with variable time-of-onset
Inability to tolerate at least 2 statins: one at the lowest starting daily dose AND another at any daily dose, due to either objectionable symptoms (real or perceived) or abnormal lab determinations, which are temporally related to statin treatment and reversible upon statin discontinuation, but reproducible by re-challenge with other known determinants being excluded.
Summary and Take-Home Message

Managing statin intolerance requires a pragmatic approach that includes principles of patient-centered medicine as well as new methods for gaining scientific evidence about this commonly encountered clinical problem.