REAL-WORLD IDENTIFICATION OF EUROPEAN PATIENTS WITH STATIN-ASSOCIATED SYMPTOMS: CLINICAL PRACTICE COMPARED WITH CLINICAL GUIDELINES

G Kees Hovingh,1 Shravanthi R Gandra,2 Jan McKendrick,3 Ricardo Dent,2 Alberico L Catapano,4 Paul Oh,5 Robert S Rosenson,6 Erik S Stroes1

1Academic Medical Center, Amsterdam, the Netherlands; 2Amgen Inc., Thousand Oaks, California, USA; 3PRMA Consulting, Fleet, Hampshire, UK; 4University of Milan, Milan, Italy; IRCCS Multimedia, Milan, Italy; 5Toronto Rehabilitation Institute, Toronto, Ontario, Canada; 6Mount Sinai School of Medicine, New York, New York, USA

BACKGROUND

- Statins are the most frequently used first-line therapy for hypercholesterolemia.
- Statins are well tolerated by most patients and serious adverse events are rare in controlled clinical trials; however, some patients experience side-effects and develop statin-associated symptoms (SAS).

SAS can include muscle-related symptoms (MRS), which lead to discontinuation of therapy in 5–20% of patients; other side-effects occur in 1–2% of patients (e.g., gastric symptoms, persistent elevation in transaminases).1,2

- In 2014, we conducted a web-based survey to understand how doctors identify and manage patients with SAS in clinical practice. At the time of the study, clinical guidelines did not provide detailed criteria for the diagnosis of SAS. A consensus statement on this topic has since been published by the European Atherosclerosis Society.3

OBJECTIVE

- In this analysis, we compared results from European participants in our survey with published guidelines, to assess how real-world practice aligns with the latest clinical consensus.

METHODS

- The European component of this web-based survey included clinicians in France, Germany, Italy, the Netherlands, Poland, Spain, Sweden, and the UK. The survey was conducted in February–March 2014.
- Sixty clinicians were recruited in each country with pre-specified quotas to ensure representation from different regions. Two-thirds of clinicians were specialists consultants (from here on referred to as specialists) and the remaining third were general/family physicians (GPs).
- All clinicians were required to have: at least 2 years’ experience in their current clinical role, treated at least 75 patients (specialists) or 50 patients (GPs) with hypercholesterolemia in the previous 12 months, treated at least 5 patients with SAS in the previous 12 months.
- All participants provided informed consent.
- Ethics approval was obtained from the Human Research Ethics Committee of the University of Technology, Sydney, Australia.
- The survey was developed in collaboration with clinical advisors, and included questions about diagnostic criteria, the estimated number of patients diagnosed with SAS, and clinicians’ choice of treatment for patients with SAS, based on their clinical experience.
- The methodology for developing the questionnaire and conducting the survey is summarized in Table 1.

RESULTS

- The criteria for identifying patients in real-world practice reported by the participants were compared with those recommended in the 2015 European Atherosclerosis Society (EASCPS) Consensus Panel Statement (EASCP5) on statin-associated muscle symptoms, in order to assess their alignment.

Table 1  Study overview

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Pilot phase</th>
<th>Main phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Literature review</td>
<td>Online questionnaire reviewed</td>
<td>Statistical analysis</td>
</tr>
<tr>
<td>Draft questionnaire reviewed</td>
<td>Online survey completed (June 2014) by three clinicians from each country, followed by a telephone interview</td>
<td>Plan developed before conducting the survey</td>
</tr>
<tr>
<td>Questionnaire validated through interviews with clinicians</td>
<td></td>
<td>Online survey conducted (Feb–March 2014) with 60 clinicians from each country</td>
</tr>
<tr>
<td>Ethics approval from the University of Technology, Sydney</td>
<td></td>
<td>Statistical analysis of the results</td>
</tr>
<tr>
<td></td>
<td>Survey translated into relevant languages and online version programmed</td>
<td></td>
</tr>
</tbody>
</table>

- Baseline demographics: A total of 480 clinicians (161 GPs and 319 specialists) from Europe completed the survey; the majority of clinicians were specialists (65%); the remaining third were general/family physicians (35%).

- Most clinicians (average 74%, range 63–85%) reported rechallenging patients with the same statin to confirm whether MRS were SAS (Figure 4).

- An average of 61% of clinicians (range 50–67%) reported discontinuing the statin to test whether MRS resolved.

- Overall, an average of 38% of clinicians (range 22–45%) reported using a combination of rechallenging, discontinuing, and decreasing the dose of statin to confirm SAS.

- A small number of clinicians (15%, 3%) selected none of these three options as part of their minimum criteria for establishing SAS.

- The majority of clinicians (average of 82%, range 73–99%) required known elevated CK levels to decrease after modifying or stopping a statin in order to establish SAS (Figure 5).

CONCLUSIONS

- Our survey establishes that clinicians are familiar with SAS; however, in the absence of clear clinical guidance, they developed individual practices to identify affected patients.

- The reported clinical criteria used to identify patients with SAS across eight European countries are broadly consistent with the current clinical consensus in Europe.4

- Based on clinicians’ responses and individual criteria for diagnosis, the estimated proportion of patients with SAS in this study (average 5%) is consistent with the range of 5–10% reported in literature.5

REFERENCES


Figure 1 Proportion of clinicians who reported observing MRS that may indicate SAS in patients prescribed statins.

Figure 2 Reasons for creatine kinase testing in patients newly prescribed statins.

Figure 3 Proportion of clinicians who reported using ≥2 or ≥3 statins before considering a patient with MRS to have SAS.

Figure 4 Proportion of clinicians who rechallenge as a minimum requirement to confirm SAS.

Figure 5 Proportion of clinicians who require a demonstrated association between CK level and statins before considering a patient with MRS to have SAS.