



# Rhabdomyolysis and statins: an analysis of spontaneous case reports using a three-dimensional classification scheme



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## Introduction

- In order to obtain a complete analysis of an adverse drug reaction (ADR) it is necessary to understand the major features that relate to (a) the drug that causes the reaction, (b) the reaction itself, and (c) the patients in whom it is most likely to occur
- A three-dimensional classification of ADRs according to dose-relation, time-course, and susceptibility factors (DoTS) has been proposed <sup>(1)</sup>

## Aim of Study

- To investigate how the DoTS classification scheme might be used to interpret and classify an ADR, using rhabdomyolysis and statins as an example

## Methods

- We searched the Canadian Adverse Drug Reaction Monitoring Program (CADRMP) Adverse Reaction Database <sup>(2)</sup> (1965 to 2006) for spontaneous reports with statins using the search terms: rosuvastatin, Crestor<sup>®</sup>, simvastatin, Zocor<sup>®</sup>, atorvastatin, Lipitor<sup>®</sup>, fluvastatin, Lescol<sup>®</sup>, lovastatin, Mevacor<sup>®</sup>, Altacor<sup>®</sup>, pravastatin, Pravachol<sup>®</sup>, cerivastatin, or Baycol<sup>®</sup>
- We reviewed suspected ADRs to any statin to identify reports of rhabdomyolysis
- Data were abstracted onto a data sheet for (1) dose; (2) time; and (3) any susceptibility factors such as gender, age, and concomitant medications
- Dose data were normalized to a daily dose of simvastatin 20 mg <sup>(3)</sup>
  - simvastatin 20 mg  $\equiv$  atorvastatin 10 mg  $\equiv$  rosuvastatin 5 mg  $\equiv$  pravastatin 40 mg  $\equiv$  lovastatin 40 mg

## Results

- We identified 205 cases of reports of rhabdomyolysis with statins
- Atorvastatin was the most commonly cited statin (79/205 reports)

Table 1 – Number of reports of rhabdomyolysis with statins

Statin	No. of case reports
atorvastatin	79
cerivastatin	74
rosuvastatin	24
simvastatin	14
lovastatin	8
pravastatin	6

## Dose

- Information on statin dose was available from 163 reports
- Rhabdomyolysis occurred at both high and low doses
- Only 12 cases developed rhabdomyolysis at less than the dose equivalent of 20 mg daily

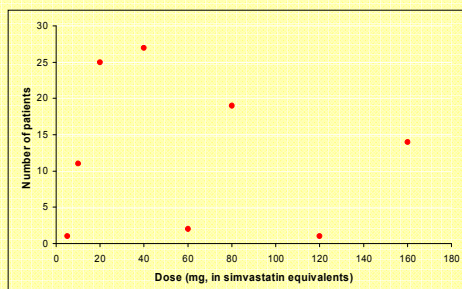


Figure 1 – Dose relationship of statins to number of patients with rhabdomyolysis. One patient on 60 mg rosuvastatin ( $\equiv$ 240 mg simvastatin) and patients on cerivastatin are not shown on the graph.

## Time

- 55% (112/205) of the reports provided data on the time from statin initiation to adverse reaction
- Although rhabdomyolysis occurred at various times following statin initiation, it occurred most frequently after several months of therapy

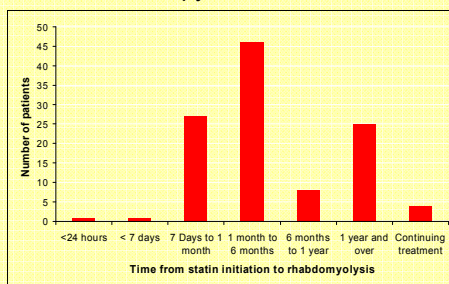


Figure 2 – Duration of statin therapy prior to rhabdomyolysis

## Dose and time

- Only 61 reports contained data on both dose and time
- Patients receiving low doses of statin were susceptible to developing rhabdomyolysis early on during treatment

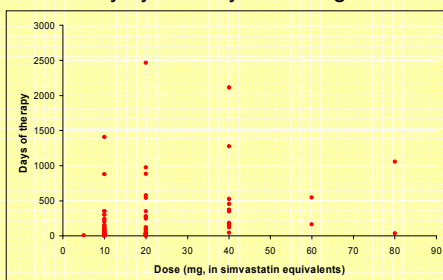


Figure 3 – Dose and duration of statin therapy prior to rhabdomyolysis

## Susceptibility

### Age

- 166 reports provided data on the age of the patient
- The mean age was 65 years (range 26–89)

Table 2 – Age ranges of patients with rhabdomyolysis

Age ranges	No. of case reports
under 45	8
45 to 59	38
60 to 74	80
75 and over	40

### Gender

- 51% (96/188) of reports were from female patients

### Concomitant medications

- Patients were taking on average 5 concomitant medications (range 0–33)
- The 5 concomitant drugs most commonly reported were:
  - ACE-inhibitors
  - Beta-blockers
  - Fluids and electrolytes
  - Acetylsalicylic acid
  - Calcium-channel blockers

## Limitations

- The results are, however, limited by the under-reporting of spontaneous reports, the lack of a known denominator, and the limited information reported for certain parameters
- Moreover, these data cannot be used to determine the incidence of rhabdomyolysis

## Discussion

- These data suggest that patients taking statins at low doses may develop rhabdomyolysis after several months of treatment
- However, the results are limited as spontaneous reports rarely contain sufficient data for the satisfactory analysis of an ADR
- Without improved reporting of the dose, time, and susceptibility factors relating to an ADR, clinicians will be unable to make a sensible assessment of risk

## Acknowledgements

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## References

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