Does Risk Tolerance to MS Therapies Change Over Time: A NARCOMS Survey

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Background

Newer and more effective therapies are now available for treatment of multiple sclerosis (MS). However, they are often accompanied by greater risk of complications, with some being potentially fatal. Some patients influence the decision to accept an effective but risky therapy. Additionally, with disease progression and changes in other factors (such as side effects, personal beliefs, insurance etc.) there may be changes in risk acceptance attitudes. In order to guide patient behavior in their treatment choices, healthcare providers need to understand not only MS patients’ tolerance of risks, but also changes in risk tolerance (RT) through the disease course as well as the factors that influence such changes.

We performed two surveys, a year apart, of MS patients through the North American Research Committee on Multiple Sclerosis (NARCOMS) MS Patient Registry. We evaluated risk tolerance to the same scenarios in both surveys using standard gamble (SG) that is validated tools for assessing patient preference. We collected patient demographic information and also assessed current disability, MS therapies and other medical conditions besides MS.

Objective

To determine how tolerance risk in MS therapies changes over time in MS patients.

Methods

- All 16,259 MS patients from the All active MS patients from the NARCOMS Registry’s online cohort who had completed at least one survey in the past two years were invited to complete two years (1) 1 and 2) web-based questionnaires on MS treatment decision making. Questionnaires were completed in August of 2010 and 2011.
- We used standard gamble paradigm to evaluate RT in two different scenarios:
  - curing MS (CureMS), with permanent reversal of all MS symptoms but a risk of immortality.
  - natalizumab (NAT), with risk of reduction of relapses by 68%, progression of disability by 42% and new brain lesions on MRI by 50% (malignant demyelinating PML) and an overall sell of brain function.
- The odds of the risk within the scenarios were adjusted iteratively to identify the maximum RT as described in Figure 1.
- We collected MS disease and behavior characteristics and demographic information.
- For this analysis, we classified patients into responders as being tolerant or intolerant of therapy as follows:
  - "Intolerant" = RT=1:1000
  - "Tolerant" = RT=1:1000
- Statistical analysis used

![Figure 1: Standard gamble Risk Tree](image)

Results

- 3,825 participants took part in both years of the web-based questionnaire, with a mean age of 56.3 years, 77% female, disease duration 14.3 years, PDDS score (Table 1).
- Using the 1:1000 cut point to define tolerance versus intolerance to treatments, the majority of patients (90%) were intolerant of CureMS, 79% NAT remained in the same risk category from Y1 to Y2 (Table 1).
- For individuals changed from being intolerant in Y1 to becoming tolerant in Y2 had a greater increase in standard gamble scores from Y1 to Y2. CureMS, a mean PDDS increase of 0.17 + 0.64 vs. 0.055 + 0.63 for the other groups (p=0.1) for NAT a mean PDDS increase of 0.14 + 0.61 vs. 0.305 + 0.64 for the other groups (p=0.2).
- The total number of respondents taking natalizumab changed little between Y1 and Y2. SCI (8.4%) in Y1 and 8.5% (1.7%) in Y2. However, some respondents either stopped or started taking natalizumab as shown in Figure 2.
- Risk attitudes changed for some respondents who were tolerant in one year but intolerant in the other year (Figure 3).
- A total of 403 were taking natalizumab other than Y1 or Y2 and 53 (12%) of them reported intolerance to NAT while taking natalizumab.
- Median RT of those taking natalizumab in both years increased, but there was no change in the median RT of those who either stopped natalizumab or started natalizumab during the two years of the study (Table 3).
- For both scenarios and in both years (Tables 5), we observed:
  - >50% had a 1 in 1000 fold greater risk tolerance to both scenarios than females.
  - Respondents, with greater disability (higher PDDS score) reported being more tolerant of newer therapies than those with little or no disability lower PDDS score.
  - Respondents currently taking natalizumab remained a much greater RT (up to 1000-fold for NAT) than those who were not taking natalizumab for both scenarios and in both years.
  - Respondents who were not on any MS therapy indicated 5-10 fold greater RT for CureMS scenario in both years.
- No change was observed for the NAT scenario.
- Respondents who had experienced a relapse in the last 12 months exhibited a 5-fold greater RT for the CureMS scenario in both years.
- Although respondents who had had lower RT for the CureMS scenario in Y1, there was no such difference in RT in Y2.

Discussion

- A threshold of 1-1000 (which was the estimated risk of natalizumab-related PML at the time of this survey), about 77% of respondents reported no change in their tolerance across that threshold but about 21% of respondents reported change in their risk tolerance attitudes over two years.
- With respect to the NAT scenario, about 13% of the respondents reported taking natalizumab while being intolerant of its risks, which may be related to their understanding of the risk of their understanding of the standard gamble (SG).
- For both scenarios, those respondents who were intolerant in Y1 but changed to tolerant in Y2, also had a greater increase in self-reported disability over the intervening year.
- We observed a number of key differences between respondents as follows:
  - Male sex: Males tolerated higher risk than females across both scenarios.
  - Age: The threshold of 1-1000 was violated when respondents aged 50+.
  - A higher PDDS score was associated with greater risk tolerance.
  - Not currently on MS therapy: MS patients who were not on MS therapy had greater risk tolerance. This may reflect that those who are not on MS therapy are more likely to have received less effective treatments. Therefore, this patient population may be willing to take greater risk for their MS therapy.
  - Currently taking natalizumab: Respondents currently receiving natalizumab showed a greater RT for both scenarios.

Conclusion

- About 17% of respondents reported changes in their risk tolerance overall over one year.
- Specific characteristics of MS patients correlate with their risk tolerance and appear to be consistent across the two years.
- Future studies may enable healthcare providers to better understand the changes in risk attitude in patient populations throughout the disease course.

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