and valid scale for semi-quantitative assessments of MSA patients with known rates of change associated with natural history. These rates can be used to power models of disease progression with the caveat that changes in slope vary with length of disease with steeper rates can be used to power models of disease progression with the caveat that changes in slope vary with length of disease with steeper rates can be used to power models of disease progression with the caveat that changes in slope vary with length of disease with steeper rates can be used to power models of disease progression with the caveat that changes in slope vary with length of disease with steeper rates can be used to power models of disease progression with the caveat that changes in slope vary with length of disease with steeper

disease progression.

Additionally, accelerated UMSARS progression was predicted not only by shorter symptom duration at baseline, but also by an absent levodopa response. It appears that UMSARS-related disease progression slows down as early as the second year of follow-up, which is important to consider when embarking on therapeutic trials of long duration. Of note, a minimal clinically important change using the UMSARS has not yet been established for MSA patients making it difficult to appreciate the relationship between statistical significance and clinical importance. As the scale was initially validated in Europeans, its validity and applicability across various populations requires further examination. In particular, some items regarding cutting food, handling utensils, and dressing may not apply to some rural and geographically isolated cultures. Furthermore, due to the need to design a scale that was reasonably simple, short, and user-friendly, some prominent features of MSA are not fully covered by the UMSARS and other validated scales may need to be supplemented to evaluate items not covered by the UMSARS that may have an impact on the overall function of MSA subjects, such as bradyphrenia, anhedonia, depression, sleep disorders, fatigue, and overall quality of life.

Finally, the long-term follow-up of MSA patients is restricted by the rapid neurodegenerative process resulting in reduced life expectancy. This may help explain the high rate of attrition and serious adverse events often seen in MSA trials. Given the rapid disease progression, survival rates might be considered as an outcome measure particularly when inclusion criteria are not restricted to early stages of the disease. In contrast, choosing patients earlier in the disease course should help improve attrition. Utilising the correct analysis that takes into account attrition patterns coupled with limiting the sites to those experienced investigators and demanding rigorous training on diagnostic and outcome measures which minimise error variance will help to ensure the chosen sample sizes will be able to detect treatment effects should they exist.

REFERENCES


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