EFFECT OF ACETYL-DL-LEUCINE IN PATIENTS WITH MULTIPLE SYSTEM ATROPHY OF THE CEREBELLAR TYPE (MSA-C)

G.M. Scigliuolo[1], A. Sagnelli[1], C. Pisciotta[1], G. Brenna[2], D. Pareyson[1], E. Salsano[1]

[1] *Department of Clinical Neurosciences, IRCCS Foundation, "C. Besta" Neurological Institute, Milan, Italy*
[2] *Scientific Directorate, IRCCS Foundation, "C. Besta" Neurological Institute, Milan, Italy*

Introduction

Acetyl-DL-leucine is a drug mainly used in France for the symptomatic treatment of acute vertigo and dizziness, and seems to be a promising, symptomatic treatment in inherited and sporadic degenerative diseases with prominent cerebellar ataxia [1-3].

Our aim was to evaluate the effect of acetyl-DL-leucine in a small cohort of patients with Multiple System Atrophy of the Cerebellar type (MSA-C), a common cause of progressive sporadic ataxia in adulthood.

Methods

Eleven clinically probable MSA-C patients asked for a pharmacological treatment of unsteadiness. **Nine** of them (**Table 1**) agreed to take off-label therapy with acetyl-DL-leucine (Tanganil®) at a dosage of **3 g/day (2 x 500 mg tablets, TID) for the first week, and then 4.5 g/day (3 x 500 mg tablets, TID)**[1]. A functional evaluation was performed at **baseline**, before the beginning of the treatment, and after **4 and 12 weeks from the start of the treatment**. We used sensitive clinical endpoints, based on quantitative measures of function, which may provide similar advantages compared to traditional ordinal scales, the Timed Up and Go test (TUG) and Nine-Hole-Peg-Test (9HPT) of dominant and non-dominant hand, and subjective rating scales such as a Visual Analogue Scale (VAS) for unsteadiness, and Patient's Global Impression of Change (PGIC).

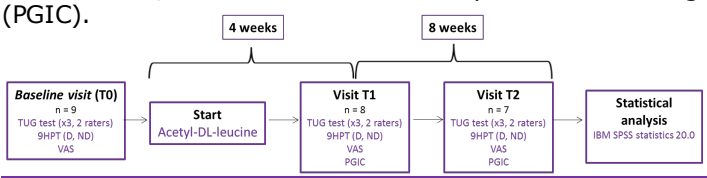


Table 1 - Patient characteristics

Patient ID	Sex	Age at onset	Age at evaluation	Walking
1	F	57	59	Without support
2	F	58	63	With support (walker)
3	M	53	55	Without support
4	F	58	61	Without support
5	M	39	44	Without support
6	M	48	52	Without support
8	M	55	56	Without support
9	F	61	63	Without support
11	F	38	42	With support (walker)

Abbreviations: M = male, F = female

Results

Fig. 1 Mean values for TUG test, VAS, 9HPT_D, 9HPT_ND at T0, T1 and T2 visits

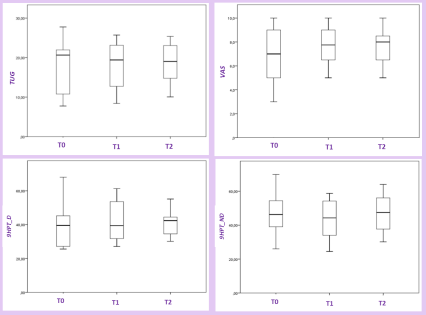
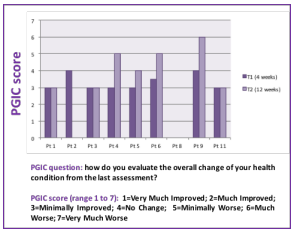


Fig. 2 Patient's Global Impression of Change



Results

We observed: **no significant difference for TUG test, 9HPT of the dominant hand and VAS** (significant if p - value < 0,05); **a slightly significant difference of the scores in 9HPT of non-dominant hand**. The **effect size** (the mean of change scores divided by the standard deviation of the baseline scores) revealed small changes of the scores (**Fig. 1, Table 2**). TUG test in MSA-C patients has an **excellent intra-rater** (Interclass Correlation Coefficient, ICC = 0.978) **and inter-rater reliability** (ICC = 0.998). Five patients reported a minimal improvement after 4 weeks, and three of them reported further minimal improvement after 12 weeks **(Fig. 2). Two patients discontinued the treatment**, one because of vague malaise, the other because of lack of improvement. Four patients (Pts 3, 5, 6, 11) decided to continue the therapy after 12 weeks as self-medication.

Table 2 – Results

TEST	T0 Mean (SD) - - - Median (min – max)	T1 Mean (SD) - - - Median (min – max)	T2 Mean (SD) - - - Median (min – max)	p-value (Friedman test for repeated measures)	Effect Size (T0-T1)	Effect Size (T0-T2)
TUG (s)	18.37 (6.90) - - - 20.64 (9.74 – 27.75)	16.98 (5.97) - - - 16.58 (8.40 – 23.83)	18.58 (5.63) - - - 19.04 (10.05 – 25.36)	0.37	0.20	-0.03
9HPT_D (s)	39,80 (12.69) - - - 39.58 (25.59 – 62.90)	39,54 (11.57) - - - 37.65 (27.12 – 60.52)	40,83 (8.62) - - - 42.40 (30.13 – 55.15)	0.87	0.02	-0.08
9HPT_ND (s)	47,98 (17.16) - - - 46.29 (26.02 – 69.87)	42,65 (13.31) - - - 38.87 (24.50 – 58.74)	47,02 (12.99) - - - 47.50 (30.15 – 64.00)	0.05	0.31	0.05
VAS (1-10)	8.00 (1.83) - - - 8.00 (5.00 – 10.00)	7.36 (1.60) - - - 7.50 (5.00 – 10.00)	7.57 (1.72) - - - 8.00 (5.00 – 10.00)	0.51	0.35	0.23

Conclusions

1) These observations, despite the small sample size, suggest that there is no effect of acetyl-DL-leucine on the functional motor disability (i.e., unsteadiness and finger dexterity) of MSA-C patients and **discourage larger, well-designed studies** to assess acetyl-DL-leucine as a symptomatic therapy for MSA-C patients; 2) **these results are not generalizable** to other forms of degenerative ataxia, due to their different pathomechanisms, and this may explain contradictory results especially when heterogeneous case series are assessed [1-3].

References

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