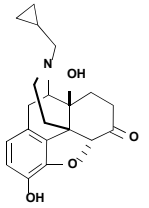


A Single Center, Randomized, Placebo-Controlled, Double-Crossover Study of the Effects of Low Dose Naltrexone on Multiple Sclerosis Quality of Life

Bruce Cree, Michael Ross, Ivo Violich, Brendan Berry, Azadeh Beheshtian, Elena Kornyeveva, Douglas Goodin

Department of Neurology, UCSF, San Francisco, CA

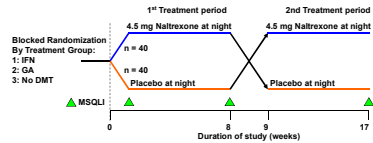


Introduction

- Naltrexone is a mu opiate receptor antagonist US FDA approved for treatment of opiate addiction
- More recently naltrexone in low dose was found to enhance the effects of opiate agonists¹
- In 1985 Dr. Bernard Bihari found that HIV infected patients had low levels of endogenous endorphins and hypothesized that increasing their levels would be beneficial
- Dr. Bihari began using a low dose of 4.5 mg naltrexone taken nightly in the treatment of HIV infected patients with the goal of "normalizing" endogenous endorphin levels
- Anecdotal reports suggest that this low dose of naltrexone (LDN) might also benefit MS patients
- A small (N=17) open label study in Crohns disease found that LDN improved active disease as measured by the Crohns disease activity index²

Materials and methods

Randomized, double-blinded, single center, double-crossover, single center, clinical trial



- Inclusion criteria**
- Clinically definite MS by current International Panel Criteria
 - 18 and 75 years of age
 - Willingness to not change or start disease modifying or symptomatic therapies of MS during the trial
 - Patients currently on a disease modifying therapy should not anticipate changing or discontinuing this medication during the 17 week study
 - Patients not currently on a disease modifying therapy
 - For women of childbearing potential, willingness to use a barrier method of contraception during the trial
- Exclusion criteria**
- Start of a disease modifying therapy within 3 months of entry in the trial
 - Planned start of DMT during the clinical trial
 - Pregnancy
 - Current chronic opioid agonists use
 - Patients currently on both interferon and glatiramer acetate
 - Patients currently taking LDN
 - Patients currently taking immunosuppressive medications

- Trial Participants**
- 80 subjects were enrolled
 - 9 withdrew voluntarily, 1 withdrew secondary to unrelated medical condition
 - 70 completed both treatment periods, 60 with complete data
 - 10 subjects dropped secondary to incomplete data
 - 4 data management errors, 6 uncompleted surveys

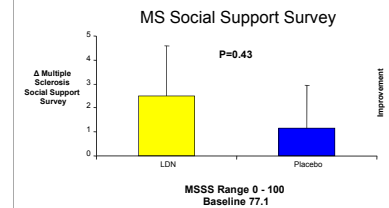
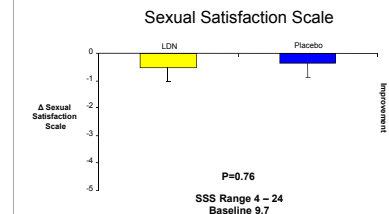
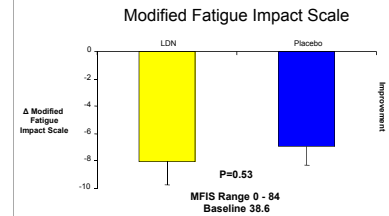
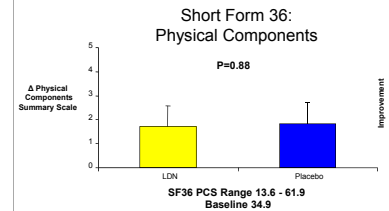
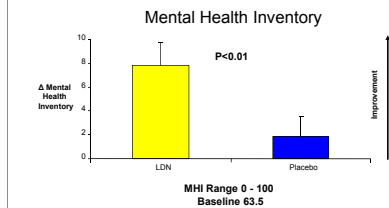
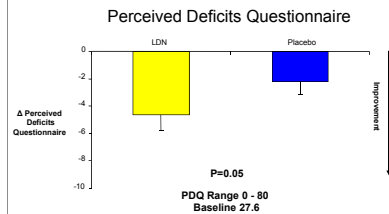
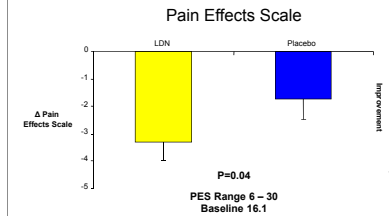
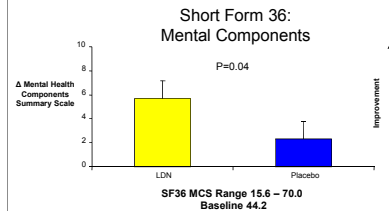
	♀	♂	RR	SP	PP	PR	IFN	GA	No DMT
	36	24	31	13	15	2	14	14	32

Outcome Measure: The Multiple Sclerosis Quality of Life Inventory (MSQLI)

Statistics

- Pre-specified analysis adjusted for sex, age, disease course (RR, SP, PP, PR), current treatment (IFN, GA, no DMT), race, baseline score and study drug order using a time series regression equation modeled for random effects and clustered by study subject
- The only baseline covariate that had a statistically significant impact on the model was the baseline score

Results



Conclusions

- 8 weeks of treatment with LDN significantly improved quality of life indices for mental health, pain, and self-reported cognitive function of MS patients as measured by the MSQLI
- An impact on physical quality of life indices including fatigue, bowel and bladder control, sexual satisfaction, and visual function was not observed
- The benefits of LDN were not affected by disease course, age, treatment order, or treatment with either interferon beta or glatiramer acetate
- The only treatment related adverse event reported was vivid dreaming during the first week of the study drug in some patients
- Potential effects of LDN beyond 8 weeks of treatment were not addressed in this study
- Multicenter RCTs of LDN in MS are warranted

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Acknowledgments

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For further information

Information on this and related projects at UCSF can be obtained at <http://www.ucsf.edu/msdb>.

Please visit <http://www.ldners.org> for more information on this patient funded initiative.

