Effect of Naltrexone on Spinal and Supraspinal Pain Mechanisms and Functional Capacity in Women with Fibromyalgia: Exploratory Outcomes from the Randomized Placebo-Controlled FINAL Trial

Running head: Effect of Naltrexone on central sensitization, pain inhibition, and muscular fatigue.

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Supplementary Table 1. Change in pain tolerance, temporal summation of pain (pain facilitation), conditioned pain modulation (pain inhibition), and functional capacity at 12 Weeks from Baseline for 30% pain responders versus non-pain responders in the LDN Treated Group.

	Change from baseline to after 12 weeks of treatment (95% CI)		**Difference between groups (95% CI)**	***P*-value**
	30% pain responders ***N=20***	**Non-pain responders** ***N=25***		
Exploratory Outcomes:				
Pressure pain tolerance left leg (kPa)	-2.2 (-5.6 to 1.2)	-4.0 (-7.0 to -0.9)	1.8 (-2.8 to 6.3)	0.44
Pressure pain tolerance right leg (kPa)	1.3 (-1.5 to 4.0)	-3.6 (-6.1 to -1.1)	**4.9 (1.1 to 8.6)**	**0.012**
Temporal summation of pain (VAS cm)	0.16 (-0.6 to 0.9)	-0.09 (-0.8 to 0.6)	0.2 (-0.8 to 1.3)	0.63
Conditioned pain modulation (kPa)	0.9 (-0.8 to 2.6)	1.6 (0.1 to 3.0)	-0.7 (-1.6 to 2.9)	0.55
30 sec chair stand test (count)	2.6 (1.8 to 3.3)	0.3 (-0.4 to 1.0)	**2.3 (1.2 to 3.3)**	**0.001**
Shoulder raise time (sec)	19.0 (-3.3 to 41.4)	-26.7 (-45.8 to -7.7)	**45.8 (15.5 to 76.0)**	**0.004**

Values are presented as least squares means (95% confidence interval) per group, and the difference between groups

Supplementary Table 2. Change in pain tolerance, temporal summation of pain (pain facilitation), conditioned pain modulation (pain inhibition), and functional capacity at 12 Weeks from Baseline for 30% pain responders versus non-pain responders in the Placebo Treated Group.

	Change from baseline to after 12 weeks of treatment (95% CI)		**Difference between groups (95% CI)**	***P*-value**
	30% pain responders ***N=13***	**Non-pain responders** ***N=34***		
Exploratory Outcomes:				
Pressure pain tolerance left leg (kPa)	0.4 (-3.9 to 4.7)	-0.9 (-3.5 to 1.8)	1.3 (-3.8 to 6.3)	0.61
Pressure pain tolerance right leg (kPa)	-0.6 (-4.2 to 3.0)	-1.4 (-3.7 to 0.8)	0.8 (-3.5 to 5.1)	0.70
Temporal summation of pain (VAS cm)	0.7 (-0.4 to 1.8)	-0.3 (-1.0 to 0.3)	1.0 (-0.3 to 2.3)	0.12
Conditioned pain modulation (kPa)	-0.2 (-2.7 to 2.3)	-1.0 (-2.6 to 0.5)	0.8 (-2.1 to 3.8)	0.57
30 sec chair stand test (count)	1.7 (0.8 to 2.6)	0.9 (0.3 to 1.4)	0.8 (-0.3 to 1.9)	0.14
Shoulder raise time (sec)	0.6 (-18.3 to 19.5)	-12.1 (-23.9 to -0.4)	12.7 (-9.9 to 35.3)	0.26

Values are presented as least squares means (95% confidence interval) per group, and the difference between groups.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Title page
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Abstract
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	Page 3
	2b	Specific objectives or hypotheses	Page 4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Page 4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	Page 4
	4b	Settings and locations where the data were collected	Page 4
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Page 5
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Page 5-6
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	N/A secondary analysis
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	Page 5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Page 5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Page 5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Page 5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Page 5
	11b	If relevant, description of the similarity of interventions	Page 5

Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Secondary analysis only (Page 5)
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	N/A
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Page 7
	13b	For each group, losses and exclusions after randomisation, together with reasons	Page 7
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Page 6
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Page 7
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	N/A Secondary analysis
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A Reported in primary report
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Page 9
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Page 9
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Page 8-9
Other information			
Registration	23	Registration number and name of trial registry	Abstract and Page 4
Protocol	24	Where the full trial protocol can be accessed, if available	Page 4
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Page 9

Citation: Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Medicine. 2010;8:18.

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up-to-date references relevant to this checklist, see www.consort-statement.org.