

Feasibility and Safety of Lumbar Punctures in the Parkinson Progression Marker Initiative

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INTRODUCTION

- Lumbar Punctures (LPs) are a routine clinical test that may be useful in research in biomarker development in Parkinson disease (PD) and other neurodegenerative diseases (1).
- Parkinson Progression Marker Initiative (PPMI) is a longitudinal observation study to identify PD progression biomarkers and includes the collection of cerebrospinal fluid (CSF) at multiple time points (2).
- The safety of LPs in the research setting has not been systematically studied in subjects with PD.
- There are multiple types of needles, positions, methods and sites that may be considered when performing an LP.
- The purpose of this analysis, is to determine the feasibility, safety and tolerability of LPs in early Parkinson disease (PD), healthy volunteer (HV) and SWEDD participants in PPMI.

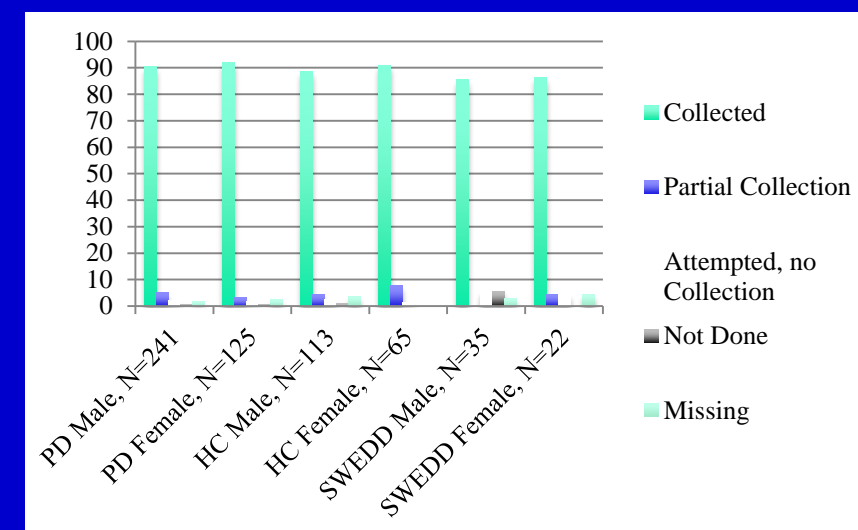
METHODS

- All subjects enrolled in PPMI undergo LP at baseline, 6, 12 months and yearly (7 total). For this analysis, only baseline data as of 1 Mar 2013 was used.
- Preferred study LP technique is: acquisition of at least 15 mls CSF using a 24 gauge Sprotte needle in the L4-5 interspace in the seated position.
- The small gauge needle requires aspiration of CSF, although gravity collection method was used for some LPs.
- Subjects were instructed to remain horizontal for at least 30 minutes following the procedure and minimize intense physical activity.
- Adverse events were monitored by phone one week after LP completion.
- In addition to descriptive data, multivariate analysis was used to determine factors that contributed to AEs related to LPs.

Baseline Clinical Data (as of 1 Oct 2012)

	All Subjects (N = 495)	PD Subjects (N = 298)	Healthy Controls (N = 155)	SWEDD Subjects (N = 42)
Age Mean (SD)	61.1 (10.42)	62.1 (9.53)	59.3 (11.7)	60.4 (10.9)
Weight, kg Mean (SD)	81.0 (16.7)	81.7 (17.2)	78.7 (15.4)	84.7 (17.0)
CSF Volume collected, mL Mean (SD)	17.4 (18.7)	18.7 (22.5)	14.6 (3.2)	19.7 (22.3)
Completed Lumbar Puncture N (%)	478 (96.6%)	287 (96.3%)	151 (97.4%)	40 (95.2%)

Percent of LPs Completed



1930's era spinal needles (2 superior) compared to 25g Sprotte Needle (arrow) with introducer



RESULTS

- There was collection (total or partial) of 568 subjects (94.5%).
 - 24g Sprotte was used in 413 (72.7%) of subjects
 - 2.7% required collection under fluoroscopy.
 - Mean volume (SD) collected was 17.4 (18.7) cc.
- Adverse events related to LPs
 - No SAEs
 - No association with more frequent or more severe AEs based on volume removed.
 - The most common AE was headache
 - Mean duration = 4.4 days
 - Higher rate of AEs when performed at L4-5 (vs. L3-4 or L2-3, p=0.0339) and in the seated position (p=0.0003).
- In female (but not male) subjects with PD, there was a higher age in those with AEs vs no AEs (60.9 vs. 56.5 years, p=0.0139)
- In subjects with PD, there was a trend toward more headaches with higher BMI in females (p=0.059).
- There were **no differences** in baseline LP AEs related to BMI, weight, or duration of disease.
- The risk of AEs was *significantly higher for the first 10 LPs* compared to the subsequent LPs when at least 20 LPs were completed [RR=2.05 (CI 1.29, 3.27)]
- Based on a multivariate analysis of LP collection methods, adjusted for age and gender on incidence of LP-related headaches, incidence of post-LP headaches was significantly higher in younger subjects, females, and subjects who were in a sitting position during their LP.

Frequencies of two specific AEs: Headache and Back Discomfort

AE Type	PD (N = 349)			HC (N = 169)			SWEDD (N = 50)		
	# of Events	# of Subjects	% of Subjects	# of Events	# of Subjects	% of Subjects	# of Events	# of Subjects	% of Subjects
Total	57	43	12.3%	48	36	21.3%	11	8	16.0%
Headache	23	22	6.3%	21	18	10.7%	6	6	12.0%
Back Discomfort	7	7	2.0%	10	10	5.9%	3	3	6.0%

Frequencies of LP-Related AEs by Group

	N	# of AEs	# Subjects with AEs	% of Subjects
PD	366	57	43	11.7
HC	178	48	36	20.2
SWEDD	57	11	8	14
Total	601	116	87	14.5

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SUMMARY AND CONCLUSIONS

- Obtaining CSF in a cohort of newly diagnosed PD and HV subjects with a mean age about 60 years is safe and feasible.
- Specific LP techniques (gauge and type of needle, subject position and level of insertion) may reduce the overall incidence of adverse events.
- Incidence of AEs was highest in the HC cohort, but still lower than other published reports using cutting needles.
- Among all cohorts, incidence of headaches was significantly higher in younger subjects, females, and subjects who were in a sitting position during their LP.
- There was no association of weight and any LP-related AE, including headache.
- Retention in the study may not be dependent on LP-related AEs.
- With experience, there appears to be a reduced risk of AEs.

References

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