A multicenter European comparative survey of motor and non motor effects of subcutaneous apomorphine infusion and intrajejunal levodopa infusion in Parkinson's disease *(The EuroInf survey)*

Prashanth Reddy[1], Pablo Martinez-Martin[2], Per Odin[3], Angelo Antonini[4], Daniela Calandrella[4], Manuela Pilleri[4], Anne Martin[1], Tove Henriksen[5], Alexandra Rizos[1], Regina Katzenschlager[6], Narissah Bryndum[5], Arne Glad[5], Lars Timmermann[7], Haidar Salimi Dafsari[7], Georg Ebersbach[8], Milica G Kramberger[9], Maja Trost[9], Zvezdan Pirtosek[9], Karoline Wenzel[10], Volker Tomantschger[11], Alexander Storch[12], Heinz Reichmann[12], Andres Ceballos-Baumann[13], K Ray Chaudhuri[1,14]

1. King's College London, National Parkinson Foundation Centre of Excellence and Regional Movement Disorders Unit, London, UK, 2. Alzheimer Disease Research Unit and CIBERNED, Alzheimer Center Reina Sofia Foundation, Carlos III Institute of Health, Madrid, Spain, 3. Department of Neurology, Central Hospital Bremerhaven, Germany and Department of Neurology, University Hospital, Lund, Sweden, 4. IRCCS San Camillo Venice and University of Padua, Italy, 5. Department of Neurology, University Hospital of Bispebjerg, Copenhagen, Denmark, 6. Department of Neurology and Landsteiner Institute for neuroimmunological and neurodegenerative disorders, Danube Hospital/SMZO, Vienna, Austria, 7. Department of Neurology, University Hospital Cologne, Cologne, Germany, 8. Movement Disorders Clinic, Beelitz-Heilstaetten, Germany, 9. Centre for extrapyramidal disorders, Neurology department, University Medical Centre Ljubljana, Ljubljana, Slovenia, 10. Department of Neurology, Medical University of Graz, Graz, Austria, 11. Centre for Neurorehabilitation, Gailtal-Klinik, Hermagor, Austria, 12. Department of Neurology, University of Dresden, Dresden, Germany, 13. Parkinson Centre Schoen Klinik Muenchen Schwabing, and Department of Neurology TUM, Munich, Germany, 14. Department of Neurology, University Hospital Lewisham, London, UK;

OBJECTIVE/ BACKGROUND:

- Intrajejunal levodopa infusion (IJL) and sub-cutaneous apomorphine infusion (Apo) are two different approaches for the treatment of advanced Parkinson's disease (PD)
- To date minimal comparative data is available
- Using validated motor and non-motor scales, we have compared multicenter European data of the motor and non-motor effects of intrajejunal levodopa infusion therapy (IJL, 43 patients) and apomorphine infusion (Apo, 37 patients) in PD patients with severe motor fluctuations and dyskinesia
- This is a real life study, hence no randomisation was possible; however the data for the two groups were matched for disease duration, age, NMSS, PDQ-8, although UPDRS III was higher at baseline in the Apo arm

To our knowledge this is the first such study reported

(The study is still recruiting, aiming to have 50 patients in each arm).

METHODS:

- IJL: 43 advanced PD (32 males, mean age: 60.5 ± 9.7 yrs, mean duration of disease:15.5 ± 5.9 yrs), average L-dopa dose: 1862 mg, average hrs on infusion 16.9 hrs
- Apo: 37 advanced PD patients (16 males, mean age 61.2 ± 11.7 yrs, disease duration 4.5 ± 4.7 yrs), average Apo dose: 107.9 mg, average hrs on infusion 14.8 hrs
- Outcome measures:
  - Unified PD Rating Scale (UPDRS) III and IV (in on state)
  - Non Motor Symptoms Scale (NMSS)
  - PD questionnaire (PDQ-8 for quality of life)
- Scores were collected before initiation of therapy and after 6 months of therapy in both groups
- Owing to baseline difference in UPDRS 3 between two group "effect size" of therapy as well as NNT (numbers needed to treat) analysis was used to avoid bias

RESULTS:

Table 1: Baseline and 6 months FU scores of observed parameters.
IJL = intrajejunal levodopa infusion, Apo = apomorphine infusion

	IJL			Apo		
	Baseline	Follow-up	p	Baseline	Follow-up	p
UPDRS-III	22.22 (11.78)	12.21 (8.19)	0.0001	32.03 (11.16)	15.43 (7.38	0.0001
UPDRS-IV	9.72 (3.14)	4.30 (3.01	0.0001	9.54 (5.57)	4.94 (3.17)	0.0001
NMSS	82.35 (48.88)	47.84 (38.94)	0.0001	80.51 (57.41)	48.24 (34.93)	0.0001
PDQ-8	43.97 (17.63)	29.58 (17.00)	0.0001	50.34 (19.33)	32.26 (18.44)	0.0001

Mean (SD). Wilcoxon test. Bonferroni correction, p<0.0125

Table 2: Effect size of intervention, and NNT values for intrajejunal levodopa infusion and apomorphine infusion.

	IJL				Apo			
	Relative change	Effect size	% who improved ≥1/2 SD	NNT to improve ≥1/2 SD	Relative change	Effect size	% who improved ≥1/2 SD	NNT to improve ≥1/2 SD
UPDRS-III	-45.05	0.85	60.47	1.65	-51.79	1.49	86.49	1.15
UPDRS-IV	-55.76	1.73	86.05	1.16	-48.15	0.82	59.46	1.68
NMSS	-41.91	0.71	60.47	1.65	-40.10	0.56	35.14	2.85
PDQ-8	-32.73	0.82	58.14	1.72	-35.90	0.93	75.68	1.32

Number needed to treat (NNT) determines the number of patients needed to treat for obtaining benefit in one of them.

Effect Size: <0.20 – negligible
0.20 – 0.49 – small effect
0.50 – 0.79 – moderate effect
≥0.80 – large effect

CONCLUSIONS:

- Although not randomized, this multicentre European survey of real life practice of advanced therapies in PD has compared groups of advanced PD patients in the largest cohort studied to date
- To reduce bias of non randomization, effect size and NNT have been calculated and both Apo and IJL therapies in similarly advanced groups of PD patients result in robust improvement in motor, non-motor scores with a large effect size matching published effects of DBS in Parkinson's
- In particular a large "effect size" on Quality of life is seen with both interventions based on multi-centre clinician led data capture in clinics
- Apo arm shows a greater motor improvement but less dyskinesia reduction compared to IJL and may be due to Apo being used concomitantly with oral treatment in most centers and Apo monotherapy was rarely used in this survey
- We are now addressing if there are any differential effects of these therapies on NMSS with larger numbers (being recruited)
- This novel data has important implications on the choice of infusion therapies and DBS in advanced PD