Clinical Neurology and Neurosurgery 160 (2017) 101–104

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Eradication of Helicobacter pylori infection might improve clinical status of patients with Parkinson's disease, especially on bradykinesia

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ARTICLE INFO

Keywords:
Helicobacter pylori
Parkinson's disease
Eradication
Bradykinesia

ABSTRACT

Objectives: Previous studies have shown that Helicobacter pylori infection might make clinical status worse in patients with Parkinson's disease and Helicobacter pylori eradication might improve clinical status by modifying the pharmacokinetics of L-dopa. Here, we investigate whether Helicobacter pylori eradication could benefit idiopathic parkinsonism and Helicobacter pylori infection will effect which aspect of motor symptom significantly.

Patients and methods: A cohort study involving idiopathic Parkinson's disease patients, screened for Helicobacter status by ^{13}C urea breath test. Clinical status was evaluated by using the Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn-Yahr stage. If patients had motor complications, they were quantified at the "on" time. The Helicobacter pylori positive patients could choose to receive Helicobacter pylori eradication or not by themselves. Group 1 was Helicobacter pylori negative patients. Group 2 was Helicobacter pylori positive patients who didn't receive eradication treatment. Group 3 was Helicobacter pylori positive patients who received successful eradication treatment. Repeat clinical assessments and ^{13}C urea breath test was performed at 1 year later. Numerical data were expressed as mean ± standard deviation (SD)

Results: Ninety-four consecutive patients with Parkinson's disease were recruited and underwent the initial ^{13}C urea breath test, but only forty-eight patients successfully completed the total study. In Group 3, the UPDRS-III scores (=Motor Examination Section Scores) were significantly lower 1 year later compared to baseline (18.3 ± 8.38 vs. 25.9 ± 8.37, P = 0.007). The differences were main in UPDRS-23 (=Finger Taps) (1.7 ± 1.16 vs. 2.4 ± 1.51, P = 0.045), UPDRS-25 (Rapid Alternation Movements of Hands) (1.6 ± 1.35 vs. 2.4 ± 1.71, P = 0.031) and UPDRS-26 (=Leg Agility) (1.3 ± 1.25 vs.2.1 ± 0.99, P = 0.011). There was difference among three groups in the UPDRS-26 (P = 0.040) of clinical status change of one year.

Conclusion: The eradication of Helicobacter might improve the clinical status of idiopathic parkinsonism, especially on bradykinesia.

1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease [1]. Levodopa (L-dopa) is still recognized as the most widely used and effective medication for Parkinson's disease, but long period therapy is often associated with the development of motor complications, which are difficult to treat [2]. One of the reasons to induce the motor complications is due to drug concentration fluctuation [3]. Helicobacter pylori (HP) is a common bacterial infection of the digestive tract and highly associated with duodenal and gastric ulcers [4]. In theory, Helicobacter pylori may affect the bioavailability of L-dopa by disrupting the duodenal mucosa, [5] which is the site of L-dopa primary absorption. Previous studies suggested that HP infected patients with PD might have worsen clinical status and HP eradication might improve clinical status by modifying the pharmacokinetics of L-dopa [6–8]. Most studies evaluated the patients' disability by the motor complications, UPDRS total score or UPDRS-III score. Few experts do further research to evaluate which aspect of motor syndrome HP infection influence mostly in PD patients. Dobbs et al. reported in 2010 [9] that, in a randomized, double blind, placebo controlled trial (RCT), the hypokinesia of idiopathic parkinsonism improved after Helicobacter pylori eradication, with overall clinical benefit. However there was a measurable increase in rigidity. Their longitudinal observational study of antimicrobial use in PD,

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http://dx.doi.org/10.1016/j.clineuro.2017.07.003
Received 14 January 2017; Received in revised form 2 July 2017; Accepted 4 July 2017
Available online 05 July 2017
0303-8467/

reported in 2013 [10], showed that this effect was indication specific, since antimicrobials for other indications did not improve hypokinesia. Eradicating H. pylori did not influence rigidity in the relatively small number of cases arising, but routine antimicrobial use in general increased it. However we have not found other studies to support this study. For these reasons, the aim of our study was to investigate whether HP eradication could contribute to idiopathic parkinsonism and which aspect of motor symptom HP would effect significantly.

2. Material and methods

2.1. Participates

Eligible patients had a diagnosis of idiopathic PD according to the UK Parkinson's Disease Society Brain Bank criteria. All patients was from Beijing Hospital and Pinggu Hospital of Traditional Chinese Medicine of Beijing.

Exclusion criteria were: 1) Showed atypical features, such as gaze palsy, cerebellar ataxia or pyramidal signs, or had a history of neuroleptic drug intake or other possible identifiable causes of secondary parkinsonism. 2) A history of recent proton pump inhibitors (PPIs) or histamine (H2) antagonist use for at least 4 weeks prior to the Urea Breath Test. 3) A history of recent antibiotics use Within 6 months prior to the UBT. 4) A diagnosis of inflammatory or neoplastic bowel disease, or a history of surgery to the gastrointestinal tract. 5) Cardiovascular/respiratory symptoms during normal activities. 6) Inability to perform the Urea Breath Test (UBT).

2.2. Design

The study was approved by local ethics committees and written informed consent obtained from all participants.

At the time of enrollment, demography and medication details were recorded via a face-to-face interview. Patients' clinical status was evaluated by neurologists using the Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn-Yahr stage. If patients had motor complications, they were quantified at the "on" time.

Participates were eligible for screening of Helicobacter status which was defined by ^{13}C urea breath test (UBT). Each patient took a ^{13}C-urea standard tablets after collection of a baseline breath sample. Then collected a breath sample 30 min post-administration of 13C urea standard tablets. The concentrations of isotope-labeled carbon dioxide ($^{13}CO2$ and $^{12}CO2$) analyzed using an IRIS infra-red isotope analyzer. A delta-over-baseline value (DOB) > 4% indicates HP positive.

The HP positive patients could choose to receive HP eradication or not by themselves. The treatment was a 14-day therapy with omeprazole 20 mg, amoxicillin 1 g and clarithromycin 500 mg 12-hourly.

All the participants were divided into three groups. Group 1 was HP negative patients. Group 2 was HP positive patients who didn't receive eradication treatment. Group 3 was HP positive patients who received successful eradication treatment.

Clinical assessments and UBT were obtained at baseline and 1 year later.

2.3. Statistical analysis

All data were analyzed by SPSS 19.0. Numerical data were expressed as mean ± standard deviation (SD). Within three groups' analysis were using the ANOVA. Bonferroni correction was used in post hoc analysis. The normal distribution is tested by the K-S method. Between two groups' analysis were using the independent *t*-test. Paired *t*-tests were used to compare between the parameters at baseline and during the 1 year follow-up. If it didn't obey the normal distribution or didn't go through homogeneity of variance test, non-parametric test was used (kruskal wallis). Chi-square test was used to compare categorical variables. Multiple linear regression analysis was used to assure factors whether influence the results. A p value of 0.05 was taken as being statistically significant.

3. Results

Ninety-Four consecutive PD patients were recruited and underwent the initial UBT, but only forty-eight patients successfully completed the total study. Forty-one patients had difficulty coming for follow-up-visits at 1 years later in the fasting state to screen the statue of HP for the second time. Two patients who didn't receive any treatments, were HP positive at baseline but HP negative 1 year later. One patient was HP negative at baseline but HP positive 1 year later. Two patients who HP positive at baseline received HP eradication, but failed. Those patients were excluded from the study.

The mean age of the patients in our study was 63.4 ± 8.42 (mean ± standard deviation) years old. The mean duration of PD from diagnosis was 6.4 ± 3.89 years. 23 patients were males (47.9%) and 25 were females (52.1%).

Group 1 had 26 HP negative patients (14 males and 12 females). Group 2 had 12 HP positive patients who didn't receive eradication treatment (4 males and 8 females). Group 3 had 10 HP positive patients who received successful eradication treatment (5 males and 5 females). There were no differences within three groups in sexual, age, disease duration, levodopa daily dose and H-Y stage (Table 1).

3.1. Comparison of clinical status between baseline and 1 year later in HP positive patients who received successful eradication treatment group (Group 3)

The UPDRS-III scores, which refers to the motor examination section scores, were significantly lower 1 year later compared to baseline (18.3 ± 8.38 vs. 25.9 ± 8.37, P = 0.007) only in Group 3. The difference was main in UPDRS-23 (Finger Taps) (1.7 ± 1.16 vs. 2.4 ± 1.51, P = 0.045), UPDRS-25 (Rapid Alternation Movements of Hands) (1.6 ± 1.35 vs. 2.4 ± 1.71, P = 0.031) and UPDRS-26 (Leg Agility) (1.3 ± 1.25 vs.2.1 ± 0.99, P = 0.011). However, there were no significant differences in the Hoehn & Yahr stages, total levodopa daily dose and other questions in UPDRS-III part (Table 2).

3.2. Comparison of clinical status change of one year among three groups

The score of 1 year later minus the score of baseline means the change of one year. Positive number means the clinic status getting worse and negative number means the clinic status improved.

There was difference among three groups in the UPDRS-26 (Leg Agility) (P = 0.040). No difference in the Hoehn & Yahr stages, total levodopa daily dose, other questions in UPDRS-III part and the total score of UPDRS-III. Through the mean scores of items from 20 to 26 and the UPDRS-III, we could see the clinical status improved in Group 3 more significantly than Group 1. However the clinic status of Group 2 was little improved even getting worse in some aspects, except UPDRS-22 (Rigidity) (Fig. 1).

The scores of UPDRS-III (−7.6 ± 6.93 vs. 0.2 ± 7.02,

Table 1
The demography of three groups

	Group 1	Group 2	Group 3	P
Age[a]	63.7 ± 8.32	62.7 ± 9.97	63.2 ± 7.44	0.950
Female sex[b]	12(46.2%)	8(66.7%)	5(50%)	0.489
Disease duration[a]	6.3 ± 3.56	5.8 ± 4.65	7.3 ± 3.97	0.677
H-Y[a]	1.9 ± 0.85	1.9 ± 0.52	2.1 ± 0.64	0.521
LED[a]	470.2 ± 310.58	446.9 ± 373.86	599.5 ± 369.18	0.886

[a] ANOVA test.
[b] Chi-square test.