Research Protocol

Oxyhydrogen Nanobubble Infusion as a Complementary Therapy in Patients with Parkinsonism

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Background

This study was conducted at Brawijaya University Hospital in Malang, Indonesia, involving 35 patients with parkinsonism. The study used a prospective cohort study design. The effects of oxyhydrogen nanobubble (OHNB) infusion on the subjects were observed without comparison to a control group (placebo). Pre- and post-test results were evaluated before and after the OHNB infusion.

The variables analyzed in this study were the degree of parkinsonism using the Hoehn and Yahr scale, cognitive function using the MOCA-Ina test, and quality of life for patients with parkinsonism using the PDQ-39 questionnaire.

The hypothesis of this study is that OHNB infusion can improve disease severity, cognitive function, and quality of life in patients with parkinsonism..

OHNB is an infusion that containing H2 and O2 gas molecules in the form of nanobubbles. H2 and O2 gas molecules encapsulated in nanobubbles are more stable and can persist for longer periods in solution (Li et al., 2022) and more easily penetrate the blood-brain barrier (Owen et al., 2016; Alghamdi et al., 2022). H2 nanobubbles have superior antioxidant properties than H2 water alone (Kato et al., 2015). H2 have anti-inflammatory effects, thus reducing cellular inflammation (Cheng et al., 2023), reducing oxidative stress and protecting the brain from ischemic injury (Ohsawa et al., 2007), mitigating acute neurotoxic effects, and addressing behavioral disorders caused by MPTP exposure on dopaminergic neurons (Fujita et al., 2009). O2 is required to activate the HIF-1α pathway which can maintain neuronal integrity.(Pinilla et al, 2021)

Study Purpose

The aim of this study was to determine the effect of oxyhydrogen nanobubble infusion on the degree of disease, cognitive function, and quality of life of patients with parkinsonism.

Study Design

The study used a prospective cohort study design. The effects of oxyhydrogen nanobubble (OHNB) infusion on the subjects were observed without comparison to a control group (placebo). Pre- and post-test results were evaluated before and after the OHNB infusion.

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Inclusion Criteria

- Patients who meet the criteria for parkinsonism
- 18-70 years old

Exclusion Criteria

- Patient is unwilling to undergo examination.
- Pregnancy.
- History of malignancy and/or chemotherapy.
- History of alcohol or drug use that can induce extrapyramidal symptoms.
- Hyperthyroidism.
- Impaired kidney function.
- Impaired liver function.
- Patients with heart failure requiring fluid restriction.
- MRI results suggest a brain tumor causing parkinsonism symptoms.
- Catalase enzyme deficiency (acatalasemia).

Study Protocol

In the initial phase of the study, patients with Parkinsonism underwent a brief history taking to determine whether they met the inclusion criteria. If the patient met the inclusion criteria, informed consent was obtained.

Next, the patient was evaluated to determine whether they met the exclusion criteria, including pregnancy, a history of malignancy and/or chemotherapy, and a history of drug or alcohol use that could induce extrapyramidal syndrome symptoms. If the exclusion criteria were met, the patient was excluded from the study.

Patients included in this study then underwent a complete physical examination (internal status and neurological status), complete blood count, SGOT/SGPT, Urea/Creatinine, random blood sugar, blood electrolyte levels, thyroid function, chest x-ray, ECG, and head MRI. If exclusion criteria were found, namely hyperthyroidism, impaired heart function requiring fluid restriction, impaired liver function (increased SGOT/SGPT > 1.5 x normal), impaired kidney function (creatinine > 1.5), or head imaging results showed a brain tumor, then the patient was excluded from the study. This initial pre-treatment data was also used as the baseline data for the study subjects.

During the blood draw, a catalase enzyme test was also performed by spraying hydroxypropyl methylcellulose onto the patient's blood on a glass slide. If bubbles/foam appear in the patient's blood upon application, it indicates the presence of catalase. However, if no bubbles/foam appear, it indicates the patient has acathalasemia and is excluded from the study.

Patients who meet the inclusion criteria and do not meet the exclusion criteria will then undergo a parkinsonism severity assessment based on the Hoehn and Yahr scale, the MoCA-Ina test, and the PDQ 39 questionnaire as pre-treatment data.

Patients will then receive 12 oxyhydrogen nanobubble infusions, administered twice weekly.

Evaluation of the effects of the OHNB infusions will be conducted twice: after the sixth infusion (following the 15 ml dose) and after the 12th infusion. Patients will undergo a complete physical examination (internal and neurological status), complete blood count (CBC), SGOT/SGPT, Urea/Creatinine, random blood sugar, blood electrolyte levels, parkinsonism severity based on the Hoehn and Yahr scale, the MoCA-Ina test, and the PDQ 39 questionnaire as post-treatment data.

Data Analysis

Data regarding age, gender, duration of parkinsonism symptoms, types of medications consumed, comorbidities (hypertension, coronary heart disease, metabolic syndrome), degree of parkinsonism according to the Hoehr and Yahr classification, cognitive function according to the MoCA-Ina examination, and PDQ 38 examination results in this study will be presented in a frequency distribution table. Then, the table will be analyzed descriptively.

Data regarding parkinsonism severity examination based on Hoehn and Yahn scale, MoCA-Ina examination, and PDQ 39 questionnaire examination PDQ-39 pre and post treatment are numerical data consisting of three groups of data, namely pre-treatment data, evaluation data after the 7th injection (mid-treatment data), and evaluation data after the 12th injection (post-treatment data). will be analyzed statistically using one-way ANOVA. The data will then be analyzed whether they are normally distributed or not. If the data are normally distributed, they will be analyzed using Repeated ANOVA Test, and if they are not normally distributed, they will be analyzed using Friedman Test.

Expected Results

Oxyhydrogen nanobubble infusion can improve disease severity, cognitive function, and quality of life in patients with parkinsonism.

Ethical Considerations

This research upholds research ethics so that it can provide values that benefit the wider community. The results of this study are expected to have a positive impact on the Indonesian health system, making it more independent and accessible to the people. However, a potential risk posed by this study is the possibility of a healing crisis, in which participants experience a decline in physical condition such as fever, chills, and pain. After experiencing a healing crisis, participants can experience the benefits of oxyhydrogen nanobubble infusion, such as feeling much healthier, more energetic, and refreshed than before the infusion. This risk can be managed with the guidance and prescription of medication provided by a doctor, thereby minimizing the occurrence and severity of a healing crisis.

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