



Received: 23 December, 2019

Accepted: 03 October, 2022

Published: 04 October, 2022

***Corresponding author:** Goldstein NI, Ph.D. Department of Human and Animal Physiology, Biological Faculty, Lomonosov Moscow State University, Moscow, Russia, E-mail: dr.naum.goldstein@gmail.com

Copyright License: © 2022 Gekht BM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

<https://www.peertechzpublications.com>



Check for updates

Short communication

The results of a clinical and neurophysiological study of the effectiveness of Parkon spray in the treatment of Parkinson's Disease (PD)

Gekht BM and Goldstein NI*

Department of Human and Animal Physiology, Biological Faculty, Lomonosov Moscow State University, Moscow, Russia

Introduction

For more than 25 years, we have begun an experimental study of the physiological effect of micromolar concentrations of reactive oxygen species on the regulatory functions of the central nervous system. We found that these effects extend to the CNS centers and hormonal regulation of the hypothalamus and pituitary gland [1-4], as well as in the control of BBB permeability [5].

In long-term experimental studies, other physiological effects of exogenous ROS were discovered, of which we note first of all the effects realized through the CNS. These are the potentiation of analgesic narcotics [6] and other drugs, a decrease in the toxic effect of MPTP, and the regulation of other MAO-dependent processes [7].

It has also been surprisingly found that endonasal application of micromolar concentrations of some ROS, such as activated oxygen (superoxide) and hydrogen peroxide, reduces the symptoms of Parkinson's disease and parkinsonism [8-10]. The first drug based on micromolar hydrogen peroxide was the German and Russian medicine Parkon® [11].

Study design

We investigated 19 patients with the PD (8 males and 11 females) using the Hoehn & Yahr scale and UPDRS scale [12]. Also, we performed the neurophysiologic investigation using High-Frequency Transcranial Magnetic Stimulation (rTMS)

and electromyographic (EMG) studies. The patients were investigated in a double-blinded placebo-controlled manner. Group A (10 people) received Parkon and Group B (9 people) received a placebo during a 4-week course.

Inclusion criteria

According to the inclusion criteria all patients had hypokinesia and at least one of the following symptoms: muscle rigidity, tremor (4-6 Hz), postural instability (not connected to visual, vestibular, cerebellar dysfunction).

Patients

Due to the use of magnetic stimulation, the study excluded people with pacemakers and metallic foreign objects.

Out of 19 patients with PD, 10 had a predominantly tremor form and 9 had a predominantly rigid form of PD. The cohorts were similar in age, gender, duration and form of the disease. The mean age was 60.7 ± 9.4 years. The mean disease duration was 4.1 ± 2.3 years.

Out of 10 patients in the Parkon Group, 3 patients never used L-dopa-containing drugs, 4 patients used L-dopa-containing drugs for not more than 2 years and 3 patients used L-dopa-containing drugs for more than 2 years. In the Control Group, 2 patients never used L-dopa-containing drugs, 4 patients used L-dopa-containing drugs for not more than 2 years, and 3 patients used L-dopa-containing drugs for a period of between 2 and 3 years (Table 1).



There were no statistically significant differences on Hoehn & Yahr and UPDRS scales between the groups.

Out of 6 people with a predominate tremor form of PD in the Parkon Group, 1 patient had stage 1.5 on Hoehn & Yahr scale, 4 patients had stage 2.0 on Hoehn & Yahr scale and 1 patient had stage 2.5 on Hoehn & Yahr scale. Patients with a predominantly rigid form in Parkon Group had the following stages for the disease: 1 patient had stage 2.0 on Hoehn & Yahr scale, and 3 patients had stage 2.5 on Hoehn & Yahr scale.

In the Control Group, out of 4 people with a predominantly tremor form for PD, 2 patients had stage 1.5 on Hoehn & Yahr scale and 2 patients had stage 2.0 on Hoehn & Yahr. Out of 5 Control Group patients with a predominantly rigid form of PD, 3 patients had stage 2.0 on Hoehn & Yahr scale and 2 patients had stage 2.5 on Hoehn & Yahr.

Results of treatment with Parkon

All patients tolerated therapy very well. As a result of treatment with Parkon, patients did not experience negative ECG changes, arrhythmias, arterial hypertension, postural disorders, and mental disorders. During treatment, the patients of the Parkon group showed a statistically significant improvement in symptoms according to the UPDRS scale. The mean UPDRS score in the subgroup with tremors before treatment was 38.9 ± 11.5 , after 4 weeks of treatment it decreased to 24.7 ± 9.7 ($p < 0.05$). The average index of motor and neuropsychological disorders in the subgroup of the rigid form was 56.3 ± 12.4 ($p < 0.05$) on the UPDRS scale and decreased to 34.8 ± 12.8 ($p < 0.05$) after 4 weeks of treatment.

There were also no statistically significant changes in the control group. The mean UPDRS score in the subgroup with tremors before treatment was 36.3 ± 14.0 , after 4 weeks of treatment it decreased to 31.8 ± 12.5 ($p < 0.05$). The mean UPDRS score in the rigid form subgroup was 54.3 ± 12.6 ($p < 0.05$) and decreased to 45.7 ± 14.6 ($p < 0.05$) after 4 weeks of treatment (Table 2).

It's important to note that both cohorts showed improvements in the emotional-motivational sphere and a decrease in depression symptoms, which was reflected in the changes of the corresponding parameters on the first part of

Table 2: Dynamics of clinical & neurophysiologic parameters in patients with different forms of PD.

Group & Form of PD	UPDRS score		Silent Period (SP)		CMCT (msec)	
	before	after	before	after	before	after
Parkon						
Tremor n = 4	38.9 ± 11.5	24.7 ± 9.7	125.43 ± 16.23	146.9 ± 17.05	7.6 ± 2.5	7.47 ± 2.28
Rigidity n = 6	56.3 ± 12.4	34.8 ± 12.8	122.8 ± 17.29	129.8 ± 16.31	7.7 ± 1.96	7.3 ± 2.01
Control:						
Tremor n = 4	36.3 ± 14.0	31.7 ± 12.7	114.1 ± 21.05	112.7 ± 18.4	7.15 ± 1.59	7.96 ± 1.63
Rigidity n = 5	54.3 ± 12.6	38.9 ± 11.5	128.45 ± 11.92	131.15 ± 16.51	7.45 ± 2.24	8.05 ± 2.32

the UPDRS scale. Analysis of Parkson's efficacy revealed that statistically significant improvements were observed in all patients from Parkon Group, regardless of their history of using L-dopa-containing medications.

The neurophysiological investigation was conducted using magnetic stimulator "Maglite" and "Keypoint" devices made by Medtronic-Dantek (USA-Denmark). Transcranial stimulation (rTMS) was used for both groups. The neurophysiological examination was performed at least twice during the study: before the administration of Parkon and after 4 weeks of administration. The method of transcranial magnetic stimulation with a period of silence was used. Parameters analyzed the Silence Period (SP) and Central Motor Conduction Time (CMCT).

As a result of the comparison of CMCT parameters, no statistically significant differences were found in the parameters in patients with predominantly tremor and predominantly rigid forms, both in the Control group and in the Parkon group. As a result of magnetic stimulation of the brain, CMCT in patients of the Parkon group with a predominantly tremor form was 7.60 ± 2.50 ms before treatment and 7.47 ± 2.28 ms after treatment; CMCT in patients of the Parkon group with a predominantly rigid form was 7.70 ± 1.96 ms before treatment and 7.30 ± 2.01 ms after treatment. In the control group, in patients with a predominantly tremor form of PD, CMCT was 7.15 ± 1.59 ms before treatment and 7.96 ± 2.01 ms after treatment; in patients with a predominantly rigid form of PD, CMCT was 7.70 ± 1.96 ms before treatment and 8.05 ± 2.32 ms after treatment.

Analysis of Silent Period (SP) duration in the Parkon Group showed statistically significant differences before and after the treatment in patients with a predominantly tremor form of PD. The duration of SP in patients with a predominantly tremor form of PD significantly increased after the 4-week course with Parkon: before treatment = 125.43 ± 16.23 msec and after treatment = 146.9 ± 17.05 msec.

There were no significant changes in Parkon Group patients with a predominantly rigid form of PD. The duration before treatment with Parkon was 122.8 ± 17.29 msec and after treatment was 129.9 ± 16.31 . No statistically significant changes in SP duration were observed in the Control Group.

Table 1: General characteristics of the patients from Parkon Group and Control Group in terms of the form of the disease and length of use of L-dopa-containing medications.

Group & Form of PD	Use of L-dopa-containing medications			Total
	never used	= 2 years	> 2 years	
Parkon				
Tremor	2	3	1	6
Rigidity	1	1	2	4
Total	3	4	3	10
Control:				
Tremor	1	2	1	4
Rigidity	1	2	2	5
Total	2	4	3	9



No side effects were observed during and after the magnetic stimulation.

Conclusion

Patients with PD (both with predominantly tremors and rigid forms) showed a positive dynamic of clinical symptoms as a result of treatment with Parkon. This is reflected in a statistically significant ($p < 0.05$) reduction of the mean score on the UPDRS scale.

Neurophysiologic analysis, which showed the increased duration of SP during the treatment in patients with a predominantly tremor form of PD, allows us to conclude positive clinical dynamics in a given group of patients. The mechanisms of these changes need to be investigated further and they are possibly connected to Parkon having an inhibiting effect on MAO activity, mainly MAO-B, in the basal ganglia and hypothalamus influencing thalamocortical, rubrospinal, and reticulospinal tracts. In addition, these results confirmed the idea of the biologically important role of micromolar concentrations of exogenous reactive oxygen species, i.e. H_2O_2 [3]. Moreover (and this is interesting in itself), in recent years original and review articles on the important regulatory role of endogenous H_2O_2 in comparable concentrations have often appeared in scientific periodicals see for example [13,14].

The biological and, in particular, the established physiological role of exogenous activated oxygen and hydrogen peroxide is discussed in more detail in the works [3,4,15].

References

- Goldstein NI. Air ions: possible role of reactive oxygen species in the mechanisms of their biological action. In: Oxygen radicals in chemistry, Biology and Medicine (Goldstein, N.I., Ed.), Riga. 1988; 80-108.
- Goldstein NI, Goldstein RN, Merzlyak MN. Negative air ions as a source of superoxide. Int J Biometeorol. 1992; 36: 118-122.
- Biophysical aspects of the physiological effect of exogenous $O_2^{\bullet-}$ on animals. Dr.Thesis. Biofizicheskiye aspekty fiziologicheskogo deystviya ekzogennoy $O_2^{\bullet-}$ na zhivotnykh, Moscow, MGU, 2000 (In Russian).
- Goldstein N, Arshavskaya TV. Is atmospheric superoxide vitally necessary? Accelerated death of animals in a quasi-neutral electric atmosphere. Z Naturforsch C J Biosci. 1997 May-Jun;52(5-6):396-404. doi: 10.1515/znc-1997-5-619. PMID: 9232896.
- Goldstein N, Goldstein R, Terterov D. Blood-Brain Barrier Unlocked. Biochemistry (Moscow). 2012; 77(5):419-424.
- Goldstein N, Lewin T, Kamensky A, Dubinin V, Baumann S, Konstantinova O. Exogenous gaseous superoxide potentiates the antinociceptive effect of opioid analgesic agents. Inflamm Res. 1996 Sep;45(9):473-8. doi: 10.1007/BF02252319. PMID: 8891759.
- Goldstein N, Kamensky A, Arshavskaya T, Goldstein R. How does medicine Parkon® affect the MPTP-induced oxidation stress and MAO systems of the rat's brain. Open J Parkinsons Dis Treatm. 2021; 4(1): 001-004. DOI: https://dx.doi.org/10.17352/ojpd.000010
- Golubev VL. Parkon as a treatment of the Parkinson's disease. Open J Parkinsons Dis Treatm. 2(1): 001-005. DOI: http://doi.org/10.17352/ojpd.000006
- Goldstein NI, Naydin VI, Fedorova NV. Application of endonasal applications of Parkon in the complex treatment of Parkinson's disease in the clinic [Primenenie endonasalnih aplikatsiy preparata Parkon v kompleksnom lechenii bolezni Parkinsona v klinike] in Russian. 2002; 7(6):45-48.
- Goldstein NI, Naidin VL, Fedorova NV. The use of endonasal applications of Parkon in the complex treatment of Parkinson's disease. Journal of Neurology. 2002; 7(6):45-48.
- Parkon® (2004): In: Register of Medicinal Products of Russia (RLS). 7: 665. In Russian.
- Fahn S, Elton RL. Unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Calne D, Goldstein M, Eds, Recent Developments in Parkinson's Disease, Macmillan Health Care Information, Florham Park. 1987; 153-163.
- Groeger G, Quiney C, Cotter TG. Hydrogen peroxide as a cell-survival signaling molecule. Antioxid Redox Signal. 2009 Nov;11(11):2655-71. doi: 10.1089/ars.2009.2728. PMID: 19558209.
- Rhee SG. Redox signaling: hydrogen peroxide as intracellular messenger. Exp Mol Med. 1999 Jun 30;31(2):53-9. doi: 10.1038/emmm.1999.9. PMID: 10410302.
- Goldstein N. Reactive oxygen species as essential components of ambient air. Biochemistry (Mosc). 2002 Feb;67(2):161-70. doi: 10.1023/a:1014405828966. PMID: 11952412.

Discover a bigger Impact and Visibility of your article publication with Peertechz Publications

Highlights

- ❖ Signatory publisher of ORCID
- ❖ Signatory Publisher of DORA (San Francisco Declaration on Research Assessment)
- ❖ Articles archived in worlds' renowned service providers such as Portico, CNKI, AGRIS, TDNet, Base (Bielefeld University Library), CrossRef, Scilit, J-Gate etc.
- ❖ Journals indexed in ICMJE, SHERPA/ROMEO, Google Scholar etc.
- ❖ OAI-PMH (Open Archives Initiative Protocol for Metadata Harvesting)
- ❖ Dedicated Editorial Board for every journal
- ❖ Accurate and rapid peer-review process
- ❖ Increased citations of published articles through promotions
- ❖ Reduced timeline for article publication

Submit your articles and experience a new surge in publication services (<https://www.peertechz.com/submission>).

Peertechz journals wishes everlasting success in your every endeavours.