Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Case report

Adamantanes might be protective from COVID-19 in patients with neurological diseases: multiple sclerosis, parkinsonism and cognitive impairment

Konrad Rejdak[a,*], Paweł Grieb[b]

[a] Department of Neurology, Medical University of Lublin, Lublin, Poland
[b] Department of Experimental Pharmacology, Medical Research Center, Polish Academy of Sciences, Warsaw, Poland

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ABSTRACT

Facing the outbreak of coronavirus disease 2019 (COVID-19) pandemic, there is an urgent need to find protective or curable drugs to prevent or to stop the course of the coronavirus SARS-CoV-2 infection. Recent evidence accumulates that adamantanes, widely used in different neurological diseases, could be repurposed for COVID-19.

We hereby report on a questionnaire-based study performed to assess severity of COVID-19 in patients suffering from multiple sclerosis (n = 10), Parkinson's disease (n = 5) or cognitive impairment (n = 7). In all patients infection with SARS-CoV-2 was confirmed by rtPCR of nasopharyngeal swabs. They were receiving treatment with either amantadine (n = 15) or memantine (n = 7) in stable registered doses. All of them had two-week quarantine since documented exposure and none of them developed clinical manifestations of infectious disease. They also did not report any significant changes in neurological status in the course of primary nervous system disease.

Above results warrant further studies on protective effects of adamantanes against COVID-19 manifestation, especially in subjects suffering from neurological disease.

1. Introduction

Facing the outbreak of coronavirus disease 2019 (COVID-19) pandemic, there is an urgent need to find protective or curable drugs to prevent or to stop the course of the coronavirus SARS-Cov-2 infection. This virus shares highly homological sequence with SARS-CoV, and may cause acute, highly lethal pneumonia coronavirus disease 2019 (COVID-19) with clinical symptoms similar to those reported for SARS-CoV and MERS-CoV (Li et al., 2020). The characteristic symptom reported by patients with COVID-19 is respiratory distress, and most of the patients admitted to the intensive care could not breathe spontaneously. It has been recently described that SARS-CoV-2 has neurotropic activity with neurological consequences leading to centrally mediated respiratory insufficiency due to virus invasion into the brainstem (Li et al., 2020). The fatality rate is the highest among elderly and those with comorbidities and immunological deficiency.

Hereby we report on the result of a questionaire-based study performed to assess whether adamantanes could exert protective antiviral effect against COVID-19 among different neurological disease patients including multiple sclerosis, parkinsonism and cognitive impairment.

2. Case report

In this study, twenty-two patients (10 with multiple sclerosis, 5 with Parkinson's disease and 7 with cognitive impairment) who were tested positive for SARS-CoV-2 and were receiving treatment with either amantadine or memantine on stable registered doses (100mg q.d. and 10mg b.i.d, respectively) for at least 3 months prior to the infection exposure, were surveyed on their laboratory results and clinical status (remote contact with verbally received information). All patients gave consent on study participation and requested anonymity, which was fully guaranteed. The demographic and clinical characteristics are presented in Table 1. All patients were tested after reported person-to-person contact with SARS-CoV-2 infected subjects and had viral infection confirmed with real-time reverse transcription polymerase chain reaction (rRT-PCR) test for the qualitative detection of nucleic acid from SARS-CoV-2 in upper and lower respiratory specimens. All of them had two-week quarantine since documented exposure and none

* Corresponding author: Konrad Rejdak, Department of Neurology, Medical University of Lublin, 8 Jaczewskiego Str. 20-954 Lublin, Poland.
E-mail addresses: k.rejdak@umlub.pl (K. Rejdak), pgrieb@imdik.pan.pl (P. Grieb).

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Table 1
Patients characteristics. Abbreviations: SD = standard deviation; DMF = dimethyl fumarate; GA = acetate glatiramer; NA = natalizumab; FG = fingolimod.

Characteristics	Multiple sclerosis	Parkinson's disease	Cognitive impairment
N	10	5	7
Age (mean ± SD; years)	38 ± 10	68 ± 15	71 ± 10
Gender (male/female)	3/7	3/2	4/3
Disease duration (mean ± SD; years)	9 ± 4	6 ± 3	7 ± 2
Primary disease treatment (n, %)	10 (100%)	5 (100%)	7 (100%)
-drugs used (n)	DMF (4); GA (2); NA (2); FG (2)	L-Dopa (5)	Donepezil (5) Rivastygmine (2)
Adamantanes treatment (n, %)	10 (100%)	5 (100%)	7 (100%)
- amantadine (n)	10	5	0
- memantine (n)	0	0	7
SARS-Cov-2 positive (n, %)	10 (100%)	5 (100%)	7 (100%)

developed clinical manifestations of infectious disease. They also did not report any significant changes in neurological status in the course of primary nervous system disease.

3. Discussion

Several potential treatments have been suggested for COVID-19, ranging from experimental to established drugs, however none of them has been confirmed effective. Patients suffering from neurological disease are at risk of COVID-19. In particular, elderly patients with dementia or parkinsonism, or patients exposed to immunosuppressive treatment in the course of autoimmune-mediated demyelinating diseases might require special attention.

Adamantanes, drugs containing tricyclo-bridged hydrocarbon structure, interfere with viroporin protein channel seemingly responsible for release of RNA-viruses, such as SARS coronavirus, from infected cells (Torres et al., 2007). Recognition of modest antiviral effects shown for amantadine, rimantadine, memantine, and bananin in models for bovine coronavirus, mouse hepatitis virus, human coronavirus OC43, and SARS-CoV, led to the suggestion that adamantanes could be repurposed for COVID-19 (Cimolai, 2020). Among adamantanes, amantadine and memantine are commonly used as symptomatic treatment to alleviate fatigue, parkinsonian symptoms and cognitive dysfunction (respectively) and might be of potential to protect against COVID-19 among the most fragile patients (Tipton and Wszolek, 2020).

Very recently it has been discovered that, in a human model cell line, expression CTSL gene coding for the cathepsin L, a lysosomal protease involved in SARS-CoV-2 entry to cells, is significantly down-regulated by amantadine. Based on this result it was hypothesized that amantadine could serve as a potent therapeutic decreasing the replication and infectivity of the virus, likely leading to better clinical outcomes (Smieszek et al., 2020). Results of our present study may, indeed, corroborate clinical importance of the aforementioned in vitro findings.

4. Conclusion

Above results warrant further studies on protective effects of adamantanes against COVID-19 manifestation. Although the current study has limitations due to small sample size and cross-sectional approach, it may indicate that adamantanes could exert protective antiviral effect. If confirmed, adamantanes might prove helpful to limit SARS-CoV-2 infection and its clinical neurological sequels.

Declaration of Competing Interest

None of the authors have any conflict of interest to disclose.

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