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THE USE OF AMANTADINE IN A PATIENT WITH PNEUMONIA AND PARKINSON'S DISEASE: A CASE REPORT

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Пневмония және Паркинсон ауруы бар науқаста амантадинді қолдану: клиникалық жағдай

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Мақсаты. Паркинсон ауруы (ПА) әлемдегі екінші ең таралған нейродегенеративті ауру болып табылады, жыл сайынғы аурушаңдық деңгейі 100 000 адамға 8-ден 18-ге дейін. 60 жастан асқан адамдар арасында ПА таралуы айтарлықтай өсуде және болжамдар 2030 жылға қарай диагноз қойылған жағдайлардың саны екі есе өсетінін көрсетеді. Амантадиннің дискинезияны емдеуде тиімділігі дәлелденіп, жиі ПА-да бастапқы монотерапия ретінде пайдаланылатынына қарамастан, оның ПА-ның декомпенсациясы кезінде емдеудегі рөлі әлі де аз зерттелген. Бұл мақалада ПА-ы бар 72 жастағы азиаттық әйелде ұзаққа созылған қызбамен бірге жүретін өкпенің төменгі бөліктің екі жақты пневмониясы дамыған жағдай көрсетілген. Қозғалыс белгілерінің нашарлауымен күресу үшін оған амантадин сульфатының инфузиясы тағайындалды, нәтижесінде бұлшықет тонусы, ригидтілік және тремор жақсарды. Бұл жағдай амантадин сульфатының декомпенсацияланған ПА-да, әсіресе пневмония сияқты ауыр инфекцияларды қамтитын жағдайларда тиімді емдеу мүмкіндігін көрсетеді. Нәтижелер амантадиннің жүйелі стресстің жедел эпизодтары кезінде қозғалыс қызметін тұрақтандыруда рөл атқаруы мүмкін екенін көрсетеді, бұл ілеспе аурулары бар ПД күрделі жағдайларын емдейтін дәрігерлерге жаңа мүмкіндіктер ашады. Әрі қарайғы зерттеулер мұндай жағдайларда амантадиннің емдік ауқымын нақтылауға және қарқынды терапия кезінде ПА-ы бар емделушілер үшін неғұрлым мақсатты емдеу хаттамаларын әзірлеуге көмектесуі мүмкін.

Негізгі сөздер: *Паркинсон ауруы, пневмония, емдеу, амантадин, нәтиже*

The Use of Amantadine in a Patient with Pneumonia and Parkinson's Disease: A Case Report

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Parkinson's disease (PD) is the second most common neurodegenerative disorder worldwide, with an annual incidence of 8–18 per 100,000 individuals. Its prevalence rises significantly in populations aged 60 and older, with cases projected to double by 2030. While amantadine is well-recognized for managing dyskinesia and as initial monotherapy in PD, its utility in addressing PD decompensation remains insufficiently studied.

This report details the case of a 72-year-old Asian woman with PD who developed bilateral lower lobe pneumonia with a prolonged fever. Her condition was marked by worsening motor symptoms, including increased rigidity and tremors. An intravenous infusion of amantadine sulfate was administered, resulting in notable improvements in muscle tone, rigidity, and tremor control. This case highlights the potential role of amantadine in stabilizing motor function during acute systemic stress, such as severe infections.

The findings suggest that amantadine sulfate may serve as an effective therapeutic option for PD decompensation in complex clinical scenarios involving comorbid conditions. This case underscores the need for further investigation to define the therapeutic range and establish targeted treatment protocols for PD patients requiring critical care interventions.

Keywords: *Parkinson's disease, pneumonia, amantadine, treatment outcome, motor function stabilization*

Применение амантадина у больной с пневмонией и болезнью Паркинсона: клинический случай

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Болезнь Паркинсона (БП) занимает второе место по распространенности нейродегенеративных заболеваний в мире, с годовым уровнем заболеваемости от 8 до 18 на 100 000 человек. Распространенность БП значительно возрастает среди лиц в возрасте 60 лет и старше, и прогнозы показывают, что число диагностированных случаев удвоится к 2030 году. Хотя амантадин доказал свою эффективность в лечении дискинезии и часто используется в качестве начальной монотерапии при БП, его роль в лечении БП в стадии декомпенсации остается недостаточно изученной. В данной статье представлен случай 72-летней азиатской женщины с БП, у которой развилась двусторонняя нижнедолевая пневмония, сопровождавшаяся длительной лихорадкой. Чтобы справиться с ухудшением двигательных симптомов, ей была назначена инфузия сульфата амантадина, что привело к улучшению мышечного тонуса, ригидности и тремора. Этот случай подчеркивает потенциал амантадина сульфата как эффективного вмешательства при декомпенсации БП, особенно в сценариях, связанных с тяжелыми инфекциями, такими как пневмония. Полученные данные свидетельствуют о том, что амантадин может играть роль в стабилизации двигательной функции во время острых эпизодов системного стресса, что открывает новые возможности для клиницистов, лечащих сложные случаи БП с сопутствующими заболеваниями. Дальнейшие исследования могут помочь уточнить терапевтический диапазон амантадина в таких ситуациях и способствовать разработке более целенаправленных протоколов лечения.

Ключевые слова: *болезнь Паркинсона, пневмония, лечение, амантадин, исход*

Introduction

The effectiveness of amantadine in the symptomatic treatment of patients with Parkinson's disease, discovered accidentally more than 50 years ago, has stood the test of time, and the drug is still widely used by neurologists. Its pharmacological action is unique in its combination of dopaminergic and glutamatergic properties, which is its dual effect on the signs and symptoms of parkinson's and levodopa-induced dyskinesia. In addition, amantadine has additional and less clearly defined pharmacological effects, including anticholinergic and serotonergic activity. Data from randomized controlled trials over the past 5 years have confirmed the effectiveness of amantadine for the treatment of levodopa-induced dyskinesia in patients with Parkinson's disease, and clinical studies have also confirmed its potential for reducing motor fluctuations [1].

Parkinson's disease (PD) is the second most prevalent chronic neurodegenerative illness in the world. The incidence rates range from 8 to 18 cases per 100,000 individuals. It is estimated that the number of people diagnosed with PD will double by 2030. PD is rarely diagnosed in individuals under 50, but its occurrence increases significantly after the age of 60 [2].

In most studies, amantadine is considered an effective treatment for dyskinesia in patients with Parkinson's disease or for early initial monotherapy [3]. However, there is insufficient information regarding the use of this medication in cases of decompensation of Parkinson's disease.

In this article, we report and discuss a case of a 72-year-old Asian female with Parkinson's disease who developed bilateral congestive lower lobe pneumonia, accompanied

by a chronic fever lasting for a month (up to 39.9º C), where amanadine sulfate was used to manage the patient's condition during decompensation.

Case report

A 72-year-old Asian female with a medical history of Parkinson's disease (PD), hypertension, and a confirmed positive SARS-CoV-2 RNA test was admitted to the hospital presenting with altered consciousness, fever (39.9°C), cough, and fatigue. She denied a history

of Botkin's disease (hepatitis A), tuberculosis, and any dermatological or venereal diseases. Her surgical history includes a cholecystectomy, with no history of trauma or blood transfusion. Her family history is unremarkable. She denies any substance abuse or other harmful habits. The patient is retired, married, and has six children. She denies any personal history of myocardial infarction or cerebrovascular accident. In 2020, she was diagnosed with COVID-19-related pneumonia. Since 2020, she has been under the care of a neurologist for Parkinson's disease.

Her pre-admission medications included trihexyphenidyl (Cyclodol, 2 mg twice daily), prescribed by her neurologist, which was discontinued upon the onset of fever. Additionally, she was receiving levofloxacin (Levolet R, 500 mg twice daily).

On initial examination, the patient exhibited altered mental status with a Glasgow Coma Scale (GCS) score of 11-12, a respiratory rate of 22 breaths per minute, blood pressure of 95/60 mm Hg, heart rate of 110 beats per minute, and an oxygen saturation of 94% with an oxygen mask (88% on room air). A 12-lead electrocardiogram at the time of admission revealed sinus tachycardia with a heart rate of 130 bpm and diffuse myocardial changes. A computed tomography scan of the chest showed findings consistent with hypostatic bilateral lower lobe pneumonia.

Neurological status upon admission: The patient was in a state of deep stupor. Her GCS score was 11-12. She was responsive to examination, tracking the reflex hammer with her eyes but unable to move her limbs. The patient was able to follow simple commands but fatigued rapidly. Bilateral eyelid openings and pupils were symmetrical (D=S), with no restrictions in eye movement or presence of nystagmus. The pupillary light reflex was intact. Asymmetry was noted in the nasolabial folds. The patient attempted to imitate tongue protrusion, and there was a marked increase in oral automatism. Tendon reflexes were symmetrical (D=S) but diminished. Muscle tone was elevated in all limbs and neck muscles, with a plastic rigidity. No pathological reflexes were observed.

The patient was initially treated for pneumonia with azithromycin (500 mg for 5 days) according to the clinical protocol of the Ministry of Healthcare of Kazakhstan. Additionally, she was prescribed levodopa/carbidopa (250 mg/25 mg) three times a day for Parkinson's disease. She also received the drug Ferric (III) hydroxide destrane under the trade name CosmoFer (2.0 ml intravenously), the proton pump inhibitor Pantoprazole under the trade name PAN IV (40 mg), the direct anticoagulant heparin under the trade name name Hepasan (2500 IU four times a day), loop diuretic Furosemide (20 mg) and a drug from the expectorant group Ambroxol (2.0 ml twice a day).

During the course of treatment, no significant improvement was noted with azithromycin, prompting a switch to levofloxacin at a dosage of 1000 mg per day for 5 days. On the 10th day of hospitalization, the patient's body temperature was 37.9°C, with an oxygen saturation of 88%. She continued to exhibit increased muscle tone, neck stiffness, and tremors. As a result, an infusion of amantadine was initiated for 5 days to manage her

Table 1. General blood count indicators over time in a patient with Parkinson's disease.

Day	WBC (x10^9/L)	RBC (x10^12/L)	HGB (g/L)	HCT (%)	PLT (x10^9/L)	Segmented neutrophils (%)	PCT (%)	LYM (%)	MON (%)	GR (%)	Erythrocyte sedimentation rate (mm/h)	Color indicator
1	9.2	3.64	109	30.9	227	77.8	0.17	19.2	1.7	79.1	17	0.9
2	11.1	3.50	106	29.0	244	-	-	20.5	1.7	-	19	0.9
3	11.1	3.08	90	26.2	223	-	0.18	14.0	1.3	84.7	20	0.9
4	7.3	2.87	86	24.4	230	-	0.19	16.1	1.9	82.0	22	0.8
5	7.6	2.89	88	24.7	261	-	0.21	19.6	2.0	78.4	21	0.8
6	6.8	2.46	74	20.9	242	-	0.20	18.7	2.8	78.5	16	0.8
7	6.8	2.51	78	21.4	231	-	0.18	20.3	2.7	77.0	20	0.7
10	7.6	2.83	84	24.3	226	-	0.16	20.3	2.1	77.6	-	-

neurological symptoms. Due to the fact that the patient was simultaneously receiving several medications, we conducted a study to identify drug interactions using the international websites Drugs.com and UpToDate. No potentially dangerous drug interactions of the Major gradation were identified (Drugs.com, UpToDate.com).

Laboratory analyses indicated that against the background of the inflammatory condition, the blood parameters, including hemoglobin, hematocrit, and color index, began to decrease. As a result, iron supplements were introduced (Table 1).

On the third day in the hospital, due to the persistence of general cerebral symptoms and signs of intoxication, a cerebrospinal fluid (CSF) examination was ordered; however, no significant findings were obtained (Table 2).

Table 2. Cerebrospinal fluid parameters on day 3 in a patient with Parkinson's disease.

Parameter	Results	Normal parameters
Quantity	2.0 ml	-
Color	colorless	colorless
Transparency	slightly cloudy	transparent
Protein	0.33 g/l	0.16—0.33 g/l
Pandey's reaction	negative	negative
Cytosis	7.2 units/µl	2-10 units/µl
Red blood cells	0	0
Glucose	4.65 mmol/l	2.78—3.89 mmol/l

She was discharged home on the 14th day in a stable condition, with reduced muscle tone in the limbs, absence of rigidity, and minor tremors in the hands.

Discussion

Amantadine hydrochloride is a member of the adamantanamine class of drugs. It was originally used as an antiviral for the treatment of influenza, but was coincidentally found to improve the symptoms of Parkinson's disease. While its exact mechanism of action is unknown, amantadine is known to act as a non-competitive antagonist at the phencyclidine

(PCP) site of the NMDA receptor at therapeutic concentrations [4]. Amantadine is also known to enhance the release of dopamine from nerve endings and delay its reuptake [5]. Early clinical trials demonstrated the antiparkinsonian effects of amantadine both as an adjuvant with levodopa and when used alone. It was employed for Influenza A treatment in the early 2000s [6].

A meta-analysis conducted in 2006 indicated that amantadine reduced the duration of influenza symptoms by one day and lessened the intensity of fever and other related symptoms [7]. Besides the two FDA-approved usages of amantadine, a few other diseases can benefit from amantadine. Clinical trials have conflicting results for the reduction of chorea in Huntington disease. The 2012 American Academy of Neurology guidelines suggests amantadine is likely effective in decreasing chorea, although the degree of effect is unknown [8]. In the Kazakhstan national drug formulary, the drug belongs to group N04 (anti-parkinson drugs) [www.knf.kz].

Despite previous studies showing some effectiveness of amantadine in improving motor function, a 2003 Cochrane review concluded that there was insufficient evidence to support the efficacy of this drug. Another pharmacological feature of amantadine is the limited duration of clinical effects. Few nonrandomized studies have shown improvement in motor function, but long duration response has not been not proven [9].

The US National Institutes of Health study focused primarily on long-term oral treatment or short-term intravenous infusions. The first double-blind randomized trial of oral amantadine, conducted in 14 patients, documented significant improvement in dyskinesia after 3 weeks [4]. Since then, others have shown both acute and long-term antidyskinetic effects in >50% of patients with advanced disease. As in the previous study, oral amantadine was used [10,11]. Ү In 17 patients who were re-evaluated after 1 year of treatment with oral amantadine, the beneficial antidyskinetic effect remained almost at the level of the acute effect [12]. Acute intravenous administration of amantadine also reduced dyskinesias by almost 50%; this effect lasted for at least 5 hours[13].

Scientists from Russia analyzed their own results of using the intravenous form of the drug amantadine sulfate in 142 patients in a vegetative state and "arreactive wakefulness syndrome." Depending on the dominant neurological symptoms, patients were divided into three main groups: areactive type of course (group 1 - 61 patients), predominance of primitive limbic reactions (group 2 - 35 patients), predominance of extrapyramidal symptoms (group 3 - 46 patients) [14].

Also, doctors from Russia described cases of patients with the initial stage of PD (stage 1 according to Hoehn-Yahr - unilateral parkinsonism without postural disturbances) and noted a favorable clinical effect when prescribing amantadine sulfate in a standard dosage of 300 mg/day. In the first case, the patient took the drug as monotherapy; in the second case, amantadine was added to pramipexole to improve symptomatic control of existing movement disorders. Our experience of the successful use of amantadine at the initial stage of PD corresponds to similar observations of foreign authors [15].

Conclusion

In our patient, we used amantadine as an additional therapy to levocarbisan in the stage of decompensation of the disease and we see positive dynamics in the neurological status of the patient. As a result, on the fifth day of prescribing amantadine sulfate, the temperature dropped to 37.0 and muscle stiffness decreased.

Declarations

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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