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**Research Article** 

# Antipsychotics Use in Vascular Dementia

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#### Abstract:

**Background:** In the clinic of dementia, not only cognitive, but also non-cognitive disorders are observed. In the treatment of these symptoms, the use of antipsychotics is necessary. As the etiology and pathogenesis of vascular dementia, which is a type of dementia, is multifactorial, it requires more careful treatment while treating with antipsychotics.

**Material and methods:** The aim of the research was to study the effectiveness of neuroleptics used in the treatment of psychotic disorders in vascular dementia. A Mini-Mental State Examination (MMSI) scale and Neuropsychiatric Inventory (NPI) were completed for each patient 4 weeks before and after treatment. The dose was reduced when side effects were observed during the study.

**Result:** The mean score on the NPI scale was  $58.7 \pm 2.0$  (23-106), and in the 4th week of treatment it dropped to  $13.9 \pm 1.8$  (0-64). In other words, a decrease of 76.3% was recorded in the total scores. If the decrease between pre- and post-treatment scores on the NPI scale was more than 30%, it was considered that there was a positive dynamics in the course of symptoms, and neuroleptics were effective

**Conclusions:** The study showed that neuroleptics can be prescribed to patients with vascular dementia. But at the same time, basic conditions must be observed. Treatment should begin with a low dose and gradually increase the dose over the first 4 weeks.

Keywords: vascular dementia; psychotic symptoms; delusions; hallucinations; neuroleptics

# **Introduction:**

Dementia is a disorder of the upper cortex as a result of chronic and progressive disease of the brain. As the other types of dementia, the main symptom of vascular dementia is cognitive impairment. In many cases, along with cognitive decline, non-cognitive symptoms are also observed. Although the main focus and treatment is against cognitive decline, it is the non-cognitive symptoms that bother patients and their caregivers. The frequency of non-cognitive impairments in different types of dementia is also different [1-3,5, 7,13,14]. In vascular dementia, One psychopathological symptom is observed in 81.1% of cases, and 2 or more symptoms are observed in 15% of cases. There were reports of apathy in 56.6% anxiety and agitation in 18.9% delusions in 14-27%, hallucinations in 5-14%, depression and disinhibition in 5.6%. of patients [9-12]. However, in any case, caregivers of these patients are more concerned about psychopathological symptoms than the decline in cognitive function. Psychiatrists are often consulted for these symptoms.

Basic therapy for vascular dementia both prevents and affects the development of psychotic disorders. Sometimes such psychotic symptoms can develop and worsen against the background of basic therapy [8]. To date, the use of neuroleptics is not recommended due to the etiology and pathogenesis of dementia [6]. Randomized placebo studies were not able to prove the effect of antipsychotics on behavior and psychotic symptoms. Thus, in the meta-analysis of 15 randomized studies and in the meta-analysis of 42 placebo-controlled studies, many neuroleptics were compared, and it was found that discontinuation of treatment was more common because the expected effect was not achieved [8]. Unfortunately, most of these studies were performed on patients with other types of dementia. More research is needed to investigate the use of neuroleptics in vascular dementia. Despite the relative effectiveness of neuroleptics in the treatment of behavioral problems and mental disorders in vascular dementia, we face serious safety shortcomings. Taking neuroleptics in itself increases the risk of cardiovascular complications (stroke, heart attack, lethal outcome). Also, in patients receiving neuroleptics, prolonged QT interval on the ECG, decreased cognitive function, decreased daily activity due to sedation and extrapyramidal effects, difficulty in care and deaths are observed [4]. However, in many cases, given the severity of psychotic and behavioral disorders, the use of neuroleptics is necessary by comparing risk and benefit.

# The aim of the study:

To assess the effectiveness and safety of antipsychotics for the treatment of psychosis in people with vascular dementia

# Materials and methods:

The study was conducted at the Republican Psychiatric Hospital of the Ministry of Health of the Republic of Azerbaijan in 2019-2022. The study included patients who had been treated for "vascular dementia with psychotic disorders" over the years. Patients with mild dementia and various degrees of psychotic disorders were selected according to the requirements of the study. Patients with other types of dementia who had vascular dementia and no psychotic sympathy were not included in the study. On the recommendation of the Azerbaijan Ethics Committee patients with previous diagnoses of schizophrenia, schizoaffective disorder, delirium, bipolar disorder, cognitive decline after Intracranial injury, persistent delirium, and other types of dementia were also excluded from the study.

All patients included in the study were examined by a therapist and a neurologist and, if necessary, referred to a cardiologist, endocrinologist and surgeon. A Mini-Mental State Examination scale (MMSE; Folstein et al., 1975) and Neuropsychiatric Inventory (NPI; Cummings JL et al., 1994) were completed for each patient before and 4 weeks after. The dose was reduced when side effects were observed during the study. When side effects did not end and the patient was disturbed, he/she was excluded from the study with the patient's consent. The decision to continue treatment and research during the study was voluntary by the patient and his / her relatives. He/she was excluded from the study at their request. The data were statistically processed to objectively evaluate all the data obtained. Statistical analyss were undertaken using the SPSS statistical

software version 23. Descriptive statistics were presented as mean values and stantdard deviation or percentages, according to the nature of the variable. The level of statistical significance was set at p<0.005.

## **Results of the study:**

77 patients participated in the study. All patients were diagnosed with vascular dementia (F01.x4) according to ICD-10 criteria. Their mean age was  $72.3 \pm 0.9$  (57-91). The average score of patients on the MMSI (Mini-Mental State Examination) scale was  $20.4 \pm 0.4$ . The NPI scale (NPI; Cummings JL et al., 1994) covered 12 symptoms. These included: delusions, hallucinations, aggression / agitation, depression / dysphoria, anxiety, euphoria, apathy, disinhibition (impulsive and thoughtless actions), lability, aberrant / motor behavior, sleep and nightime behavior disorders, appetite and eating disorders. First of all, it was clarified whether there were any symptoms in the last 4 weeks. If the answer was positive, the frequency of symptoms, the degree of expression, the degree of distress were evaluated [2,15-29]. Prior to treatment, the mean score on the NPI scale was  $58.7 \pm 2.0$  (23-106), and in the 4th week of treatment it dropped to  $13.9 \pm 1.8$  (0-64). In other words, a decrease of 76.3% was recorded in the total scores. If the decrease between pre- and posttreatment scores on the NPI scale was more than 30%, it was considered that there was a positive dynamics in the course of symptoms, and neuroleptics were effective. Based on this rule, the degree of expression, degree of distress and frequency of occurrence of each symptom were calculated separately. In order to more clearly observe the effectiveness of neuroleptics, it was assumed that the change in scores had a treatment effect if it was more than 30%, and that the treatment effect was small if it was less than 30%. Cases of no change in scores were also investigated. We think that such a conditional separation allows us to draw more accurate conclusions (Table 1 and 2).

Cl	1 - 6 - 11 -	- 64 - 11	0/	>30%		<30%		D	Do not change	
Scales	before	aner	%0	N=77	%	N=77	N=77 %	r	N=77	%
Scores on the NPI scale	58,7±2,0 (23-106)	13,9±1,8 (0- 64)	76,3	68	93,2	5	6,8	p<0,001	0	0,0

Circutante	hefere	- <b>6</b> t - m	0/	>30%		<30%		л	Do nott change	
Simptoms	belore	alter	%	N=77	%	N=77	%	I	N=77	%
Delusions	11,66±0,14 (4-12)	3,78±0,48 (0-12)	67,6	66	90,4	2	2,7	p<0,001	5	6,8
severity	2,91±0,06 (0-3)	1,10±0,13 (0-3)	62,3	63	86,3	0	0,0	p<0,001	10	13,7
distress	4,81±0,09 (0-5)	1,30±0,18 (0-5)	72,9	66	90,4	0	0,0	p<0,001	7	9,6
frequency	3,87±0,06 (0-4)	1,48±0,19 (0-4)	61,8	50	68,5	10	13,7	p<0,001	13	17,8
Hallucinations	3,56±0,61 (0-12)	0,78±0,29 (0-12)	78,1	23	31,5	0	0,0	p<0,001	50	68,5
severity	0,92±0,16 (0-3)	0,19±0,07 (0-3)	79,2	22	30,1	0	0,0	p<0,001	51	69,9
distress	1,48±0,26 (0-5)	0,26±0,11 (0-5)	82,4	22	30,1	0	0,0	p<0,001	51	69,9

## Table 1. Dynamics of scores on NPI

	before	after	%	>30%		<30%			Do nott change	
Simptoms				N=77	%	N=77	%	Р	N=77	%
frequency	1,13±0,20 (0-4)	0,26±0,10 (0-4)	77,0	20	27,4	2	2,7	p<0,001	51	69,9
Agitation/Aggression	6,75±0,63 (0-12)	0,56±0,26 (0-12)	91,7	44	60,3	1	1,4	p<0,001	28	38,4
severity	1,81±0,16 (0-3)	0,15±0,07 (0-3)	91,7	44	60,3	0	0,0	p<0,001	29	39,7
distress	2,81±0,26 (0-5)	0,18±0,09 (0-5)	93,7	45	61,6	0	0,0	p<0,001	28	38,4
frequency	2,19±0,21 (0-4)	0,23±0,10 (0-4)	89,4	42	57,5	1	1,4	p<0,001	30	41,1
Depression	3,14±0,54 (0-12)	1,55±0,40 (0-12)	50,7	17	23,3	3	4,1	p<0,001	53	72,6
severity	0,81±0,14 (0-3)	0,38±0,10 (0-3)	52,4	18	24,7	1	1,4	p<0,001	54	74,0
distress	1,13±0,21 (0-5)	0,45±0,12 (0-5)	60,0	19	26,0	1	1,4	p<0,001	53	72,6
frequency	1,26±0,22 (0-5)	0,70±0,18 (0-4)	44,5	12	16,4	2	2,7	p<0,001	59	80,8
Anxiety	2,57±0,56 (0-12)	0,34±0,22 (0-12)	86,7	15	20,5	1	1,4	p<0,001	57	78,1
severity	0,65±0,14 (0-3)	0,11±0,06 (0-3)	83,1	15	20,5	0	0,0	p<0,001	58	79,5
distress	1,08±0,23 (0-5)	0,18±0,10 (0-5)	83,5	15	20,5	0	0,0	p<0,001	58	79,5
frequency	0,84±0,18 (0-4)	0,10±0,07 (0-4)	88,6	15	20,5	1	1,4	p<0,001	57	78,1
Elation/Euphoria	1,38±0,42 (0-12)	0,29±0,16 (0-8)	79,1	10	13,7	0	0,0	p<0,001	63	86,3
severity	0,34±0,10 (0-3)	0,05±0,03 (0-2)	83,8	10	13,7	0	0,0	p<0,001	63	86,3
distress	0,52±0,16 (0-5)	0,07±0,04 (0-2)	86,8	10	13,7	0	0,0	p<0,001	63	86,3
frequency	0,52±0,15 (0-4)	0,16±0,09 (0-4)	68,4	8	11,0	0	0,0	p<0,001	65	89,0
Apathy/Indifference	4,26±0,59 (0-12)	3,71±0,49 (0-12)	12,9	12	16,4	7	9,6	p<0,001	54	74,0
severity	1,08±0,15 (0-3)	0,88±0,13 (0-3)	18,7	16	21,9	1	1,4	p<0,001	56	76,7
distress	1,51±0,23 (0-5)	1,03±0,15 (0-5)	31,8	19	26,0	1	1,4	p<0,001	53	72,6
frequency	1,66±0,23 (0-4)	1,81±0,23 (0-4)	8,8	5	6,8	1	1,4	p=0,039	67	91,8

	>30%		<30%				Do nott change			
Simptoms	before	after	%	N=77	%	N=77	%	Р	N=77	%
Disinhibition	3,66±0,61 (0-12)	0,60±0,27 (0-12)	83,5	22	30,1	0	0,0	p<0,001	51	69,9
severity	0,94±0,16 (0-3)	0,15±0,07 (0-3)	83,9	21	28,8	0	0,0	p<0,001	52	71,2
distress	1,47±0,25 (0-5)	0,22±0,10 (0-5)	85,1	22	30,1	0	0,0	p<0,001	51	69,9
frequency	1,26±0,21 (0-4)	0,23±0,10 (0-4)	81,5	21	28,8	0	0,0	p<0,001	52	71,2
Irritability	3,88±0,63 (0-12)	0,16±0,16 (0-12)	95,8	24	32,9	0	0,0	p<0,001	49	67,1
severity	0,97±0,16 (0-3)	0,04±0,04 (0-3)	95,8	24	32,9	0	0,0	p<0,001	49	67,1
distress	1,58±0,26 (0-5)	0,07±0,07 (0-5)	95,7	24	32,9	0	0,0	p<0,001	49	67,1
frequency	1,32±0,21 (0-4)	0,05±0,05 (0-4)	95,9	24	32,9	0	0,0	p<0,001	49	67,1
Aberrant motor behavior	7,31±0,60 (0-12)	1,36±0,36 (0-12)	81,5	44	60,3	4	5,5	p<0,001	25	34,2
severity	1,92±0,16 (0-3)	0,37±0,10 (0-3)	80,8	44	60,3	0	0,0	p<0,001	29	39,7
distress	2,91±0,25 (0-5)	0,45±0,13 (0-5)	84,5	47	64,4	1	1,4	p<0,001	25	34,2
frequency	2,47±0,20 (0-4)	0,48±0,13 (0-4)	80,6	42	57,5	3	4,1	p<0,001	28	38,4
Sleep and Nightime Behavior Disorders	10,90±0,22 (0-12)	0,62±0,28 (0-12)	94,3	68	93,2	1	1,4	p<0,001	4	5,5
severity	2,95±0,04 (0-3)	0,19±0,08 (0-3)	93,5	68	93,2	1	1,4	p<0,001	4	5,5
distress	4,78±0,09 (0-5)	0,23±0,11 (0-5)	95,1	70	95,9	0	0,0	p<0,001	3	4,1
frequency	3,29±0,09 (0-4)	0,19±0,09 (0-4)	94,2	68	93,2	1	1,4	p<0,001	4	5,5
Appetite and Eating Disorders	1,12±0,39 (0-12)	0,23±0,18 (0-12)	79,1	7	9,6	0	0,0	p<0,001	66	90,4
severity	0,27±0,10 (0-3)	0,05±0,04 (0-3)	79,9	7	9,6	0	0,0	p<0,001	66	90,4
distress	0,43±0,16 (0-5)	0,10±0,07 (0-5)	77,6	7	9,6	0	0,0	p<0,001	66	90,4
frequency	0,42±0,14 (0-4)	0,08±0,06 (0-4)	80,2	7	9,6	0	0,0	p<0,001	66	90,4

 Table 2. Dynamics of symptoms on the NPI scale

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The side effects of neuroleptics were also studied for 4 weeks. Side effects were observed in 31 (40.3%) patients. In 46 (59.7%) patients, no side effects were observed during the first 4 weeks with the minimum dose of neuroleptics. Side effects observed during treatment were: parkinsonism,

muscle weakness, hypotension, convulsions, urination, drowsiness, gait changes (Table 3). Only 8 out of 77 patients refused treatment due to side effects. The results of the treatment are presented in the table below (Table 4). (Table 7).

Side effects	N=77	%
parkinsonism	2	2,6
muscle weakness	14	18,2
Hypotension	2	2,6
Convulsions	1	1,3
Urinary incontinence	10	13
participants with somnolence	18	23,4
participants with a change in gait	12	15,6

#### Table 3. Side effects observed in patients

The result of treatment	N=77	%
recovery	19	24,7
improvement	48	62,3
no change	10	13,0
the situation has worsened	0	0,0
died	4	5,2

**Table 4.** Outcome of treatment of psychotic symptoms observed in vascular dementia.

# **Discussions:**

These result showed that, during the first 4 weeks of treatment with neuroleptics, irritability, agitation/aggression, sleep and nightime behavior disorders respond better. Based on the results, we can say that apathy is the least effective symptom of the neuroleptics used for treatment. The effect of neuroleptics on delusions and hallucinations is almost the same. However, antipsychotics are effective to varying degrees in the treatment of all non-cognitive symptoms, Since p<0.001 is for all symptoms according to statistical calculations, smaller doses have fewer side effects, resulting in fewer treatment discontinuations. It is advisable to keep the dose as small as possible even during the first 4 weeks. This will both reduce the development of side effects that can lead to treatment rejection and reduce mortality.We can say that neuroleptics have an effect in the treatment of non-cognitive symptoms. In many cases it is necessary to use neuroleptics by evaluating the phase of harm and benefit.

#### **Conclusion:**

Antipsychotics are not recommended for patients with vascular dementia. However, in many cases it is necessary to use neuroleptics by measuring the phase of harm and benefit. In this case, it is recommended to start with a small dose and gradually increase the dose. This will both reduce the development of side effects that can lead to treatment rejection and reduce mortality.

# Limitations

This study has some limitations. Despite the obvious limitation of this study due to the small number of samples, we can argue that it shows promising data.

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