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Deprescribing antipsychotics in long term care patients with dementia

Deprescripción de antipsicóticos en pacientes institucionalizados con demencia

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Abstract

Objective: To develop a clinical protocol for the use of antipsychotic drugs in dementia patients with behavioral disturbances that includes prescribing and deprescribing criteria and to assess its applicability in long-term care institutions.

Method: The protocol was developed from an interdisciplinary perspective based on a literature search of the published proposals on antipsychotic drug use in dementia patients. Its applicability to the antipsychotic deprescribing process was assessed in a single center in a prospective before-after study with a follow-up of 6 months after the intervention study.

Results: A protocol was developed that includes prescribing and deprescribing criteria. The intervention was performed in 35 patients (21 [60%] female). Antipsychotic treatment was completely withdrawn in 28 patients (80%) and was reduced to the minimum effective dose in 7 (20%). Treatment was resumed in 2 patients due to worsening symptoms. The pre- and 6-month post-test results showed that there were no significant changes in neuropsychiatric symptoms (12.91 ± 12.80 vs 13.76 ± 16.68; $P=0.124$).

Conclusions: The establishment of a protocol that includes prescribing and deprescribing criteria, in combination with the incorporation of a pharmacist in the multidisciplinary team, can be effective in improving the use of these drugs in elderly dementia patients in long-term care institutions.

Resumen

Objetivo: Elaborar un protocolo de uso de fármacos antipsicóticos en pacientes institucionalizados que presenten alteraciones conductuales que incluya criterios de prescripción y deprescripción y valorar su aplicabilidad en el ámbito de los centros sociosanitarios.

Método: El protocolo de actuación se elaboró por consenso de un equipo interdisciplinar a partir de una búsqueda bibliográfica de las propuestas publicadas sobre el uso de antipsicóticos en estos pacientes. La valoración de su aplicabilidad en la desprescripción de antipsicóticos se realizó mediante un estudio prospectivo antes-después con un seguimiento de 6 meses tras la intervención en una residencia para personas mayores dependientes.

Resultados: Se elaboró un protocolo que incluye criterios de prescripción y desprescripción de antipsicóticos. La intervención se realizó sobre 35 pacientes, 21 (60%) de las cuales eran mujeres. La retirada del tratamiento antipsicótico fue completa en 28 pacientes (80%) y se redujo a la mínima dosis eficaz en 7 (20%). El tratamiento se reinició en 2 pacientes por agravamiento de los síntomas. Los resultados de la evaluación conductual previa y a los 6 meses indicaron que no se produjeron modificaciones significativas en dichas alteraciones (12,91 ± 12,80 frente a 13,76 ± 16,68; $p=0,124$).

Conclusiones: El establecimiento de un protocolo que incluya criterios de prescripción y desprescripción, unido a la incorporación del farmacéutico en el equipo interdisciplinar, puede ser una herramienta eficaz para mejorar el uso de este tipo de medicamentos en los pacientes institucionalizados con demencia.

Introduction

Dementia is a neurodegenerative disease that affects a large number of older persons. In 2016, there were an estimated 47 million dementia patients worldwide and it has been estimated that in 2050 this figure will rise to 131 million[1]. During the course of the disease, between 20% and 30% of these patients exhibit behavioral changes[2,3]. If the dementia patient is institutionalized, these symptoms can appear in up to 80% of patients[4,5] and they become more frequent as the disease progresses[6].

The behavioral and psychological symptoms of dementia (BPSD) comprise a group of abnormalities:
- Mood disorders, such as depression, anxiety, and apathy or indifference.
- Psychotic disorders or symptoms, such as delusions and hallucinations.
- Abnormal motor behavior, such as wandering, erratic walking, or inappropriate movements.
- Inappropriate behavior, such as agitation, aggression, disinhibition, or euphoria.

These BPSD significantly affect patients, cause stress in caregivers, increase the risk of institutionalization, and decrease the quality of life[7,8].

The main clinical practice guidelines and systematic reviews recommend the use of nonpharmacological therapies as the first therapeutic option after the first appearance of these symptoms or when the patient has mild symptoms[8-11]. If the symptoms cannot be controlled, there are delusions or hallucinations, or the symptoms are so severe that they place an immense burden on the caregiver or the patient, the guidelines recommend the use of antipsychotics for their control[12]. The same guidelines also recommend starting treatment at low doses with close titration until reaching the dose needed to control the symptoms[9-12].

The use of antipsychotics to treat behavioral symptoms in dementia patients has been associated with severe adverse effects, the worsening of cognitive symptoms[13], and increased risk of mortality[8,14,15]. Regarding their efficacy, different studies have presented modest evidence of control of symptoms, such as disorientation, withdrawal, incontinence, and erratic walking[5]. For all these reasons, the clinical guidelines suggest that antipsychotic treatment should be tapered or withdrawn after 3 months to 6 months of symptom control[8,9].

Despite these suggestions, antipsychotic use in institutionalized dementia patients remains elevated and their use rate ranges from 20% to 30%[2,7,16-18]. If the patient has severe dementia their use rate can increase to 45%[17].

Several studies have addressed the issue of deprescribing antipsychotic treatment in dementia patients in different clinical situations[14,19-21]. Other studies have suggested that the use of nonpharmacological therapies may reduce antipsychotic use in institutionalized dementia patients[22], and several clinical studies have suggested that the withdrawal of antipsychotic treatment does not worsen BPSD[20,23].

Given the foregoing aspects, the main objective of this study was to develop a protocol for antipsychotic use and assess its applicability to the deprescription of these drugs in institutionalized patients with dementia.

Methods

The protocol for antipsychotic use in elderly dementia patients was designed by a multidisciplinary team comprising pharmacists specialized in hospital pharmacy working in hospital pharmacy services integrated in nursing homes, nursing home physicians, nursing coordinators, and psychologists. Firstly, a literature search was conducted of MEDLINE in English and Spanish for the period 1966 to February 2013. The search strategy included the following terms: antipsychotics, behavioral symptoms, dementia, Alzheimer's disease, elderly patient, and neuropsychiatric symptoms. After reviewing and assessing the available evidence[9,18,20,22,24], a draft protocol was proposed and examined by the multidisciplinary team in four face-to-face meetings. It was considered that consensus had been reached when each of the points of the protocol were agreed by more than 90% of the team.

To assess the applicability and efficacy of the protocol in deprescribing antipsychotic drugs in dementia patients, a prospective 1-year before-after study was conducted in a nursing home with 120 residents in the Valencian Community (Spain).

The study assessed the efficacy of tapering or withdrawing antipsychotic treatment in institutionalized dementia patients who met the deprescription criteria included in the protocol. These criteria are listed in the results section. The study included the gradual tapering of antipsychotic treatment according to the standardized deprescription guideline set out in the protocol. After the intervention, patients were followed up for 6 months, assessing variations in BPSD using the Cummings Neuropsychiatric Inventory adapted to nursing homes (NPI-NH)[25] and the need to resume treatment due to the reappearance of behavioral symptoms.

The inclusion and exclusion criteria were as follows:
- Included: elderly dementia patients treated with one or more antipsychotics who met the deprescription criteria defined in the protocol.
- Excluded: dementia patients treated with antipsychotics with delusions or hallucinations at the start of the study or who had a previous psychiatric condition.

The following variables were collected from the study population: age, sex, type of dementia, cognitive state as assessed using the Mini-examen cognoscitivo de Lobo (MEC)[26] functional status assessed using the Barthel index, and presence and intensity of BPSD using the pre- and 6-months post-intervention NPI-NH scores. Data were also collected on the type of antipsychotic used, dose, treatment duration, and indication for which it was prescribed. If treatment needed to be resumed, data were collected on the selected drug, dose, and reason for resuming treatment. Data were obtained from each resident's clinical history available in the nursing home, from the information obtained in the comprehensive geriatric assessment, and from the pharmacotherapeutic history available in the pharmacy service.

Statistical analysis

Quantitative variables are expressed as arithmetic mean, standard deviation, and minimum and maximum range. Categorical variables are expressed as frequencies. The effectiveness of the intervention was analyzed using the Student t-test for paired data using the NPI-NH scores pre- and post-intervention. All statistical analyses were conducted using the SPSS 15.0 software package (SPSS, Chicago IL).

Results

The aforementioned multidisciplinary team designed and reached a consensus on a protocol for the use of antipsychotic drugs in elderly patients with dementia and associated behavioral disorders. The protocol incorporated criteria for their prescription and deprescription. After reviewing the literature and the available evidence, the protocol was drafted and a decision algorithm was designed that includes the following points (Figure 1):
1. Discard organic/environmental causes that could potentially produce behavioral disturbances.
2. Initiate nonpharmacologic strategies established by the center's psychologist.
3. If nonpharmacological strategies are ineffective, start antipsychotic treatment, report the cases where these strategies were ineffective, and provide supporting evidence.
4. Establish the main prescription criteria for an antipsychotic as follows: the disorder is especially dangerous for the patient or caregiver; and agitation is associated with delirium or psychosis.
5. Establish antipsychotic selection criteria, initial doses, maximum doses, and minimum periods of treatment before gradually increasing doses.
6. Outline warning signs and adverse effects which will be monitored by the healthcare team during antipsychotic treatment.
7. Assess treatment effectiveness and safety after start the treatment, after dose modifications and stabilization achieved using the clinical history, NPI-NH records, and nursing and auxiliary records.
8. Establish periodic examinations once the patient has stabilized with the aim of tapering or withdrawing treatment. A 6-month period after the stabilization of symptoms was established before starting deprescription.
9. Establish selection criteria for patients with antipsychotic treatment who are suitable for the tapering or withdrawal of treatment. Inclusion criteria included were as follows:
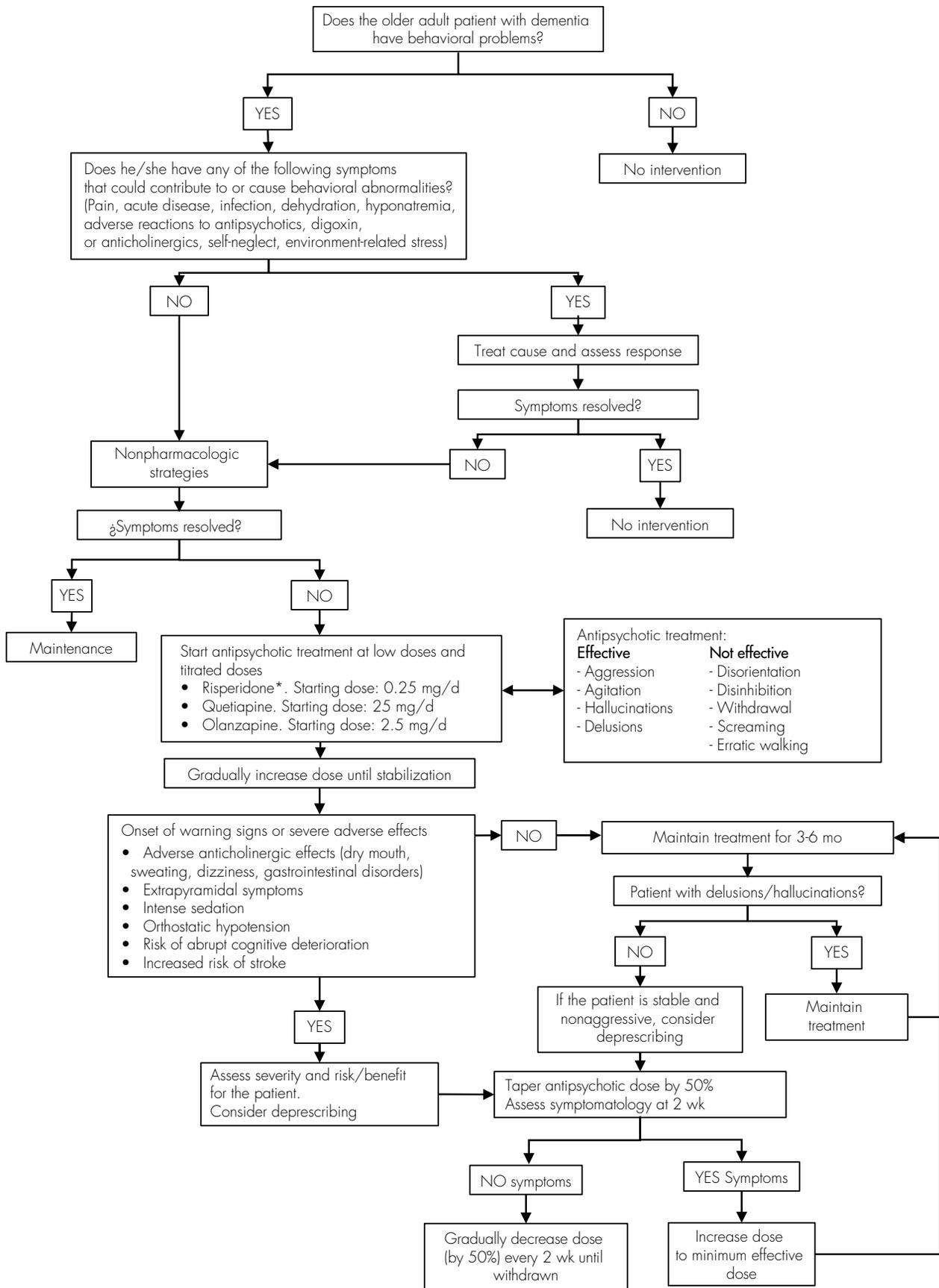   - Patients without antipsychotic treatment modification for more than one year.

Figure 1. *Algorithm for antipsychotic use in institutionalized patients with dementia. *First election drug.*

– Stable patients after 6 months of treatment.
– Patients with severe adverse reactions to antipsychotic treatment.
– Patients under treatment with a typical antipsychotic.
– Patients prescribed with more than one antipsychotic.
– Patients with advanced functional impairment and advanced dementia (stage 7 on the Global Deterioration Scale).

10. Establish standardized guidelines for tapering treatment (see Figure 1).
11. Follow up if symptoms recur. If needed, increase dose or resume antipsychotic treatment.
12. After 6 months, try deprescription again.

The outcomes of applying the antipsychotic deprescription protocol were as follows:

The deprescription criteria were met by 38 institutionalized patients residing in a nursing home with 120 residents. Of the 38 patients, 35 underwent intervention (29.1% of all the residents). Three patients were excluded because they had delusions or hallucinations at the time of the intervention. Table 1 shows the baseline characteristics of the patients. The patients who underwent intervention had a mean age of 82.31 ± 5.81 years and 21 (60%) of these patients were women. They had moderate to severe cognitive deterioration (9.74 ± 10.21) and severe dependence in relation to activities for daily living as measured using the Barthel index (33.29 ± 28.62). The participants were diagnosed with Alzheimer's disease (16 patients, 45.7%), vascular dementia (5 patients, 12.3%), and non-specific dementia (14 patients, 40%). According to the clinical history, antipsychotic treatment was prescribed for the following reasons: agitation or aggression (24 patients), insomnia (5 patients), apathy and anxiety (2 patients), and other behavioral symptoms (4 patients).

Antipsychotic treatment was withdrawn in 28 patients (80%) and treatment was tapered to the minimum effective dose in the remaining 7 patients (20%). The most commonly used antipsychotics were risperidone and quetiapine. Table 2 shows the antipsychotics to which the intervention was applied and the average number of treatment doses at the start of the intervention.

A minimum follow-up period of 6 months was established to assess the effectiveness of withdrawal of treatment, the need to resume treatment, and behavioral symptomatology pre- and post-intervention using the NPI-NH.

During the follow-up period, only 2 patients experienced a significant worsening of behavioral symptoms such that antipsychotic treatment had to be resumed. The remaining patients did not experience significant behavioral abnormalities. No statistically differences were found in symptomatology between the pre- and post-intervention periods as assessed using the NPI-NH (12.91 ± 12.80 vs 13.76 ± 16.68; P = 0.1245) (Table 3).

Table 2. Type of antipsychotic used during the intervention and average dose

Prescribed antipsychotic	No. of patients, %	Average dose, range
Risperidone	14 (40.0%)	1.2 mg/d (0.5-2.0 mg/d)
Quetiapine	10 (28.6%)	80.0 mg/d (50.0-200.0 mg/d)
Olanzapine	5 (14.3%)	5.5 mg/d (2.5-7.5 mg/d)
Haloperidol	4 (11.4%)	1.0 mg/d (0.5-2.0 mg/d)
Others	2 (5.7%)	

Table 3. Behavioral symptoms pre- and post-intervention

NPI-NH score pre-intervention	NPI-NH score post-intervention	Student t for paired data (significance)
12.91 ± 12.80	13.76 ± 16.68	P = 0.125 (Non significant)

NPI-NH: Neuropsychiatric Inventory Nursing Homes.

Discussion

This study shows the feasibility of designing and applying a consensual protocol for the use of antipsychotics in patients with dementia. The protocol incorporates data collected from the comprehensive geriatric assessment that healthcare professionals can easily obtain. This protocol follows the recommendations of the main guidelines for the use of antipsychotics in dementia patients, is adapted to the institutionalized patient care setting, and provides useful evidence-based tools[9-12]. This interdisciplinary protocol allows to evaluate residents from a multidimensional perspective.

The present study shows that the establishment of standardized criteria and guidelines for the deprescription of these medications can be effective. The results of a recent study[27] are similar to those of the present study: the tapering or withdrawal of antipsychotics in selected institutionalized patients is effective and does not cause significant behavioral changes in these patients.

The Cochrane Collaboration recently published an update on withdrawal vs continuation of antipsychotic treatment in dementia patients[28]. It suggested that patient selection and standardized criteria for the gradual tapering of dose can contribute to treatment reduction in these patients. This update suggested that deprescription may make little or no difference to overall cognitive function, has a small effect on psychological and behavioral symptoms, and that there is insufficient evidence to suggest that it may decrease mortality. The results of the present study show that there were no statistical differences in BPSD between the pre- and post-intervention periods as assessed using the NPI-NH. In addition, the results of the 6-month

Table 1. Baseline characteristics of the patients undergoing intervention and reasons for their inclusion in the deprescription protocol

	Mean ± SD n = 35 patients	Percentage n = 35 patients
Age, years	82.31 ± 5.81	
Sex:		
Men		14 (40%)
Women		21 (60%)
Cognitive state (MEC)	9.74 ± 10.21	
Activities of daily living (Barthel index)	33.29 ± 28.62	
Pre-intervention NPI-NH score	12.91 ± 12.80	
Reason for deprescription	**Number of patients**	
Patients without treatment modification at > 1 year	16	
Stable patients after 6 months treatment	7	
Severe adverse effects associated with antipsychotic treatment	6	
Patients treated with a typical antipsychotic	4	
Patients treated with > 1 antipsychotic	2	

MEC: Miniexamen cognoscitivo de Lobo; NPI-NH: Neuropsychiatric Inventory Nursing Homes; SD: standard deviation.

follow-up period showed that it was not necessary to resume or increase the dose again in 33 of 35 patients (94%). The present study did not address the effect of treatment withdrawal on cognitive capacity and therefore no conclusions can be drawn in this regard.

Systematic reviews have shown that short-term interventions to reduce inappropriate antipsychotic prescriptions in institutionalized patients can be effective. Although the results of these interventions should be confirmed by long-term studies[29], in highly dependent elderly people, such as those included in the sample, this need is a secondary priority compared to the need to match treatment to the patient's condition while optimizing patient safety. This intervention study found no significant changes in behavior after the tapering or withdrawal of antipsychotic treatment during a 6-month follow-up period.

Patients with delusions or hallucinations were excluded from the intervention. It is recommended that the treatment management of these patients should aim to reduce the dose by 6 months: however, if this is not possible, then the minimum effective dose should be maintained indefinitely[24] because of the high relapse risk in these patients compared to those who do not have this symptomatology[30].

Limitations

This study was a non-comparative interventional study with no control group, and therefore no causal relationships can be inferred. The number of patients was low and the study was conducted in a single center. Thus, although the results were satisfactory and in line with other studies[31], it may not be possible to extrapolate them to all institutionalized dementia patients. However, the results suggest the need to address the treatment of these symptoms and their periodic examination to improve treatment in elderly dementia patients.

Conclusions

The results of this study show that a multidisciplinary team can reach consensus and apply a protocol for the use of antipsychotics that includes their deprescription in institutionalized dementia patients. The establishment of criteria for deprescription, standardized withdrawal guidelines, and patient follow-up contributes to the development of a clinical protocol for the use of antipsychotic drugs in elderly institutionalized dementia patients.

Funding

Conflict of interests

No conflict of interest.

Presentation in Congresses

VI Congreso de Atención Sanitaria al paciente Crónico, organized by Sociedad Española de Medicina Interna and Sociedad Española de Medicina Familiar y Comunitaria. Seville (Spain): 27, 28, and 29 March, 2014.

Contribution to the scientific literature

Antipsychotics are used in clinical practice to control and manage behavioral and psychological symptoms that may appear throughout the course of dementia. Antipsychotic use rates are elevated in this group of patients. Once the behavioral symptoms are controlled, treatment with these drugs is typically maintained for long periods despite the main clinical guidelines for the treatment of dementia recommending their gradual reduction and withdrawal whenever possible.

The present study describes an antipsychotic prescribing and deprescribing protocol used in clinical practice. It includes guidelines on deprescribing. It also describes follow-up by a multidisciplinary team that includes a pharmacist specialized in hospital pharmacy. The study shows that the protocol is effective for the reduction and withdrawal of treatment, thereby decreasing the risk of adverse effects.

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