Digoxin prescription in geriatric patients of the primary health care

Leidys Cala-Calviño¹, MD; Sandra Casas-Gross¹, MD, MSc; Miguel E. Sánchez-Hechavarría¹, MD; Tania Hernández-Lin², MD, MSc; Deylis Jardines-Cala³, BSc; and Sibelis Calderín-Figueroa², BSc

¹ Clinical Sciences Department, Medicine Faculty Nº 1, University of Medical Sciences. Santiago de Cuba, Cuba.
² Policlínico Docente “José Martí Pérez”. Santiago de Cuba, Cuba.
³ Centro de Toxicología y Biomedicina (TOXIMED), University of Medical Sciences. Santiago de Cuba, Cuba

ABSTRACT

Introduction: Digoxin is one of the most used drugs in cardiovascular diseases, frequent in the geriatric patient, characterized by its narrow therapeutic margin.

Objectives: To characterize the prescription of digoxin and identify problems related to its prescription in geriatric patients.

Method: A descriptive and cross-sectional study was carried out on the use of drugs, indication-prescription type, in 23 patients with digoxin indication, treated at the Policlínico José Martí in Santiago de Cuba, from April to June 2017.

Results: In the case study, women (78.26%), ages between 70-74 years (26.08%), and patients with one or two associated diseases were more likely to use it. Diagnosis of cardiovascular diseases by Comprehensive General Medicine was prevalent, associated with a greater frequency of diuretics and antiplatelet drugs intervention group. The group with the lowest probability of survival was that of late treatment.

Conclusions: The prescription of digoxin may be considered as rational, although there is a possibility of drug interactions that could lead to toxic effects or therapeutic failure.

Keywords: Digoxin, Drug prescriptions, Geriatric patients, Drug interactions

Prescripción de digoxina en pacientes geriátricos de la atención primaria de salud

RESUMEN

Introducción: La digoxina es un medicamento muy empleado en algunas enfermedades cardiovasculares, que son frecuentes en el paciente geriátrico, y está caracterizada por su estrecho margen terapéutico.

Objetivo: Caracterizar la prescripción de digoxina e identificar problemas relacionados con su prescripción en pacientes geriátricos.

Método: Se realizó un estudio descriptivo y transversal, de utilización de medicamentos, de tipo indicación-prescripción, en 23 pacientes con indicación de digoxina, atendidos en el Policlínico José Martí de Santiago de Cuba, Cuba, desde abril hasta junio de 2017.

Resultados: En la casuística predominó su uso en el sexo femenino (78.26%), entre 70 y 74 años (26.08%), con una o dos enfermedades asociadas. Fue prevalente
el diagnóstico de las enfermedades cardiovasculares por especialistas de Medicina General Integral, y la indicación de digoxina se asoció con mayor frecuencia a diuréticos y antiagregantes plaquetarios.

**Conclusiones:** La prescripción de digoxina puede considerarse como racional, aunque existe posibilidad de interacciones medicamentosas, que pudieran conllevar efectos tóxicos o falla terapéutica.

**Palabras clave:** Digoxina, Prescripciones de medicamentos, Pacientes geriátricos, Interacciones medicamentosas

### INTRODUCCIÓN

Entre los objetivos de los profesionales de la salud es el uso racional de medicamentos y su promoción. Conocer cómo se utilizan es un paso necesario para promover su uso racional. A veces se prescriben medicamentos inefectivos, se selecciona el medicamento más costoso, o se inicia un tratamiento sin atención debida a medidas no farmacológicas y recomendaciones. En estos casos, nos referimos al uso irracional de medicamentos.

El aumento de la esperanza de vida junto con la disminución creciente de las tasas de natalidad ha llevado, en décadas recientes, a un aumento significativo en la población envejecida en todo el mundo. La Organización Mundial de la Salud estimó que en el año 2026, habrá alrededor de dos millones de personas mayores con problemas de dependencia, lo que duplicará la cifra actual, y específicamente en Cuba, 17% de la población es de 60 años o más.

La prevalencia e incidencia de la insuficiencia cardíaca congestiva (ISC) continúan aumentando, especialmente en la persona mayor, que es un problema geriátrico importante. En pacientes mayores, la etiopatogenia, epidemiológica y hasta las características clínicas de la ISC difieren significativamente de las encontradas en pacientes más jóvenes, pero el tratamiento aplicado deriva del resultado de ensayos clínicos con poca participación de pacientes mayores. Algunas décadas de la enfermedad, es esencial evaluar al paciente entero, poner en cuenta la interrelación entre la ISC y diferentes síndromes geriátricos de los pacientes mayores.

Muy pocos medicamentos han sobrevivido al paso del tiempo y son todavía utilizados hoy por más de un siglo: dentro de la medicación cardiovascular, sin duda, los extractos digitalis. El uso de digital es documentado desde 1785. Las infusiones de hojas de zanahoria, *Digitalis purpurea* según su taxonomía oficial, dieron paso a la extracción y purificación de los extractos digitalis, entre los que se encuentra digoxina, el digoxina y el lanatoside C, y, en menor grado, el ouabain, obtenido de otra planta, tuvo más éxito. La digoxina es uno de los medicamentos más utilizados en el corazón, debido a sus indicaciones y demostrada efectividad en algunos de estos episodios para el control de la frecuencia cardíaca. Este medicamento es caracterizado por la estrecha margen terapéutica y se considera uno de los tres medicamentos que pueden causar los efectos adversos más graves, independientemente del uso.

En el envejecimiento, la adecuación en la dosis, frecuencia y ruta de administración de los medicamentos es de suma importancia para un uso racional. En gran medida, la necesidad de adecuación se debe a los múltiples cambios fisiológicos que presentan los pacientes y su impacto en la farmacocinética y farmacodinámica de los medicamentos; ejemplo: la disminución del volumen de distribución, la disminución del flujo sanguíneo y menor metabolización, así como la eliminación.

Como parte de las recomendaciones sobre el uso de medicamentos, los llamados criterios Beers incluyen una lista de medicamentos cuyo uso se limita en la población geriátrica, o cuya dosificación debe modificarse. Relevante para hombres mayores es en este caso la digoxina. Es la responsabilidad del médico mantener una buena relación médico-paciente, que lleva tiempo para una adecuada explicación de la importancia del tratamiento, sus beneficios y riesgos, incluyendo reacciones adversas, para permitir la prescripción de medicamentos adecuados.

Con el presente estudio, se delineó para caracterizar la prescripción de digoxina y identificar problemas relacionados con la indicación de este medicamento en pacientes mayores, en asistencia primaria de salud.

### MÉTODO

Un estudio descriptivo y observacional fue realizado, concerniente al uso de medicamentos indicados en pacientes mayores, quienes fueron pre-
scribed digoxin. The population was constituted by
39 patients with digoxin prescription, controlled and
registered in the Farmacia U-646, located in the Bloque H of the Policlínico José Martí's health area
in Santiago de Cuba, from April to June 2017. A sam-
ple of 23 patients belonging to the Family Doctor’s
Office #37 of this town was selected; all the medical
certificates of the National Program of Medications
were reviewed, and the medical records of family
and individual health, from where the necessary
data were extracted, were registered in a survey
made for such purpose, as an empirical research
method.

Variables
The chosen variables were: age, sex, associated dis-
eases, diagnoses of cardiovascular diseases per-
formed by specialties, risk of therapeutic failure or
toxic effects, and groups of prescribed drugs. These
variables were properly classified and conceptual-
ized. The risks of therapeutic failure or toxicity asso-
ciated with the use of digoxin were identified ac-
cording to the disease for which it was indicated and
the comorbidities, dose and interval of prescribed
dose, as well as individuality of the prescription; in
the same way, there was taken into account any
other medication used by the patient.

Analysis and statistical processing of data
The statistical package SPSS version 23.0 was the
one used and also the percentage and the arithmetic
mean as summary measures of information. In order to
test if there was an association among the characteris-
tics of interest, the X^2 statistician was applied. All data
were expressed in contingency tables and figures, and for
report writing, theoretical analysis and synthesis and
inductive-deductive methods were employed.

Bioethical parameters
All research participants agreed and showed their
agreement by signing the informed consent model. The
study met the ethical criteria in accordance with
institutional policy and the principles of the Declara-
tion of Helsinki.

RESULTS

The female sex (18, for 78.26%) was predominant, as
well as the age group of 70-74 years (6, for 26.08%),
followed by that of 65-69 (5, for 21.73%) (Table 1).
It is worth noting that in patients under the age of 64,
the number of prescriptions is lower, for both sexes
they were made in those with more advanced ages.
These differences between the two groups were not
statistically significant (p=0.378).

As shown in Table 2, there was a predominance
of patients with only one (43.48%) or two (39.13%) associated diseases, who received pharmacological
treatment for them, together with digoxin, mean-
less from a statistical standpoint regarding sex (p=
0.062).

Diagnoses made by the Comprehensive General
Medicine specialty for all cardiovascular diseases
(Table 3) prevailed, and it is worth noting that the
Cardiology specialty only made it for one patient, for
whom digoxin was not a primary indication (6.3%),
being a cardiomyopathy without CHF. There were
no statistically significant differences among the dis-
eases described (p=0.105). It is also worth noting
that in total, there were 4 patients diagnosed with
CHF, 9 with high blood pressure (HBP) and 16 with

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N°</td>
<td>%</td>
<td>N°</td>
<td>%</td>
</tr>
<tr>
<td>55 – 59</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>60 – 64</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>65 – 69</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>70 – 74</td>
<td>6</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>75 – 79</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>80 – 84</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>85 – 90</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>5</td>
<td>23</td>
</tr>
</tbody>
</table>

Table 1. Patients with digoxin prescription according to sex and age.

Source: Survey
p=0.378
Digoxin prescription in geriatric patients

**Figure.** Patients at risk of treatment failure or toxic effects when considering the dosing interval and the prescribed dose of digoxin.

**Table 2.** Patients with digoxin prescription, according to sex and number of associated diseases with pharmacological treatment.

<table>
<thead>
<tr>
<th>Number of associated diseases</th>
<th>Female</th>
<th>Sex</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N°</td>
<td>%</td>
<td>N°</td>
<td>%</td>
<td>N°</td>
</tr>
<tr>
<td>1</td>
<td>7</td>
<td>3.04</td>
<td>3</td>
<td>13.04</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>3.04</td>
<td>2</td>
<td>8.7</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>13.04</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>More than 3</td>
<td>1</td>
<td>4.35</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>78.26</td>
<td>5</td>
<td>21.74</td>
</tr>
</tbody>
</table>

p=0.062

**Table 3.** Patients with digoxin prescription, according to diagnosis and specialty that prescribed it.

<table>
<thead>
<tr>
<th>Specialty</th>
<th>CHF Nº</th>
<th>CHF %</th>
<th>Diagnóstico HBP Nº</th>
<th>Diagnóstico HBP %</th>
<th>Other CVD Nº</th>
<th>Other CVD %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGM</td>
<td>3</td>
<td>75.0</td>
<td>8</td>
<td>88.9</td>
<td>13</td>
<td>81.2</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>1</td>
<td>25.0</td>
<td>1</td>
<td>11.1</td>
<td>2</td>
<td>12.5</td>
</tr>
<tr>
<td>Cardiology</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>6.3</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>100</td>
<td>9</td>
<td>100</td>
<td>16</td>
<td>100</td>
</tr>
</tbody>
</table>

p=0.105

CGM, Comprehensive General Medicine; CHF, congestive heart failure; CVD, cardiovascular diseases; HBP, high blood pressure.

Other cardiovascular diseases. Digoxin was prescribed to treat CHF (17.3%) and to control heart rate in patients with atrial fibrillation (AF) (13.04%), diseases for which use it is indicated. It was also indicated in patients with ischemic heart diseases (39.13%) and hypertensive heart diseases (21.7%).

The prescribed doses of digoxin were 0.25-0.125 mg/day, with a general dosage range of 24 hours. No diseases, that compromised the effect of this drug, were detected; however, 100% of the sample was exposed to drug interactions that could lead to toxic effects or therapeutic failure in 30.4% (7 patients), associated with irregular intervals dosing, 2 days at the week of rest and doses above the recommended therapeutic guidelines (Figure).

Among the most used pharmacological groups for the control of the diseases presented by the studied patients (Table 4), in general, antiplatelet agents (69.5%) and diuretics (65.2%) predominated. It draws attention that only in 1 patient of 4 with CHF, the diuretics and angiotensin-converting enzyme inhibitors (ACE inhibitors) are used. A 12.5% of antiplatelet agents and 71.4% of calcium channel blockers were used in patients with HBP.

**DISCUSSION**

Older adults present a series of physiological changes that determine alterations in the pharmacokinetic and pharmacodynamic processes of many medications of frequent prescription. This population also has a high prevalence of comorbidities, polypharmacy and prescription of potentially inappropriate medications. Aging is a natural process that involves degenerative changes, which can affect the efficacy and safety of the drugs that the patient uses. There are two important factors when choosing the best treatment: the time from the onset of symptoms and the age of the patient. This latter is of great importance, in order to contribute to reducing adverse effects and rates of hospitalization.

Lo Presti et al9 suggested that several concomitant cardiovascular diseases increase the risk of in-
interactions, and they found that the acute coronary syndrome (68.9%) and high blood pressure (12.6%) were the most frequent conditions, which was similar to a research that evaluated interactions among medications prescribed at discharge in an internal medicine department, where HBP and CHF predominated. This last, in its acute phase, is one of the most frequent causes of hospitalization and leads to difficulties in choosing the best treatment. As indicated by international guidelines, the usual therapeutic approach aims at the improvement of signs and symptoms, to correct volume overload and to improve cardiac hemodynamics in order to increase perfusion to vital organs. The recommended treatment is characterized by the use of diuretics and vasodilators, which, although alleviate symptoms, do not have a favorable influence on mortality at short and long terms.

The correct selection of a drug must be made taking into account the criteria of efficacy, safety, convenience and cost, by a qualified staff. The consumption of drugs has increased associated with the development of the pharmaceutical industry over the last 50 years and, therefore, the likelihood of unwanted effects, as well as iatrogenies caused for its misuse. On the other hand, there is a great interindividual variability in the response to drugs, due to physiological and pathological changes observed in older adults. In this sense, some authors have described that, in older ages, there is a decrease in the cerebral expenditure and regional blood flow to different organs, mainly brain, kidney and liver. Consequently, decreasing the blood flow and the hepatic mass, as well as the activity of its enzymes, can cause a fall in the metabolic capacity of the organ. Likewise, the CHF can increase this liver dysfunction. Moreover, there are drugs, such as digoxin, captopril, enalapril, atenolol and furosemide whose renal elimination may be decreased in the elderly, which may favor more intense adverse reactions in this age group.

The main indication of the digital was the CHF since its start. A better use of the drug, the background about interactions with other drugs and the need to reduce the dosage in patients with failure of the renal function, the ability to determine blood levels, disappearance of digitoxin, and obviously, decreased use of digoxin, have determined a clear

**Table 4.** Patients with digoxin prescription, according to found diagnosis and other prescribed pharmacological groups.

<table>
<thead>
<tr>
<th>Pharmacological groups</th>
<th>Diagnosis</th>
<th>Other CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CHF</td>
<td>HBP</td>
</tr>
<tr>
<td>Diuretics (n=15 [65.2%])</td>
<td>1</td>
<td>6.7</td>
</tr>
<tr>
<td>Nitrates (n=9 [39.1%])</td>
<td>1</td>
<td>11.1</td>
</tr>
<tr>
<td>CCB (n=7 [30.4%])</td>
<td>1</td>
<td>14.3</td>
</tr>
<tr>
<td>ACE inhibitors (n=7 [30.4%])</td>
<td>1</td>
<td>14.3</td>
</tr>
<tr>
<td>Antiplatelet agents (n=16 [69.6%])</td>
<td>3</td>
<td>18.8</td>
</tr>
<tr>
<td>Beta-blockers (n=2 [8.7%])</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Antiarrhythmic agents (n=1 [4.3%])</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

ACE, angiotensin-converting enzyme; CCB, calcium channel blockers; CVD, cardiovascular diseases; HBP, high blood pressure; HCF, congestive heart failure.
Digoxin prescription in geriatric patients
decrease in the incidence of digitalis toxicity. During the last decades, the treatment of CHF in adults was more aimed to treat it as associated neurohormonal changes than to improve the contractile function of the myocardium, and most recommendations are based in randomized multicenter studies. The digoxin is currently indicated in frequency controls for supraventricular tachyarrhythmias, refractory CHF to treatment with diuretics and angiotensin-converting enzyme inhibitors (ACE inhibitors) and cardiac failure. Practice guidelines relegated digital symptomatic control of CHF in patients that do not respond to other drugs that have shown themselves survival benefits. According to Scheuermeyer et al, the US guideline on CHF, of 2013 establishes, as a class IIa recommendation, that digoxin may be beneficial unless contraindicated in patients with CHF and low ejection fraction to reduce hospitalizations.

There is no doubt that the digital decreases ventricular rate and thus, improves cardiac output of the tachycardic patient. The AF is the most prevalent arrhythmia in hospital emergency, which is a disease with severe implications for double mortality and morbidity and it has a high, primarily relation with the CHF and arterial thromboembolism. Drugs that block the atrioventricular node are used as a general strategy of heart rate control, such as beta-blockers, calcium channel blockers or digoxin. According to Bonino et al, a study conducted by García López et al, in 2013, revealed that digoxin was the most used drug (42%) at the emergency department of the Hospital Obispo Polanco de Teruel, in patients with AF and CHF for the heart rate control. However, it has also been used in patients without CHF (21%), although studies suggest, as first choice, the beta-blockers or calcium channels. It is also noted that there is no evidence that the use of digoxin in patients without clinical CHF reduces morbidity and mortality of AF.

According to Scheuermeyer et al, the AF guidelines of the American College of Cardiology, American Heart Association and Heart Rhythm Society recommend, as indication I, digoxin or intravenous amiodarone for rapid control of heart rate in patients with CHF, in the absence of preexcitation; they indicate that digoxin is effective in controlling the resting heart rate in patients with CHF and reduced ejection fraction, and that it may be considered, as a class IIb recommendation, the administration of amiodarone or digoxin to slow a rapid ventricular response in patients with acute coronary and AF syndromes, associated with severe left ventricular dysfunction and CHF or hemodynamic instability. Other publications, derived from the AFFIRM and TREAT-AF studies, show opposite conclusions, since the first one found that the administration of digoxin in patients with AF can increase mortality; and the second, quite the opposite.

The dosage of this drug should be individualized according to age, renal function, severity of the condition and other factors; sometimes, it is necessary to rest two days a week for the risk of digitalis toxicity. In general, the dose in the elderly is usually lower than in younger adults. For these reasons, its contraindications, precautions, situations where it is necessary to control the blood levels and electrolyte, and drug interactions must be well known.

The gastrointestinal absorption in the geriatric patient is very similar to that of the young patient; however, the maximum plasma digoxin time lasts from 38 to 69 hours, which prolongs the time required to reach a steady state of 7 to 12 days. Likewise, it usually requires a 20% decrease in dose. For this reason, the evaluation of treated patients requires not only measurement of the plasma levels of the drug, but also an evaluation of renal function and body weight; as the renal dysfunction, reduced muscle mass and the high percentage of presenting another cardiac disorder, present in the elderly, may increase the susceptibility to the effects of this drug and the risk for digitalis toxicity.

Ortega López et al highlighted the importance of the interaction of digoxin with loop diuretics and ACE inhibitors with potassium-sparing diuretics, which can promote the occurrence of serious adverse drug reactions. Moreno Pérez et al associate this drug with ophthalmological manifestations such as dyschromatopsia (yellow-green), blurred vision and flashes, photophobia and amblyopia. On the other hand, Montoya et al state that in the SOLVD study, digoxin, together with other medications such as ACE inhibitors, diuretics and beta-blockers, contributed to improve the survival of these patients.

Some recently published studies suggest that digoxin is not associated with an increase in mortality for any reason, regardless the presence of underlying cardiac failure. All medications carry a risk of causing adverse effects. However, there are some that have a greater potential to cause problems when used by the elderly. It has been shown that inappropriate prescription in elderly people is highly prevalent but preventable.
CONCLUSIONS

The digoxin prescription is considered as rational, although there is a possibility of drug interactions, which may lead to toxic or therapeutic failure.

REFERENCES


