

Cardiovascular medication scheduling patterns in light of chronopharmacology: A descriptive nursing study

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Abstract

Objective: To describe the schedules for administering cardiovascular medications in light of chronopharmacology.

Materials and methods: This prospective, cross-sectional, and descriptive study reviewed the medication records of adult patients discharged from a hospital ward who received systemic cardiovascular drugs prescribed once daily.

Results: A total of 753 once-daily prescriptions were analyzed across seven therapeutic drug groups. Most medications were scheduled for morning administration, with 08:00 being the most frequent time. Statins were administered almost exclusively at night, whereas diuretics, beta-blockers, and angiotensin II receptor antagonists were mainly given in the morning. Notable variation was observed within medication groups, indicating the lack of chronopharmacological criteria in the scheduling.

Conclusions: The administration of once-daily cardiovascular medications showed distinct timing patterns across therapeutic groups, with variability even among drugs within the same group, highlighting the lack of systematic chronopharmacological criteria for their scheduling. These results underscore the importance of integrating chronopharmacology into nursing practice to promote safer, more effective administration of cardiovascular medications and to strengthen evidence-based decision-making in pharmacological care.

Descriptors: Chronotherapy; Drug Chronotherapy; Circadian Rhythm; Cardiovascular Drugs; Nursing (source: DeCS, BIREME).

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Patrones de programación de medicamentos cardiovasculares a la luz de la cronofarmacología: estudio descriptivo de enfermería

Resumen

Objetivo: describir los horarios de administración de los medicamentos cardiovasculares a la luz de la cronofarmacología.

Metodología: estudio prospectivo, transversal y descriptivo. Se analizaron tarjetas de medicamentos de pacientes adultos que egresaron de un servicio de hospitalización y recibieron fármacos cardiovasculares de administración sistémica en régimen de una sola dosis diaria.

Resultados: se analizaron 753 prescripciones de medicamentos cardiovasculares administrados una vez al día, distribuidas en siete grupos terapéuticos. La mayoría de los fármacos se programaron en horarios matutinos y las 8:00 fue la hora más frecuente. Las estatinas se administraron casi exclusivamente en la noche, mientras que los diuréticos, los bloqueadores beta y los antagonistas del receptor de angiotensina II mostraron una marcada preferencia por la mañana. Se observaron variaciones significativas entre los medicamentos de cada grupo, lo que evidencia la ausencia de criterios cronofarmacológicos en la programación.

Conclusiones: la administración de medicamentos cardiovasculares una vez al día presentó patrones temporales diferenciados según el grupo terapéutico, con variabilidad entre fármacos de un mismo grupo, lo que evidencia la ausencia de criterios cronofarmacológicos sistemáticos en su programación. Estos resultados destacan la importancia de integrar la cronofarmacología en la práctica de enfermería para favorecer una administración más segura y eficaz de los medicamentos cardiovasculares y para fortalecer la toma de decisiones basada en la evidencia del cuidado farmacológico.

Descriptor: Cronoterapia; Cronoterapia de Medicamentos; Ritmo Circadiano; Fármacos Cardiovasculares; Atención de Enfermería (fuente: DECS, BIREME).

Padrões de programação de medicação cardiovascular à luz da cronofarmacologia: um estudo descriptivo de enfermagem

Resumo

Objetivo: Descrever os horários para a administração de medicamentos cardiovasculares à luz da cronofarmacologia.

Metodologia: Este estudo prospectivo, transversal e descriptivo revisou os registros de medicamentos de pacientes adultos egressos de uma enfermagem hospitalar que receberam medicamentos cardiovasculares sistêmicos prescritos uma vez ao dia.

Resultados: Um total de 753 prescrições de dose única diária foi analisado em sete grupos terapêuticos de medicamentos. A maioria dos medicamentos foi programada

para administração matinal, sendo às 8h o horário mais frequente. As estatinas foram administradas quase exclusivamente à noite, enquanto diuréticos, betabloqueadores e antagonistas dos receptores da angiotensina II foram administrados principalmente pela manhã. Observou-se variação notável dentro dos grupos de medicamentos, indicando a ausência de critérios cronofarmacológicos no agendamento.

Conclusões: A administração de medicamentos cardiovasculares de dose única diária apresentou padrões de administração distintos, dependendo do grupo terapêutico, com variabilidade até mesmo entre medicamentos do mesmo grupo, evidenciando a falta de critérios cronofarmacológicos sistemáticos em sua programação. Esses resultados reforçam a importância da integração da cronofarmacologia à prática de enfermagem para promover uma administração mais segura e eficaz de medicamentos cardiovasculares e fortalecer a tomada de decisões baseada em evidências no cuidado farmacológico.

Descritores: Cronoterapia; Cronofarmacoterapia; Ritmo Circadiano; Fármacos Cardiovasculares; Enfermagem (fonte: DECS, BIREME).

Introduction

Biological rhythms are periodic fluctuations in physiological and behavioral processes, classified as circadian (24 h), ultradian (<24 h), and infradian (>24 h). They are regulated by internal biological clocks, the most important of which is the suprachiasmatic nuclei of the hypothalamus, which coordinate other clocks in organs such as the liver, intestine, and kidney through hormonal and neural signals (1, 2).

Biological rhythms influence the expression of genes that regulate pharmacokinetics and therapeutic targets, thereby affecting plasma drug concentrations, pharmacological effects, and treatment response. Therefore, the timing of drug administration can impact therapeutic efficacy (3).

Even when specific drug characteristics, chronotype, or individual variability are not considered, circadian rhythms are known to modulate key pharmacokinetic processes (2, 4). Fluctuations in gastrointestinal motility, enzyme secretion, pH levels, and membrane transporters affect drug absorption and bioavailability. Drug distribution is influenced by variations in blood flow, plasma protein expression such as albumin and α 1-acid glycoprotein, and tissue permeability (4). Metabolic processes also follow circadian patterns, particularly those mediated by the activity and expression of cytochrome P450 enzymes, which affect the biotransformation of prodrugs and active pharmaceutical ingredients (4–7). Finally, hepatobiliary and renal excretion demonstrate rhythmicity due to variations in transporter expression, renal blood flow, glomerular filtration, tubular secretion, reabsorption, and urinary pH (4).

Biological rhythms also influence the incidence and severity of cardiovascular events, as well as the onset or exacerbation of symptoms, which has given rise to the concept of chronotherapy: administering drugs at specific times of the day to synchronize their effects with periods of higher risk. For example, the risk of angina, myocardial infarction, sudden death, ischemic stroke, arrhythmias, and aortic dissection increases in the morning due to increased sympathetic activity and blood pressure. Conversely, heart failure, vasospastic angina, vagotonic atrial fibrillation, and Brugada syndrome worsen during sleep due to parasympathetic predominance (8–10).

Nevertheless, in clinical practice, drugs are often administered according to standardized routines, with little consideration for biological rhythms. Furthermore, pharmaceutical product information rarely provides guidance on optimal dosing times (11).

In the hospital where this study was conducted, as in many other hospitals across Colombia, nursing professionals are responsible for planning and selecting medication administration schedules. Therefore, knowledge of specific chronopharmacological principles may support clinical decision-making regarding the most appropriate time of day to administer certain medications, contributing to therapeutic optimization, improved adherence, and reduced risks associated with medication use, such as adverse effects or suboptimal therapeutic outcomes (3).

In Colombia, Law 911 of 2004 (12) requires nursing professionals to ensure safe, high-quality care. In the context of cardiovascular diseases, this responsibility is heightened by the risks associated with inappropriate administration and dosing times outside those indicated by chronotherapy. This study describes the schedules and patterns of cardiovascular drug administration in hospitalized adults, with a focus on chronopharmacology, providing valuable information for nursing professionals. Beyond its technical aspects, this work highlights the importance of scientific knowledge in managing therapeutic plans and achieving clinical objectives (13–15).

Materials and methods

This was a prospective, cross-sectional, descriptive study conducted in the adult general hospitalization service of a high-complexity hospital in Colombia, intended for patients who did not require care in critical or intermediate units or specialized care. The study analyzed medication records of adult patients who received systemic cardiovascular drugs prescribed once daily.

The inclusion criteria were medication records of adult patients discharged between October 2023 and April 2024, who at the time of hospital discharge were actively treated with systemically administered drugs of conventional biopharmaceutical design, prescribed on a once-daily regimen, from the following pharmacological groups: beta-adrenergic blockers, calcium channel blockers, angiotensin II receptor blockers (ARBs), angiotensin-converting enzyme (ACE) inhibitors, statins, antiplatelets, oral anticoagulants, and diuretics.

The exclusion criteria were medication cards that were in poor condition, had incomplete scheduling, or lacked clarity regarding the pharmacological intervention, particularly where medication changes or discontinuations were not properly documented.

During the observation period, cards completed exclusively by nursing professionals were collected, and a database was created with medication name, administration route, number of doses, and scheduled times. Each patient card was assigned an ID based on the registration date. Only drugs with a daily dose were included because they are more sensitive to biological rhythms (16).

Data were recorded in Excel and imported into SPSS version 25 (IBM, Armonk, NY, USA). An exploratory analysis was conducted to determine the treatment of variables, followed by a descriptive analysis using frequencies and percentages for categorical variables. For the time-based analysis, three time intervals were defined: morning (6:00–12:00), afternoon (13:00–18:00), and night (19:00–5:00) (17, 18).

This research was approved by the Research and Ethics Committee of the participating institutions. It adhered to ethical principles that safeguard human dignity and well-being and uphold the rights enshrined in the Colombian Political Constitution and the participants' legal rights. According to Resolution 8430 of 1993 (19) of the Colombian Ministry of Health, this research was classified as risk-free.

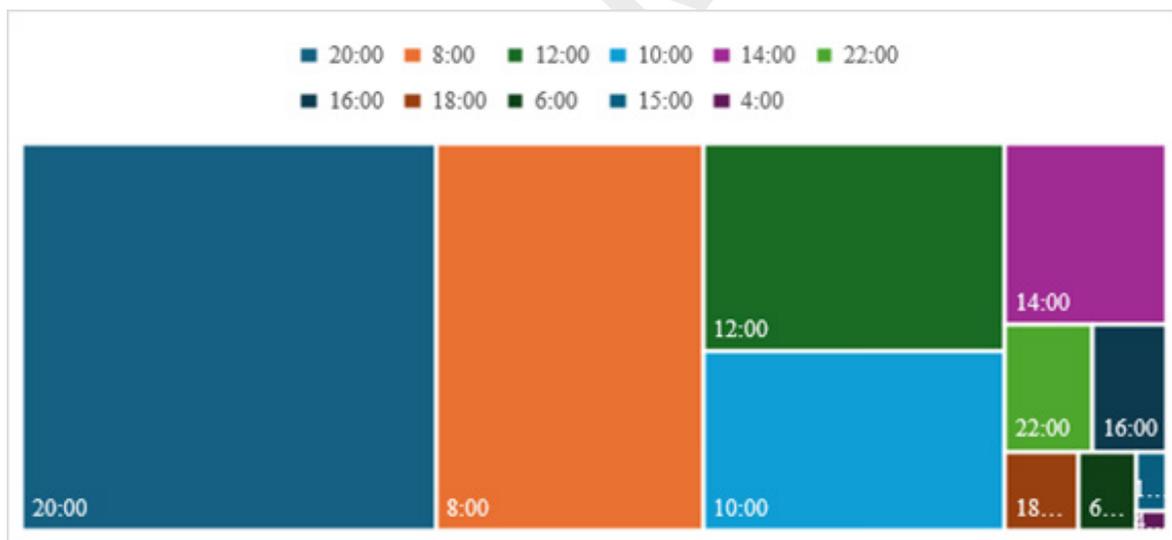
Consensus AI was used to support the literature search on chronopharmacology, and each source was manually verified. In addition, ChatGPT was used solely to improve the writing and was not employed to generate original scientific content or results.

Results

A total of 753 prescriptions for once-daily cardiovascular medications were analyzed. The prescriptions were distributed across seven therapeutic groups as follows: 69 for beta-blockers, 55 for calcium channel blockers, 46 for ARBs, 23 for ACE inhibitors, 249 for statins, 142 for antiplatelet and anticoagulant medications, and 169 for diuretics.

In the mosaic plot (Figure 1), each block represents a specific time slot, with block size indicating the proportion of medications administered during that period. The 08:00 time slot was the most frequently scheduled. However, when considering absolute frequencies and the high number of statin prescriptions, 20:00 had the greatest number of scheduled doses. In contrast, 15:00, 04:00, and 06:00 had very low scheduling frequencies.

Figure 1. Distribution of scheduled medication administration times



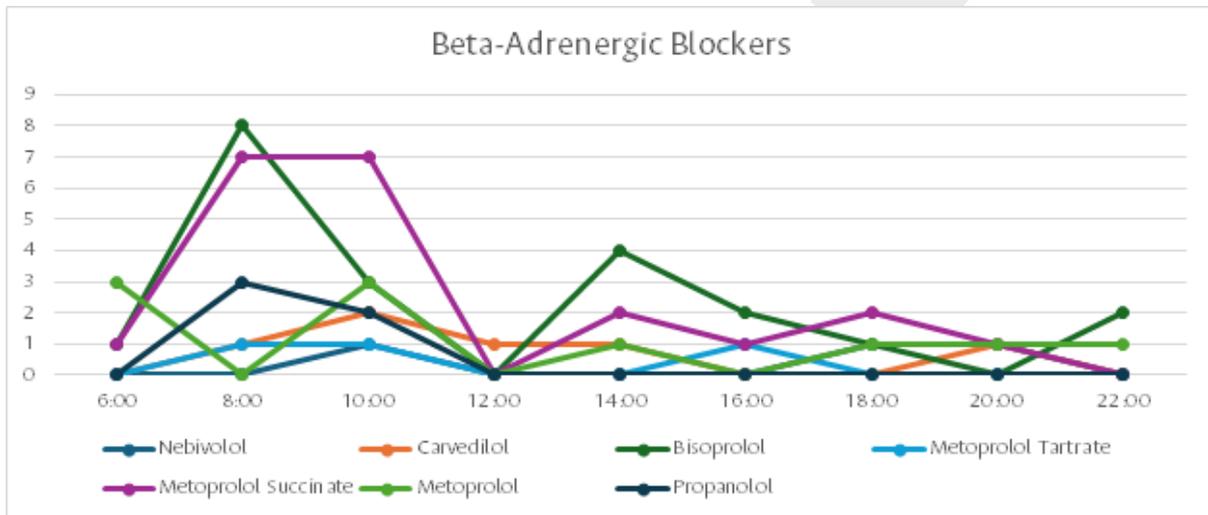
Note. Each block represents a specific time slot, and its size indicates the proportion of medications administered during that period.
Source: authors.

Figures 2–8 present a detailed breakdown of the scheduled administration times for each medication included in the study. For analysis by therapeutic group, the data were presented in heat charts to facilitate visualization of the administration schedules for each medication.

Beta-adrenergic blockers (Figure 2)

Metoprolol succinate and bisoprolol were the most frequently prescribed beta-blockers, followed in smaller numbers by metoprolol, carvedilol, propranolol, nebivolol, and metoprolol tartrate (Table 1). Considerable variation in administration times was observed among some of these beta-adrenergic blockers. For example, metoprolol succinate was mainly prescribed in the morning (71.4%), with 23.8% scheduled in the evening and 4.8% at night. Bisoprolol was prescribed more evenly, with 57.1% scheduled in the morning, approximately one-third in the evening, and almost 10% at night. Metoprolol showed similar dispersion, with 20% of prescriptions scheduled in both the evening and nighttime periods. In contrast, propranolol was scheduled exclusively in the morning in 100% of cases, suggesting greater consistency in clinical practice for this agent.

Figure 2. Schedules for cardiovascular medications on a once-daily regimen with beta-adrenergic blockers



Source: authors.

Table 1. Beta-adrenergic blockers heat chart

Time range	n	Morning 6-12	Afternoon 13-18	Night 19-5	Color Scale
Nebivolol	3	33.3	33.3	33.3	
Carvedilol	6	66.7	16.7	16.7	86
Bisoprolol	21	57.1	33.3	9.5	71
Metoprolol Tartrate	3	66.7	33.3	0.0	57
Metoprolol Succinate	21	71.4	23.8	4.8	43
Metoprolol	10	60.0	20.0	20.0	29
Propranolol	5	100.0	0.0	0.0	14
Average adjusted by n	69	65.2	17.0	12.0	0

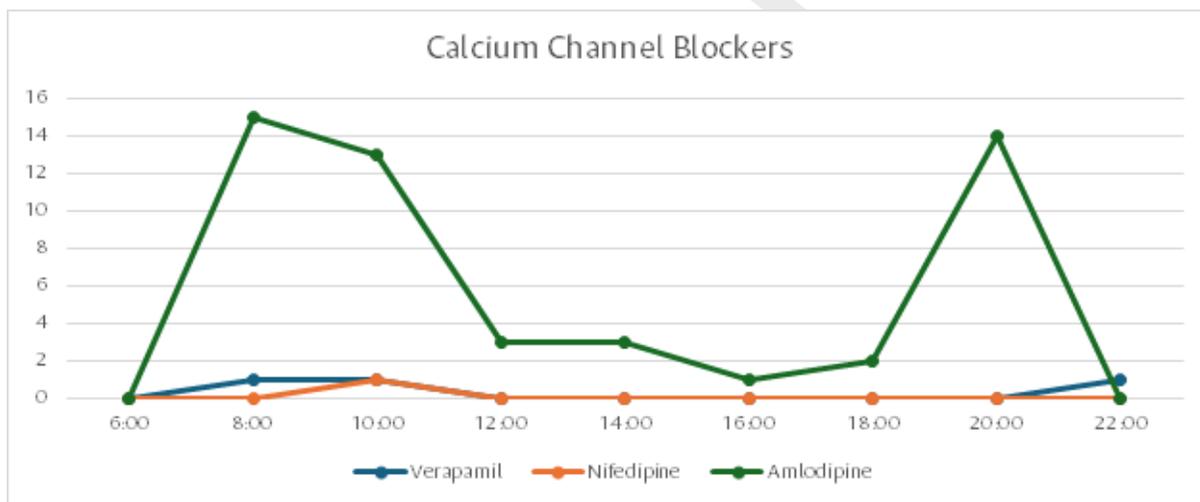
Source: authors.

The timing of beta-blocker administration showed a general tendency toward morning use, with a sample-size-adjusted mean of 65.2% in this interval. Within this group, the most frequent times were 08:00 (50%) and 10:00 (41.3%). In contrast, administration after 18:00 was generally less frequent for the beta-adrenergic blocker group (12%).

Calcium channel blockers (Figure 3)

Of the 55 patients treated with calcium channel blockers, the majority (51 patients) received amlodipine. Verapamil and nifedipine were prescribed for three and one patient(s), respectively (Table 2). Nifedipine was scheduled between 6:00 and 12:00, and amlodipine showed the widest variation in administration times, ranging from 8:00 to 20:00. However, a preference for morning administration was evident: 60.8% of prescriptions were scheduled between 6:00 and 12:00 and 27.5% were scheduled for 20:00. Verapamil administration also varied somewhat; however, two of the three prescriptions were scheduled between 6:00 and 12:00 (66.7%).

Figure 3. Schedules for cardiovascular medications on a once-daily regimen with calcium channel blockers

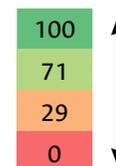


Source: authors.

Table 2. Calcium channel blockers heat chart

Time range	n	Morning	Afternoon	Night
		6-12	13-18	19-5
Verapamil	3	66.7	0.0	33.3
Nifedipine	1	100.0	0.0	0.0
Amlodipine	51	60.8	11.8	27.5
Average adjusted by n	55	75.8	3.9	20.3

Color Scale



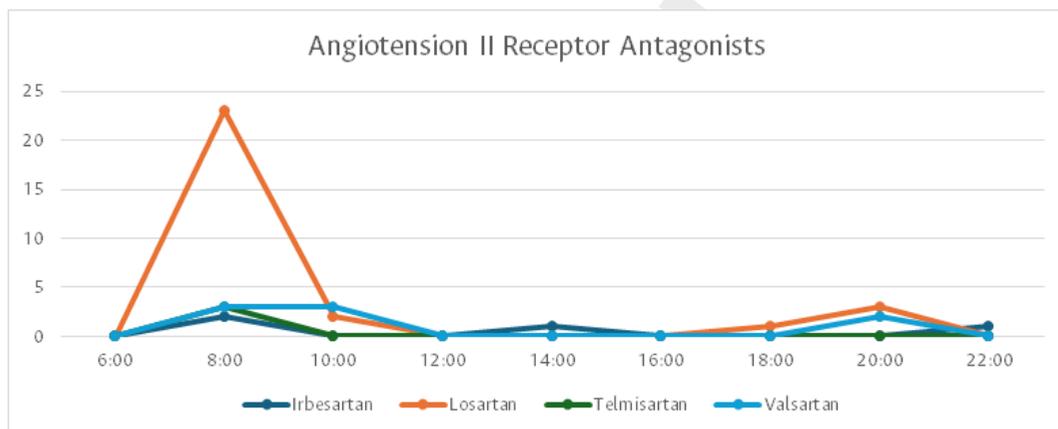
Source: authors.

In the overall analysis of calcium channel blocker scheduling, a trend toward morning administration was observed, with a sample-adjusted average of 75.8%. Within this interval, the most frequently scheduled times were 8:00 (47.06%) and 10:00 (44.12%). Nighttime administration (19:00–05:00) accounted for 20.3% of prescriptions, based on the sample-adjusted average, with 20:00 being the most frequently scheduled time.

Angiotensin II receptor antagonists (Figure 4)

Losartan was the most frequently prescribed medication in this group, followed by valsartan, irbesartan, and finally, telmisartan (Table 3). All telmisartan prescriptions were scheduled for the morning, and a similar pattern was observed for losartan (86.2%), valsartan (75%), and irbesartan (66.7%). Overall, 82.6% of ARBs were scheduled in the morning, with 08:00 being the predominant time, and nighttime administration was low (13%).

Figure 4. Schedules for cardiovascular medications on a once-daily regimen with angiotension II receptor antagonists



Source: authors.

Table 3. Angiotensin II receptor antagonists heat chart

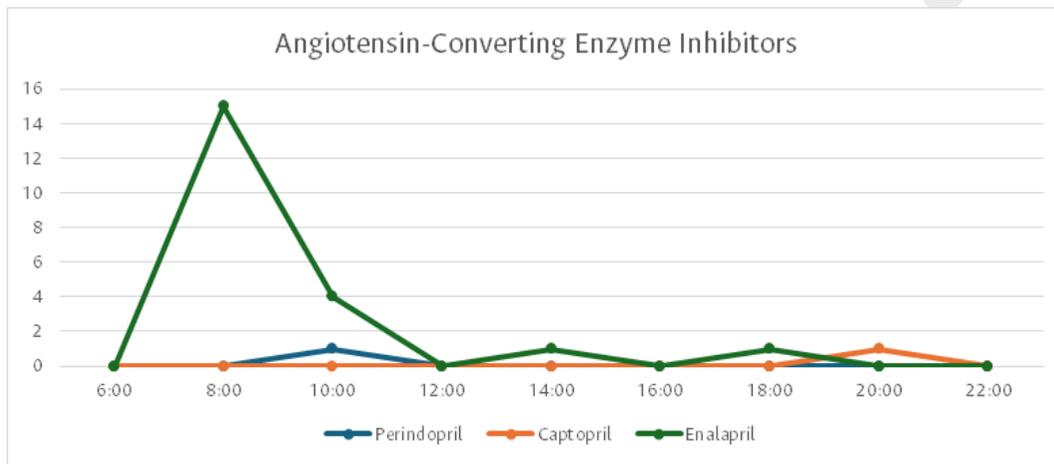
Time range	n	Morning	Afternoon	Night	Color Scale
		6-12	13-18	19-5	
Irbesartan	6	66.7	16.7	16.7	
Losartan	29	86.2	3.4	10.3	
Telmisartan	3	100.0	0.0	0.0	
Valsartan	8	75.0	0.0	25.0	
Average adjusted by n	46	82.6	4.3	13.0	

Source: authors.

Angiotensin-converting enzyme (ACE) inhibitors (Figure 5)

Enalapril was the most frequently prescribed ACE inhibitor, followed by perindopril and captopril (Table 4). Perindopril was scheduled at 10:00, whereas captopril was scheduled at 20:00. Among patients treated with enalapril, 90.5% had their medication scheduled between 06:00 and 12:00, with 08:00 being the most frequent time (71.42%). Overall, ACE inhibitor scheduling showed a tendency toward morning administration (87%).

Figure 5. Schedules for cardiovascular medications on a once-daily regimen with angiotensin-converting enzyme inhibitors



Source: authors.

Table 4. Angiotensin-converting enzyme inhibitors heat chart

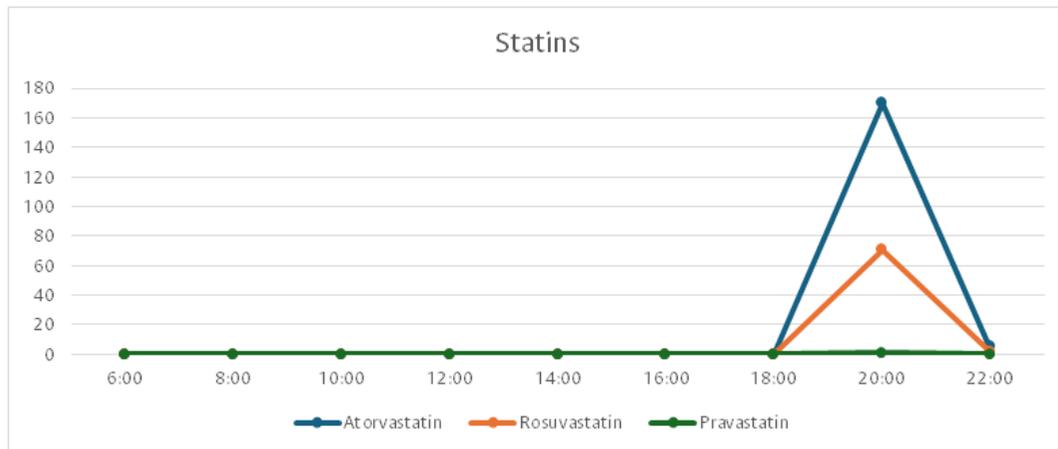
Time range	n	Morning	Afternoon	Night	Color Scale
		6–12	13–18	19–5	
Perindopril	1	100.0	0.0	0.0	<div style="display: flex; align-items: center;"> <div style="width: 20px; height: 20px; background-color: #4CAF50; margin-right: 5px;"></div> 100 <div style="width: 20px; height: 20px; background-color: #FFC107; margin-right: 5px; margin-left: 10px;"></div> 67 <div style="width: 20px; height: 20px; background-color: #FF9800; margin-right: 5px; margin-left: 10px;"></div> 33 <div style="width: 20px; height: 20px; background-color: #F44336; margin-right: 5px; margin-left: 10px;"></div> 0 </div>
Captopril	1	0.0	0.0	100.0	
Enalapril	21	90.5	4.8	4.8	
Average adjusted by n	23	87.0	4.3	8.7	

Source: authors.

Statins (Figure 6)

Atorvastatin was the most frequently prescribed statin, followed by rosuvastatin and pravastatin (Table 5). Dosing was scheduled exclusively at night, with negligible variability in timing. For atorvastatin, 97.14% of prescriptions were scheduled for 20:00, with the remaining 2.86% scheduled for 22:00. Similarly, 97.26% of rosuvastatin prescriptions were scheduled for 20:00, with the remaining 2.74% scheduled for 22:00. The single pravastatin prescription in the dataset was scheduled for 20:00.

Figure 6. Schedules for cardiovascular medications on a once-daily regimen with statins



Source: authors.

Table 5. Statins heat chart

Time range	n	Morning	Afternoon	Night	Color Scale
		6-12	13-18	19-5	
Atorvastatin	175	0.0	0.0	100.0	
Rosuvastatin	73	0.0	0.0	100.0	
Pravastatin	1	0.0	0.0	100.0	
Average adjusted by n	249	0.0	0.0	100.0	

Source: authors.

Antiplatelets and anticoagulants (Figure 7)

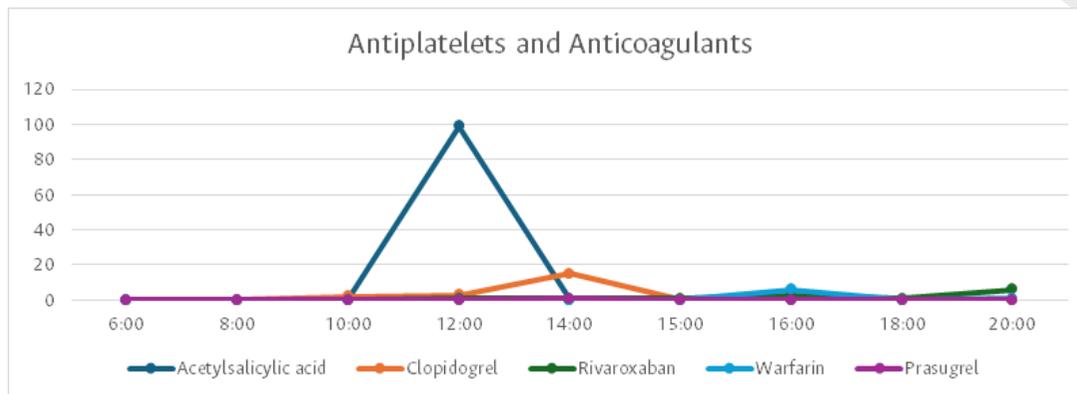
Acetylsalicylic acid was the most frequently prescribed agent in this group, followed by clopidogrel, rivaroxaban, warfarin, and prasugrel (Table 6). A standardized schedule for administering acetylsalicylic acid was observed, with all prescriptions set for 12:00. Clopidogrel showed some variation, with the most common administration time at 14:00 (68.18%). Rivaroxaban showed greater dispersion in scheduled times, with the highest frequencies at 16:00 (23.07%) and 20:00 (46.15%). Warfarin scheduling showed low variability, with 85.7% administered at 16:00, and the single prasugrel prescription was scheduled for 14:00. This group of medications showed a clear scheduling trend between 13:00 and 18:00, accounting for 61.8% of prescriptions.

Diuretics (Figure 8)

Furosemide was the most frequently prescribed diuretic, followed by spironolactone, hydrochlorothiazide, chlorthalidone, and indapamide (Table 7). A preference for morning administration was observed, though with some variability, particularly in prescribing furosemide and hydrochlorothiazide. Among patients receiving furosemide, the most frequent times were 08:00 (63.75%) and 14:00 (23.75%). For spironolactone, the highest frequencies were observed at 08:00 (52.17%)

and 10:00 (45.65%). Hydrochlorothiazide was also predominantly scheduled for 08:00 (47.36%) and 10:00 (44.73%). Overall, for diuretics, a trend toward morning administration was observed, with 87.1% being scheduled between 06:00 and 12:00.

Figure 7. Schedules for cardiovascular medications on a once-daily regimen with antiplatelets and anticoagulants



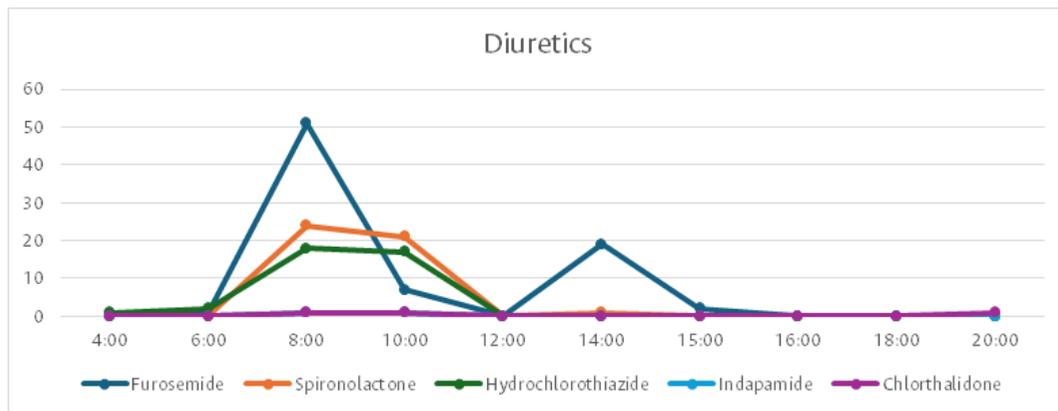
Source: authors.

Table 6. Antiplatelets and anticoagulants heat chart

v	n	Morning 6-12	Afternoon 13-18	Night 19-5	Color Scale
Acetylsalicylic acid	99	100.0	0.0	0.0	100
Clopidogrel	22	22.7	77.3	0.0	80
Rivaroxaban	13	7.7	46.2	46.2	60
Warfarin	7	0.0	85.7	14.3	40
Prasugrel	1	0.0	100.0	0.0	20
Average adjusted by n	142	26.1	61.8	12.1	0

Source: authors.

Figure 8. Schedules for cardiovascular medications on a once-daily regimen with diuretics



Source: authors.

Table 7. Diuretics heat chart

Time range	n	Morning 6-12	Afternoon 13-18	Night 19-5	Color Scale
Furosemide	80	73.8	26.3	0.0	
Spironolactone	46	97.8	2.2	0.0	80
Hydrochlorothiazide	38	97.4	0.0	2.6	60
Indapamide	2	100.0	0.0	0.0	40
Chlorthalidone	3	66.7	0.0	33.3	20
Average adjusted by n	169	87.1	5.7	7.2	0

Source: authors

Discussion

Chronopharmacology in real-world hospital practice

This study examined the time distribution and frequency of medication administration in hospitalized adults, specifically medications used for cardiovascular diseases due to their high morbidity and mortality both in Colombia and globally (20, 21). There is growing evidence that the time of day can influence plasma drug concentrations, biological responses, and both the expected and adverse effects of certain drugs (22, 23). However, this evidence does not account for interindividual factors such as age, sex, underlying pathologies, metabolic status, transporter protein levels, organ function, chronotype, or other variables that affect pharmacokinetics and pharmacodynamics (24–27).

Analysis of medication cards showed variable scheduling across several drugs, with a general trend toward morning administration (Figure 1), except for statins, which were administered exclusively at night. This tendency may be more driven by institutional dynamics, such as the start of the working day, patient admissions, and nursing shift changes at 06:00, than by chronobiological

considerations. From a behavioral perspective, the start of the day is associated with greater cognitive and operational activation, which favors the execution of clinical tasks, such as medication administration, guided by logistical criteria rather than by the circadian rhythm (28).

A critical comparison of the study's findings with scientific evidence revealed both similarities and discrepancies regarding the ideal timing of cardiovascular medication administration to optimize pharmacological intervention and patient safety. Although the evidence is inconclusive, the reviewed studies primarily compare nighttime administration with other times of day, evaluating their effect on LDL (statins), platelet aggregation and coagulation (antiplatelets and anticoagulants), blood pressure, cardiovascular risk, and target organ protection (antihypertensives).

The study was conducted in a hospital setting, allowing for the evaluation of the timed administration of cardiovascular drugs under controlled conditions. This is relevant, as factors such as care routines, nutrition, and sleep influence chronopharmacology. These conditions differ from those in the outpatient setting, where adherence to schedules and lifestyle factors may influence medication effectiveness (29).

Several studies on the optimal timing of antihypertensive drug administration have focused on blood pressure control and cardiovascular risk reduction. Clinical outcomes are often analyzed in non-dipper patients, classified by dipping status: extreme dippers ($\geq 20\%$), dippers (10% to $< 20\%$), non-dippers (0% to $< 10\%$), and reverse dippers ($< 0\%$). Selecting non-dippers as the reference group is likely because they have higher cardiovascular risk, making them an appropriate population for comparing nocturnal administration with other dosing times (30, 31). In addition, although to a lesser extent, some studies have evaluated biomarkers of myocardial and endothelial function and platelet activation as complementary indicators of efficacy, particularly at the time of administration, especially in target organs (32, 33).

Clinical evidence versus real-world drug scheduling

In our study, beta-blockers were mostly scheduled in the morning, although timing varied notably, especially among the most frequently prescribed agents. Nebivolol, one of the least commonly used, was administered evenly throughout the day, suggesting no consistent scheduling pattern, possibly due to a lack of standardized clinical criteria.

Studies by Dharani *et al.* (34) and Zaslavskaya *et al.* (35) identified clinical benefits with morning administration of metoprolol succinate, whereas propranolol and carvedilol showed better results at night. Using a pharmacokinetic–pharmacodynamic model, Cortés and Rodríguez (36) observed greater blood pressure control and cardiovascular protection with nighttime propranolol. Hermida *et al.* (37) also reported greater benefit with carvedilol administered at night.

In the calcium channel blocker group, amlodipine accounted for the majority of prescriptions, whereas verapamil and nifedipine were prescribed in very low proportions, limiting comparative analysis. Amlodipine showed wide hourly variability, with a predominance in the morning but also a considerable proportion scheduled at 20:00. In contrast to our findings, a meta-analysis concluded that nighttime administration of amlodipine was more effective in non-dipper patients, with better control of 24-hour mean arterial pressure (38). Similarly, Khalisah *et al.* (38) and Khodadoustan *et al.* (39) reported greater benefit with nighttime administration, but Lubada *et al.* (40) observed therapeutic equivalence between morning and nighttime administration in patients with primary hypertension.

For verapamil, greater blood pressure reduction was observed with nighttime administration, as reflected by a notable difference in morning indices (41).

The study found that ARBs were predominantly prescribed for morning administration, especially losartan, which accounted for the majority of prescriptions. However, telmisartan and irbesartan were underprescribed, limiting the ability to draw firm conclusions about their specific timing compared with the available evidence.

Previous research indicates that dosing time can influence ARB efficacy, especially in patients with non-dipper hypertension. Yan *et al.* (42) observed that nighttime administration of irbesartan combined with other antihypertensives improved nocturnal blood pressure control. Similarly, Huangfu *et al.* (43) reported that losartan with indapamide, administered at night, more effectively modulated morning blood pressure surge.

The findings for telmisartan were mixed: Rekovets *et al.* (44) reported greater efficacy with morning dosing, whereas Agarkov *et al.* (45) reported better blood pressure control and reversal of the non-dipper pattern with nighttime dosing. Zhang *et al.* (46) also concluded that nighttime dosing was more effective in reducing nocturnal blood pressure.

Zappe *et al.* (47) observed no substantial difference in the efficacy of valsartan between morning and evening administration. Fujiwara *et al.* (48), evaluating valsartan/amlodipine, observed sustained 24-hour control with both regimens, with a slight morning superiority in reducing nocturnal central systolic blood pressure. In contrast, Cortés-Ríos and Rodríguez-Fernández (49) concluded that nighttime administration was more effective in reducing nocturnal blood pressure, morning surge, and systemic vascular resistance.

Within the ACE inhibitor group, captopril and perindopril had only one prescription each. Enalapril was the most prescribed, enabling analysis of its predominantly morning schedule. However, studies such as that by Devangi Dharani *et al.* (34) reported a nighttime preference for ACE inhibitors in hospitalized patients, due to their greater efficacy during sleep and in the early morning. Similarly, nighttime administration of enalapril has been shown to improve blood pressure control (48), with Cortés and Rodríguez reporting that, although it can be administered at either time of day, better nocturnal blood pressure reduction is achieved when administered in the evening (49). Hermida *et al.* observed that the nighttime regimen can also reduce major cardiovascular events (50).

Agent-specific evidence is limited, preventing a comparison of all findings. However, studies with various drug groups that evaluated the ideal time of day for administering antihypertensives, including systematic reviews and meta-analyses, showed that nighttime administration can more effectively reduce systolic blood pressure, cardiovascular events, heart failure, mortality, and ambulatory blood pressure parameters than morning administration (31, 51–54).

In contrast, other studies question the widespread benefits of administering antihypertensives at night. Wu *et al.* (55), who evaluated nebivolol, metoprolol, and propranolol, concluded that the evidence is of low quality and nighttime superiority cannot be affirmed. The Harmony trial found no notable differences between dosing schedules but suggested that long-acting medications may be more beneficial and emphasized tailoring the schedule to the patient to promote adherence (56). Similarly, the TIME trial found no differences in major cardiovascular events by schedule and recommended individualizing administration based on tolerance and adherence (57).

In this study, statins were scheduled almost exclusively at night, in accordance with the traditional recommendation based on the circadian rhythm of HMG-CoA reductase activity. However, this practice originated with short-acting statins and may not be applicable to atorvastatin and rosuvastatin, the most commonly prescribed statins in this study, which have longer pharmacokinetics (58).

An observational study found no notable differences in adherence or in LDL reduction between those taking atorvastatin at night and those taking it at any time of day (59). Another study compared nighttime administration of amlodipine/atorvastatin with separate morning dosing and concluded that both regimens were equally effective (58). Similarly, another study reported no differences in lipid levels when comparing morning and evening administration of atorvastatin (60).

The limited evidence on rosuvastatin supports flexible scheduling. In one study, rosuvastatin/ezetimibe reduced LDL cholesterol at 6 and 12 weeks, regardless of the timing of administration (61).

This study identified distinct scheduling patterns for antiplatelet and anticoagulant medications. Acetylsalicylic acid was administered at a single, unvaried time, whereas clopidogrel, rivaroxaban, and warfarin showed more variable scheduling patterns. Prasugrel had minimal representation, with only one prescription in the afternoon. Several studies suggest that nighttime administration of acetylsalicylic acid improves cardiovascular protection and enhances its morning antiplatelet effect (52, 62–65). A mathematical model supports this logic, indicating that nighttime use optimizes anticoagulant action, whereas morning administration may be insufficient for nocturnal platelet production (49).

No studies were found recommending an optimal timing for clopidogrel administration, limiting guidance from a chronopharmacological perspective. The only relevant study observed increased ADP-induced platelet aggregation at 10:00, suggesting a possible circadian variation in platelet response. However, no recommendations regarding the timing of administration were made (66).

Evidence for rivaroxaban supports nighttime administration. One study found higher plasma concentrations and longer-lasting anti-factor Xa activity after the nighttime dose (67). Similarly, West *et al.* (68) noted that nighttime administration may be preferable, as it produces higher drug concentrations 12 hours later and better *in vivo* thrombin suppression in the morning.

The available evidence is limited regarding the recommended time of day for warfarin administration. One clinical trial found no notable differences in the anticoagulant effect between dosing times and recommended that warfarin should be administered at the time that best suits the patient's routine (69).

In this study, the diuretics spironolactone and hydrochlorothiazide were predominantly administered in the morning, whereas furosemide showed greater variability in timing. Indapamide and chlorthalidone were underprescribed, which precludes meaningful comparisons with existing literature. Morning administration of diuretics is traditionally recommended to minimize nocturia and sleep disorders (70). However, recent studies question this practice. One study showed that intravenous furosemide administered between 00:00 and 05:59 produced greater urine output in the following hour (71), and another found a greater diuretic response when administered between 23:00 and 04:59 than at other times of the day (72). Other sources state that morning administration of diuretics generally provides better relief of edema and congestion in cardiac and renal conditions. For hydrochlorothiazide specifically, a secondary source indicates that administration before 09:00 produces a better antihypertensive effect (34).

Evidence for spironolactone is limited, though one review noted that its actions and effects may be modulated by biological rhythms, which favor its administration in the morning (73).

Hidden nursing role in scheduling

Although data support the influence of medication administration timing on the efficacy and safety of cardiovascular drugs, the evidence remains limited and heterogeneous, so larger studies are needed. In this context, the study's findings highlight an underexplored aspect of nursing practice: medication scheduling. This variable is frequently underestimated compared with factors such as dose, route, technique, or dilution, which tend to receive greater attention in institutional protocols, safety strategies, and professional training, including undergraduate, graduate, and continuing education programs on safe medication administration (74–76).

In clinical practice, medication scheduling is frequently determined by operational rather than clinical or physiological criteria, reflecting a narrow perception of administration as a purely technical task. However, optimal scheduling requires integrating pharmacological knowledge, circadian physiology, and clinical assessment. The lack of studies on medication scheduling by nursing professionals is striking, revealing a gap in the literature and an opportunity to strengthen the disciplinary role. Research in this field could position nurses as key contributors to complementary decisions about medication administration, beyond protocol adherence, through clinical reasoning, treatment management, and collaboration (77). This, in turn, could improve therapeutic outcomes, reduce risks, promote adherence, and reinforce their autonomous and proactive role. For example, in the United States, 22 states prohibit delegating this responsibility to non-certified personnel, thereby ensuring standardized processes under professional responsibility (77).

Such studies could also motivate nursing professionals to develop research that integrates metabolites and clinical biomarkers to correlate the timing of administration with therapeutic response. Moving beyond descriptive analyses to generate evidence on the efficacy of optimized schedule administration could support the development of predictive models to guide clinical and disciplinary decisions.

Finally, the limitations of this study should be recognized as opportunities for future research with a broader scope and methodological rigor. The descriptive design prevented evaluation of clinical outcomes by time of administration. Furthermore, the low prevalence of certain medications limited the analysis of timing patterns and trends, as well as the identification of systematic practices or preferences in nursing decision-making.

Conclusion

This research demonstrates that once-daily cardiovascular medication administration follows consistent and distinct timing patterns by therapeutic group; however, the variations observed among drugs within the same group highlight the absence of systematic chronopharmacological criteria for their scheduling. From a practical perspective, these findings underscore the need to integrate the chronopharmacology approach into nursing practice, not only to ensure adherence to prescribed schedules but also as a clinical tool to guide safe and effective cardiovascular medication scheduling, optimize therapeutic outcomes, minimize adverse effects, and strengthen the role of the nursing professional in evidence-based decision-making for pharmacological care.

From a nursing perspective, the observed heterogeneity in administration schedules highlights medication timing as an underexplored component of pharmacological care. The results underscore the importance of considering chronopharmacology as an analytical framework to better understand current administration practices and to inform future research aimed at strengthening evidence-based medication management in nursing.

Conflicts of interest

We declare no conflicts of interest related to the conduct of this study.

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