

Drug Therapy Scheduling by Nurses and Resulting Potential Drug Interactions in the Hospital Care Of Adolescents: A Cross-Sectional Study

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Abstract

Background: One of the nursing activities in the hospital is the scheduling that requires a nursing specific knowledge of pharmacology to avoid potential drug interactions (PDIs). **Objective:** To analyze the characteristics of the medication schedule established by nurses and to identify PDIs. **Methods:** Retrospective cross-sectional study developed in a specialized adolescent health unit at a public hospital in Rio de Janeiro, Brazil. The sample consisted of 79 prescriptions based on a sample size calculated for a power of 0.8. Odds ratios were calculated, and a significance level of 5% was considered. The drug pairs that were scheduled at the same time were tested using the Micromedex software and analyzed using the statistical software R. **Results:** Among the prescriptions, those containing more than 5 drugs had two times the odds (OR: 2.5) of being associated with PDIs. Phenytoin was involved in 4 events. Suggested nursing care actions for PDIs include observing signs and symptoms, monitoring the therapeutic response and possible adverse reactions, and intervening according to the specific complications. **Conclusion:** It study highlighted aspects related to medication scheduling which is a routine nursing activity, and when it is done correctly can avoid PDIs and Drug Interactions promoting safety patient.

Keywords: Nursing; Potential drug interactions; Scheduling.

1. Introduction

Among the nursing activities performed by the nursing team, one of the most complex in the hospital setting is drug management. Although the scheduling and administration of drug therapy are incorporated into the work routine of the nursing team, scheduling requires nurses to have knowledge of pharmacology knowledge, including the interactions and reactions associated with drugs, which sometimes go unnoticed among nurses' numerous routines. Among the many responsibilities of the nursing team, particularly in the context of hospital care, drug therapy administration is one that requires continuous, ongoing professional training that should be implemented at the drug preparation, administration, monitoring and scheduling stages with technical and scientific rigor to promote patient recovery (Cortes & Silvino, 2019).

Potential drug interactions (PDIs) are defined as those in which the effect of the drugs involved could change, which may lead to undesirable results and increase the incidence of the adverse effects of therapy without increasing the therapeutic benefit (Bachmann, Lewis, Fuller, & Bonfiglio, 2006).

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Given the complexity of drug therapy, especially with regard to DIs and potential adverse effects, it is recommended that nurses schedule medications because scheduling is characterized as the planning of the daily administration of drugs (Carvalho et al., 2013). To properly implement drug therapy, nurses must reflect on the routinely used schedules, the conditions of the prescribed drug, the patient's clinical condition, and the PDIs and adverse effects of therapy (Secoli, 2001).

In addition, studies indicate that scheduling concentrated at pre-established times favors DIs and interferes with the efficacy of treatment, even in cases when up to five drugs are prescribed (Silva, Matos, Barreto & Albuquerque, 2013; Okuno, Cintra, Vancini-Campanharo & Batista, 2013) the prevalence of DIs is 70.6%, with a predominance of severe and moderate ones (Carvalho et al., 2013).

Based on the above, the following descriptive hypothesis was defined: nursing care during hospitalization affects PDIs in hospitalized adolescent patients. The objectives were to analyze the characteristics of the medication schedule established by nurses and to identify the PDIs resulting from the schedule. Descriptive hypothesis: The scheduling of medications by the nurse causes in PDIs, especially when in the presence of polypharmacy.

2. Methods

This was a retrospective cross-sectional study based on documentary analysis conducted in a specialized adolescent health unit of a public hospital in Rio de Janeiro. The study setting was a teaching and health care unit responsible for integrated health care for adolescents between the ages of 12 and 18 years. The unit has 16 beds, 8 for girls and 8 for boys. The multidisciplinary team consists of health professionals from the following fields: nursing, medicine, physical therapy, nutrition, social work, and psychology. The service's routine drug therapy protocol is as follows: after the drug prescription is written, it is printed and taken to the nursing station for subsequent scheduling by the nurse.

To calculate the sample size, the mean number of prescriptions/month from January and July 2017 was calculated, yielding a total of 122 prescriptions/month. Considering the mean number of prescriptions per month, the formula for cross-sectional studies with a finite population, a confidence level of 95%, α of 0.05 and a critical value of 1.96, the resulting minimum sample size was 83 prescriptions.

Based on this, 29 medical records were available for consultation; from these, the prescriptions were selected and one to five prescriptions per hospitalization were analyzed. The final sample consisted of 79 drug prescriptions, generating a sampling power higher than 80%. Data were collected in August 2017 via analysis of the medical records of patients hospitalized during the abovementioned months. The inclusion criteria were as follows: prescriptions for patients hospitalized between January and July 2017 for at least three days that included at least two prescribed intravenous drugs, including doses of emergency drugs requested by the patient for pain relief, gastrointestinal discomfort or axillary temperature $>37.8^{\circ}\text{C}$. The exclusion criteria were fluids with or without electrolytes, blood products included among the prescriptions, medical records in the billing process, and illegible prescriptions.

The variables of interest were: predictor variables - drug name, requested interval, scheduled times and outcome variable - PDIs. PDIs were identified and classified based on drug pairs scheduled at the same time, with the support of the Micromedex® Healthcare Series tool (Thomson Micromedex™, Greenwood Village, Colorado, USA) using the Drug Interactions tool, which shows the incompatibility of each drug. Micromedex is a restricted access database updated every three months that contains drug descriptions in terms of pharmacokinetics and pharmacodynamics, indications and contraindications, adverse effects and DIs; the interactions are classified in relation to severity (contraindicated, severe, moderate, secondary and unknown) and the level of scientific evidence (excellent, good, reasonable and unknown) (Micromedex, 2011).

After the PDIs were identified, the database was organized, and analyses were performed with the statistical software R. The mean number of items and doses per prescription and their respective confidence intervals (CIs) were calculated, and the proportion of PDIs was estimated using odds ratio with their respective CIs to identify an association between the number of items per prescription and the presence of DIs. For this purpose, the prescriptions were classified as "up to 5 prescribed items" and "more than 5 prescribed items". For the statistical analysis, the collected variables were organized into spreadsheets in Microsoft Excel Office XP. A significance level of 5% was used to calculate the odds ratio and CI. Next, graphs were constructed to show the distribution of the drug schedules *versus* the time slot and the resulting peaks.

The study meets the standards of the Declaration of Helsinki and was submitted to the Ethics Committee for approval; it obtained a favorable decision under number 2.022.282. This paper is reported using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist guideline (see Supplementary file 1). Could exist a recall bias because the data were taken from secondary sources, that is, medical records. This type of bias was minimized by the sample calculation with power greater than 80%.

3. Results

3.1 Scheduling profile

Based in the mean number of prescriptions/month - 122, after calculate the sample size, resulting in 83 prescriptions, this study gets 79 drug prescriptions, generating a sampling power higher than 0,8. The results showed that 503 drugs from 79 different prescriptions were scheduled, generating a total of 1043 scheduled doses. The mean number of drugs per prescription was 6.4. Patients in the studied unit were characterized as receiving polypharmacy that is, having more than 5 drugs prescribed. The mean number of doses per prescription was 13.2, and the mean number of doses per prescribed medication was 2.1. The distribution of doses according to the day and night shifts is shown in Figure 1.

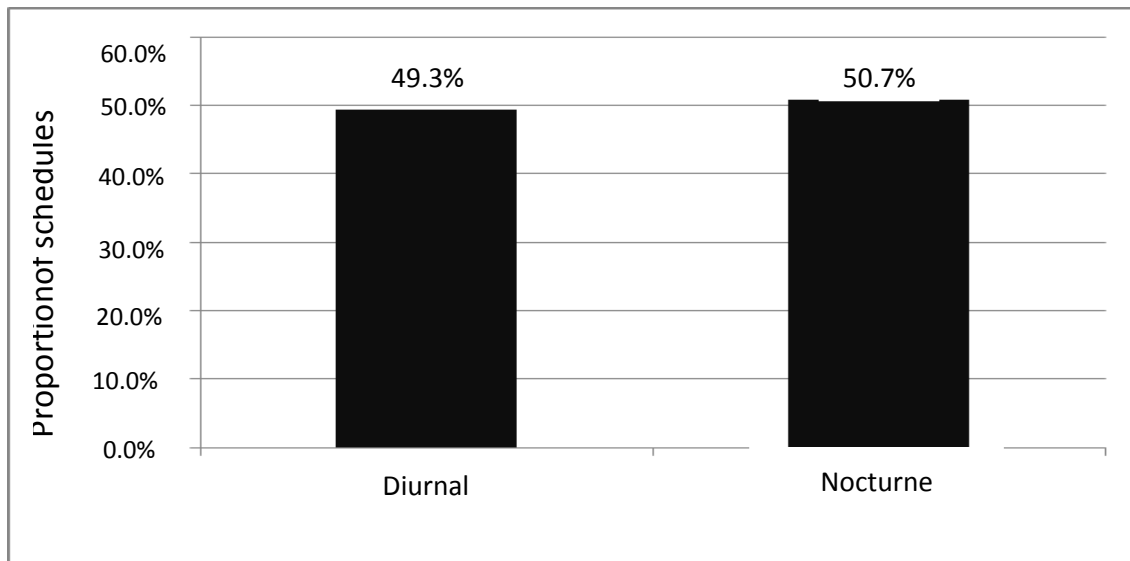


Figure 1 - Distribution of scheduled doses per shift in a specialized unit of adolescent. Rio de Janeiro - RJ. Brazil.2017.

The day shift at the study unit is between 7:00 am and 6:59 pm, and the night shift is between 7:00 pm and 6:59 am. The data show that a slightly higher proportion of doses was scheduled for the NS, with 529 doses compared to the DS, which had a concentration of 514 scheduled doses.

Another relevant finding was the distribution of the scheduled time slots in the unit, shown in Figure 2.

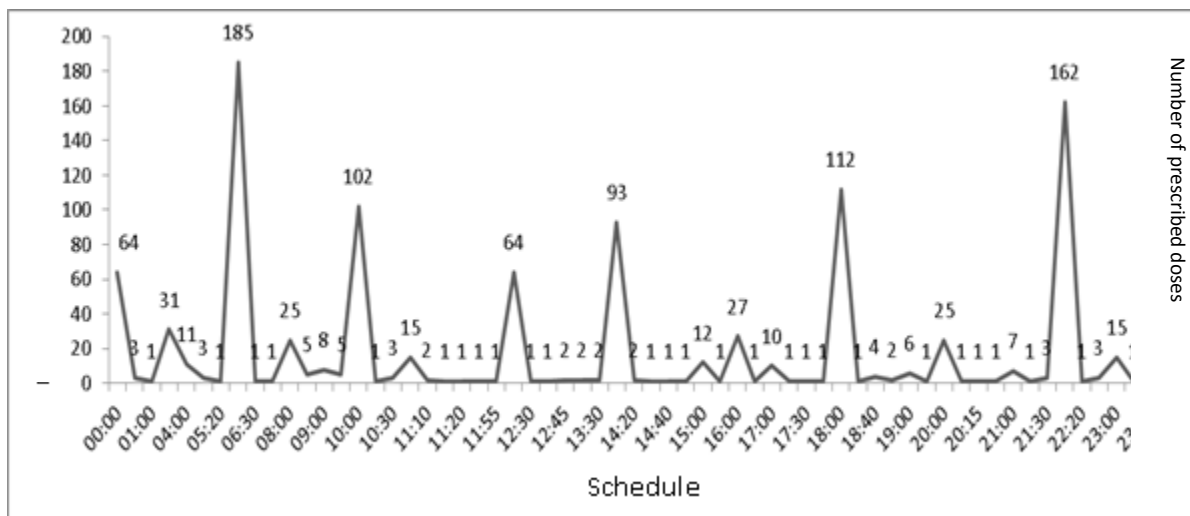


Figure 2. Distribution of doses scheduled per time slot in a specialized unit. Rio de Janeiro, RJ. Brazil. 201

Figure 2. Distribution of doses scheduled per time slot in a specialized unit. Rio de Janeiro, RJ. Brazil. 2017.

Four peak times for drug administration were identified for the DS, corresponding to 10 am (n=102 doses), 12 pm (n=64 doses), 2 pm (n=93 doses) and 6 pm (n=112 doses); for the NS, two peak hours, 10 pm (n=162 doses) and 6 am (n=185 doses) were identified. Together, these times accounted for 69% of all the scheduled doses. Doses scheduled at odd hours were found but corresponded to only 9% of all the scheduled doses identified in the study.

3.2 Potential drug interactions favored by the scheduling

With regard to the scheduling, 13 scheduled prescriptions with the potential for DIs were found. The results on table 1 shows the proportion of prescriptions scheduled without and with PDIs and the number of drugs prescribed per prescription. In addition, the table shows the distribution of prescriptions per number of items in general, regardless of whether PDIs were present in the schedule (column 3).

Table 1. Distribution of prescriptions by the presence or absence of potential DIs and number of drugs prescribed in a specialized unit. Rio de Janeiro, RJ. Brazil. 2017.

Drugs for each prescription	No drug interaction		With drug interaction		Total		OR
	N	%	N	%	N	%	
Upto 5	29	43.9%	03	23.1%	32	40.5%	1.8
More than 5	37	56.1%	10	76.9%	47	59.5%	2.5
Total	66	100.0%	13	100.0%	79	100.0%	-

OR: Odds Ratio; N: Number

Of the total of 79 prescriptions, 13 prescriptions had PDIs due to scheduling, 3 in prescriptions with up to 5 drugs (23.1%) and 10 in prescriptions with more than 5 prescribed drugs (76.9%); therefore, there was a higher prevalence of PDIs in prescriptions with more than 5 drugs. According to the odds ratio for the presence of PDIs as a function of the number of items per prescription, prescriptions with more than 5 drugs were more likely (OR: 2.5) to be associated with a schedule with potential for DIs. The OR confidence interval ranged from 0.67 to 12.6. The data in the table 2 shows the pairs of drugs that were involved in PDIs as well as the absolute frequency of schedules involving the pairs.

Table 2. Drug pairs that were scheduled at the same time and absolute frequency of schedules with drug pairs with potential for drug interaction in a specialized unit. Rio de Janeiro, RJ. Brazil. 2017.

Pairs of medications scheduled at the same time	Number of schedules
Phenytoin 50 mg/ml and Acyclovir 250mg	03
Dipyron 500mg/ml and Dexamethasone 4mg/ml	03
Meropenem 500mg and Vancomycin 500mg	02
Morphine (Chloridate or Sulphate) 10mg/ml and Tramadol (Chloridate) 50mg/ml	02
Tramadol (Chloridate) 50mg and Ondansetron (Chloridate) 2mg/ml	02
Ketoprofen 100mg and Dipyron 500mg/ml	02
Clarithromycin 500mg and Ondansetron (Chloridate) 2mg/ml	01
Dexamethasone 4mg/ml and Ketoprofen 100mg	01
Phenytoin 50mg/ml and Omeprazole 40mg	01
Methylprednisolone 125mg and Dipyron 500mg/ml	01
Nalbuphine (Chloridate) 10mg/ml and Ondansetron (Chloridate) 2mg/ml	01
Absolute frequency of schedule with PDI	19

Eleven pairs of drugs with PDIs were found, with an absolute frequency of schedules equivalent to 19 PDIs. Phenytoin was involved in 4 events, in association with acyclovir and omeprazole.

After the analysis of 11 mapped drug pairs performed with the Micromedex® Healthcare Series software, the following PDIs classified as severe were identified: tramadol-morphine, tramadol-ondansetron, nalbuphine-ondansetron, meropenem-vancomycin, clarithromycin-ondansetron, dexamethasone-ketoprofen. The identified PDIs classified as moderate were for phenytoin-acyclovir and phenytoin-omeprazole.

4. Discussion

4.1 Scheduling profile

The highest incidence of drug schedules found in the study occurred at night (50.7%); this finding is consistent with another study, in which 74.6% of the doses were scheduled at night, with higher frequencies at 10 pm and 6:00 am (Silva, Matos, Barreto & Albuquerque, 2013). A previous study indicated that scheduling several drugs at the same time is associated with the institutional organization and culture and with the praxis of nursing and that such standardization does not consider the possibility of DIs. Concentrated scheduling of drugs at pre-established times favors the occurrence of interactions, even in prescriptions of five drugs or fewer (Silva, Matos, Barreto & Albuquerque, 2013).

These findings are corroborated by a study that reported the administration of drugs at only four times, 2 pm, 6 pm, 10 pm and 6 am, and that also indicated that organizational aspects related to the work routine influence the use of a few specific drug administration times and that diversifying the schedules would lead to an increase in workload (Silva, Matos, Barreto & Albuquerque, 2013). Additionally, regarding the routine, the study found that visiting and shift change times were not used.

It can be inferred that the nursing work process and work organization contribute to the scheduling of drug administration at predetermined times. The present study identified that few drugs were scheduled for 7:00 am and 7:00 pm given that, as a rule, shift changes occur at these times, and official communication between the teams leaving and entering the unit during which the conditions of each patient are reported and the additional actions taken for them must occur to ensure continuity of care, even in the presence of written records. It is understood that not scheduling drugs at these times is a strategy to avoid information overload, delays or forgetting (e.g., omission of doses) (Silva, Matos, Barreto Albuquerque, 2013). Between 8 am and 9 am, few drug schedules were also identified, which suggests that the demand for nursing care related to personal hygiene, material collection/referral for exams, and the establishment of diagnoses and the care plan/prescription, among other needs, and the administrative-managerial actions of the unit are determinants of this finding.

As mentioned, there was a concentration of drug schedules at 10 am (n=102 doses), 12 pm (n=64 doses), 2 pm (n=93 doses), 6 pm (n=112 doses), 10 pm (n=162 doses) and 6 am (n=185 doses), corroborating the referenced studies; these schedules favor the occurrence of PDIs (Fontenele& Araújo, 2006; Barreto, 2010; Carvalho, 2011). In summary, the data show that drug scheduling is sometimes performed according to the institutional routine and a minimally valued activity, although this practice requires knowledge to avoid PDIs and negative effects on the patient's therapy (Silva, Matos, Barreto & Albuquerque, 2011). Lima and Cassiani(2009) corroborate the finding of the present study; they observed that 61.8% of drugs were scheduled for the same time, with 6:00 am being the most frequent time, and that up to nine drugs were administered at the same time. Regarding the route of administration, it was also observed that many of these drugs were administered at the same time via the same route, which could have undoubtedly precipitated the occurrence of DIs.

Regarding the clinical management of PDIs, a study identified the main care actions through which health professionals can intervene: observing signs and symptoms (211-47.9%), monitoring the therapeutic response (95-20.6%), adjusting the drug dose (85-18.4%), adjusting the drug administration time (38-8.2%), avoiding combining drugs (15-3.3%), changing the drug (4-0.9%) and changing the drug administration route (3-0.7%)(Lima &Cassiani, 2009). Researchers reinforce the need for integrated actions among the health team and knowledge of pharmacological mechanisms to avoid DIs (Carvalho et al., 2013) Additionally, equipping nurses to rationally use drugs can increase the safety of patient care(Okuno, Cintra, Vancini-Campanharo& Batista, 2013).

4.2 Potential drug interactions favored by scheduling

Of the total of 79 prescriptions, 13 prescriptions presented PDIs due to scheduling; 3 of these involved up to 5 prescribed drugs (23.1%), and 10 involved more than 5 prescribed drugs (76.9%). This finding indicates that PDIs were more prevalent in prescriptions with more than 5 drugs. However, the mean number of prescription drugs found was lower than that reported in other reference study (Moreira, Mesquita, Stipp&Paes, 2017). The quantitative definition of polypharmacy varies widely in the literature, with the most commonly used definition referring to the use of five or more drugs(Vieira et al., 2012).

The number of drugs per prescription is an indicator of risk because the greater the number of drugs the patient receives and the longer the hospital stay, the greater the possibility of DIs and adverse effects (Secoli, 2001). Corroborating the present findings, a study points to a prevalence of interactions associated with the clinical condition in hospitalized patients because severity and clinical instability favor the concomitant use of drug therapies (Melgaço, Carrera, Nascimento & Maia, 2011).

A retrospective cohort study (Feinstein, 2015) that included infants, children and adolescents hospitalized in a children's hospital in the United States concluded that PDIs are common among this population. Opioids were involved in 25% of all PDIs, followed by anti-infective agents (17%), neurological agents (15%), and cardiovascular agents (13%). The most common potential adverse drug events included additive respiratory depression (in 21% of the PDIs), bleeding risk (5%), chemotherapy interval prolongation (4%), reduced iron absorption/availability (4%), nervous system depression (4%), hyperkalemia (3%) and altered diuretic effectiveness (3%). Regarding the association between drug pairs and PDIs in terms of severity, level of evidence and adverse reactions, of the 11 DI pairs found, most were classified as severe, and there was a prevalence of reasonable evidence. However, none of these DIs generated an adverse reaction in the patient.

The severity found reveals the clinical importance of DI analysis, given that the Micromedex® software defines a severe interaction as one that can pose risks to patient life and requires immediate medical intervention, whereas moderate interactions may result in exacerbation of the patient's clinical condition that require a change of treatment(Micromedex, 2011). Regarding the level of evidence, the most frequent category was reasonable level of evidence, which was present in 9 of the 11 analyzed pairs. A good level of evidence was found for two tested pairs, whereas excellent and unknown levels of evidence were not found in this study.

So, it is important to the nurse to treat drug scheduling as a singular activity that considers the specific clinical and drug needs of each patient and to perform it with autonomy and responsibility, opting for safer administration schedules that enable better provision of patient care and freedom from risks and harm avoiding PDIs and DIs. The limitations of this study include the reduced number of nurses at the study unit. There is also a shortage of literature addressing adolescent health in hospitalization units to support the findings, as well as a lack of information on adolescent wards for the comparison and replication of the study.

5. Conclusion

Based in this results, could perceive that PDIs are common and is necessary in the clinical practice the following efforts by the nursing to reduce the combination of drugs that are harmful: knowing the drug, evaluating the list of drugs prescribed to each patient, considering the clinical, understanding the expected effect of therapy, diversifying the schedules of administration, and promoting education and awareness among professionals, such as the use of programs to identify DIs. Suggested nursing actions for PDIs include observing signs and symptoms, monitoring the therapeutic response and possible adverse reactions and providing specific interventions according to the complications. This research has external validity because it follows methodological and statistical rigor for cross-sectional studies and addresses thematic that covers the worldwide nursing activity.

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