

POTENTIAL MEDICATION INTERACTIONS AT A PSYCHIATRIC EMERGENCY SERVICE OF A GENERAL HOSPITAL: ANALYSIS OF THE FIRST TWENTY-FOUR HOURS

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Medication interaction happens when the power or efficiency of one drug is altered by the presence of another. The medication used during psychiatric emergencies is aimed at reducing and/or putting an end to symptoms related to the behavioral change, almost always symptoms of psychomotor agitation and aggressiveness. The use of multiple drugs is common to increase the potential interaction. The objective in this study was to survey the potential pairs of drug interactions administered at the same time at a psychiatric emergency service of a general hospital during the first twenty-four hours of care. A descriptive, exploratory, documentary, retrospective and quantitative study was undertaken. The population relates to the histories of patients attended at the emergency service of the HCU-UFU, in the specialty area psychiatrics, in 2012. In total, 725 histories were selected of patients who visited the emergency service of the Hospital de Clínicas at Universidade Federal de Uberlândia in 2012. The possible drug interactions were analyzed based on the crossing of the drugs in the databases Drugs® and Micromedex®. The most frequent interaction in the histories analyzed was Haloperidol + Promethazine, totaling 17.7% of all 1,537 pairs of drugs administered at the same time during the research period. The database Drugs® informed that, of all pairs administered during that period, 559 (36%) presented possible interactions, while 978 (64%) had no signs of interaction risk. Micromedex® evidenced that, in 329 (21%) of the drug pairs administered, some type of drug interaction took place while, in 1,208 (79%) pairs, no interaction possibility was found. The predominant drug classes of possible interactions were Benzodiazepines

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+ Antipsychotics, an association commonly used in psychiatric emergencies, alerting to the need to monitor the possible adverse effects of these drugs. Based on the findings, a figure was elaborated with the main care for possible interactions between drugs used in psychiatric emergency care.

Descriptors: Drug Interactions; Psychotropic Drugs; Emergency Medical Services.

POTENCIAIS INTERAÇÕES MEDICAMENTOSAS EM UM SERVIÇO DE URGÊNCIA PSIQUIÁTRICA DE UM HOSPITAL GERAL: ANÁLISE DAS PRIMEIRAS VINTE E QUATRO HORAS

A interação medicamentosa ocorre quando uma droga tem sua potência ou eficiência alterada pela presença de outra. A medicação utilizada nas urgências psiquiátricas tem como objetivo diminuir e/ou cessar sintomas relacionados à alteração do comportamento, quase sempre sintomas de agitação psicomotora e agressividade. É comum a utilização da polifarmácia para aumento do potencial de interação. O objetivo do estudo foi levantar as possíveis duplas de interações medicamentosas administradas no mesmo horário, em um serviço de urgência psiquiátrica de um hospital geral, durante as primeiras vinte e quatro horas de atendimento. Trata-se de um estudo descritivo, exploratório, documental, retrospectivo e de caráter quantitativo. A população refere-se aos prontuários de pacientes atendidos no PS HCU-UFU, na especialidade de psiquiatria, durante o ano de 2012. Selecionaram-se 725 prontuários de pacientes que buscaram o pronto-socorro do Hospital de Clínicas da Universidade Federal de Uberlândia no ano de 2012. As possíveis interações medicamentosas foram analisadas a partir do cruzamento dos fármacos nas bases de dados Drugs[®] e Micromedex[®]. A interação mais frequente nos prontuários analisados foi de Haloperidol + Prometazina, totalizando 17,7% de todas as 1.537 duplas de medicamentos administrados no mesmo horário, no período pesquisado. A base de dados Drugs[®] informou que, do total de duplas administradas no período, 559 (36%) apresentaram possibilidade de interação e 978 (64%) não apresentaram indícios de risco de interação. O Micromedex[®] evidenciou que, em 329 (21%) das duplas de medicamentos administrados houve algum tipo de interação medicamentosa, mas em 1.208 (79%) duplas não foi encontrada qualquer possibilidade de interação. A classe de medicamentos das possíveis interações que predominou foram os Benzodiazepínicos + Antipsicóticos, associação comumente utilizada nas emergências psiquiátricas, alertando para a necessidade de monitoramento dos possíveis efeitos adversos destes medicamentos. A partir dos achados, elaborou-se um quadro com os principais cuidados de potenciais interações entre medicamentos utilizados na urgência psiquiátrica.

Descritores: Interações de Medicamentos; Psicotrpicos; Serviços de Saúde de Emergência.

POTENCIALES INTERACCIONES MEDICAMENTOSAS EN UN SERVICIO DE URGENCIA PSIQUIÁTRICA DE UN HOSPITAL GENERAL: ANÁLISIS DE LAS PRIMERAS VEINTICUATRO HORAS

La interacción medicamentosa ocurre cuando una droga tiene su potencia o eficiencia alterada por la presencia de otra. La medicación utilizada en las urgencias psiquiátricas visa a disminuir y/o cesar síntomas relacionados a la alteración del comportamiento, casi siempre síntomas de agitación psicomotora y agresividad. Es común la utilización de la polifarmacia para aumento del potencial de interacción. La finalidad del estudio fue levantar las posibles parejas de interacciones medicamentosas administradas a la misma hora en un servicio de urgencia psiquiátrica de un hospital general durante las primeras veinticuatro horas de atención. Se trata de un estudio descriptivo, exploratorio, documental, retrospectivo y cuantitativo. La población se refiere a los archivos de pacientes atendidos en el PS HCU-UFU, en la especialidad de psiquiatría, durante el año de 2012. Fueron seleccionados 725 archivos de pacientes que buscaron el servicio de emergencia del Hospital de Clínicas de la Universidade Federal de Uberlândia en 2012. Las posibles interacciones medicamentosas fueron analizadas a partir del cruce de los fármacos en las bases de datos Drugs[®] y Micromedex[®]. La interacción más frecuente en los archivos analizados fue de Haloperidol + Prometazina, totalizando 17,7% de todas las 1.537 parejas de medicamentos administrados a la misma hora, en el período investigado. La base de datos Drugs[®] informó que, del total de parejas administradas en el período, 559 (36%) presentaron posibilidad de interacción y 978 (64%) no presentaron señales de riesgo de interacción. El Micromedex[®] evidenció que, en 329 (21%) de las parejas de medicamentos administrados ocurrió algún tipo de interacción medicamentosa, pero en 1.208 (79%) parejas no fue encontrada cualquiera posibilidad de interacción. La clase de medicamentos de las posibles interacciones que predominó fueron los Benzodicepinas + Antipsicóticos, asociación comúnmente utilizada en las emergencias psiquiátricas, alertando a la necesidad de monitoreo de los posibles efectos adversos de estos medicamentos. A partir de los hallazgos, fue elaborado un cuadro con los principales cuidados de potenciales interacciones entre medicamentos utilizados en la urgencia psiquiátrica.

Descriptores: Interacciones de Drogas; Psicotrópicos; Servicios Médicos de Urgencia.

Introduction

Urgency is defined as a health problem and potential death risk that needs immediate medical care; the emergency happens when the health problems imply an imminent risk of death or intense suffering, demanding immediate medical treatment⁽¹⁾.

According to Cruz et al. (2010), psychiatric

emergency can be defined as any change in feelings, behaviors or thoughts that can cause damage to other people or the individual, requiring an immediate diagnosis and rapid intervention for the sake of efficient care in this acute phase⁽²⁾.

The Psychiatric Emergency Service in General Hospital (SEPHG) is active in psychiatric emergencies, regulated by Decrees

No. 1.863 from September 29th 2003 and No. 224 from January 29th 1992, which guarantee patients the right to be attended in accordance with the principles of the Unified Health System (SUS) and regulate the Mental Health services, ranging from outpatient/hospital services to emergency care services⁽³⁾.

The emergency service team should be properly trained to cope with peculiar situations of agitation and violence. Mantovani (2010) considers some action plans: environmental or organizational management, behavioral or attitudinal management, physical management and pharmacological management. The latter was the focus of this study⁽⁴⁾.

In psychiatry, the use of drugs with symptomatic therapeutic efficacy is more common, that is, when the goal of the intervention is to control or minimize the patient's problem⁽⁵⁾. Thus, pharmacological management is used to calm down the patient rapidly, reducing the risk of self and hetero-aggressiveness and the occurrence of side effects, but permitting the continuity of the diagnostic investigation and therapeutic approach, maintaining the patient fully or partially responsive⁽⁴⁾.

The psychotropic drugs used in cases of psychiatric symptoms affect the Central Nervous System (CNS) and can selectively relieve pain, reduce fever, suppress disordered movements, induce sleep or awakening, reduce the desire to eat or decrease the trend to vomiting. Drugs with this type of action can be used to treat anxiety, mania, depression or schizophrenia, without altering the patients' awareness⁽⁶⁾.

One type of treatment psychiatrists use is multiple drug treatment, called medication interaction. Medication interaction can be defined as the combination of two or more drugs so that the power or efficiency of one drug is significantly changed by the presence of the other⁽⁷⁾.

In medication therapy, drug interaction is one of the causes of adverse reactions. These represent a severe risk for patients' health and increased costs for the health service. Therefore, attentive monitoring of care while in hospital is fundamental⁽⁸⁻¹⁰⁾.

For the sake of greater treatment efficacy, multiple drug therapy is commonly used to induce sedation, calm down the patients quickly and,

consequently, reduce the risks involved in this type of episode. Nevertheless, this treatment entails potential risks, which may cause irreversible damage to the patient. The objective in this study was to survey the pairs of potential drug interactions administered at the same time at a psychiatric emergency service of a general hospital during the first 24 hours of care. In addition, the data analysis permitted the construction of a tool to inform the professionals on the main care related to the potential interactions among drugs used in psychiatry emergency care.

Method

A descriptive, exploratory, documentary, retrospective and quantitative study was undertaken. Preliminary approval was obtained from the Ethics Committee for Research Involving Human Beings at Universidade Federal de Uberlândia (CEP/UFU), under opinion 691.206, in compliance with National Health Council – NHC Resolution No. 466 on December 12th 2012. The paper presented is part of the main study "Psychiatric Emergency Care at General Hospitals: the care profile in the first 24 hours". The Statistics Service of the HC-UFU supplied the number of patient histories of interest to the research.

The study was undertaken at the emergency service of the Hospital de Clínicas at Universidade Federal de Uberlândia (HC-UFU).

Stratified probabilistic sampling was used for the study. The strata considered were the months of the year in function of the unequal distribution of patient histories in each month. The population refers to the histories of patients attended at the Emergency Service of HCU-UFU, in the specialty area psychiatrics, in the course of 2012 (2,265 histories). Based on the calculation of a 3% errors and a 95% confidence level, a sample of 725 histories was calculated.

In the research, the histories of patients were included who visited the emergency services of the Hospital de Clínicas at Universidade Federal de Uberlândia in 2012 and were forwarded for care in the specialty area psychiatrics during the first 24 hours of care at the health service. These histories were accessed through the ALERT® system⁽¹¹⁾ (electronic patient history tool) used at the investigated hospital.

For this study, a tool was used with information on the prescribed drug, dose and administration route, time of prescription and administration and professional category of the professional administering the drug. The data were stored in Microsoft Office Excel 2007[®] and distributed in graphs and tables. The possible medication interactions were analyzed based on the crossing of the drugs in the databases Drugs[®] and Micromedex[®], which provide information on medication and possible medication interactions, ranking them according to their severity under: “Contraindicated”, associations rejected for concomitant use; “Major”, interaction that can represent a death threat and/or require medical interaction to reduce or avoid severe adverse effects; “Moderate”, when the interaction can result in an exacerbation of the patient’s health problem; and “Minor”, of minimal clinical significance; and classified in terms of clinical management⁽¹²⁾.

Results

The drugs administered at the same time and registered in the files selected for the research, after the collection, were grouped and consulted regarding the potential and severity of the interaction.

The findings revealed 248 pairs, administered

Table 1 – Distribution of drug pairs administered at the same time, per frequency (superior to 1%), and their classifications based on Drug[®] and Micromedex[®], of the severity of possible interactions (Uberlândia, 2012) (N=1537)

Interactions	Quantity	%	Classification				
			Drugs			Micromedex	
			MO	MA	SI	MA	SI
Folic Acid + Thiamine	15	1.0			x		X
Clonazepam + Haloperidol	21	1.4	x				X
Clonazepam + Promethazine	16	1.0	x				X
Diazepam + Haloperidol	152	9.9	x				X
Diazepam + Promethazine	152	9.9	x				X
Diazepam + Risperidone	29	1.9	x				X
Diazepam + Thiamine	41	2.7			x		X
Diazepam + Complex B vitamin	22	1.4			x		X
Haloperidol + Midazolam	41	2.7	x				X
Haloperidol + Promethazine	271	17.7		x		x	
Haloperidol + Thiamine	51	3.3			x		X
Haloperidol + Complex B vitamin	15	1.0			x		X
Midazolam + Promethazine	34	2.2	x				X
Promethazine + Risperidone	29	1.9	x				X
Promethazine + Thiamine	44	2.9			x		X
Thiamine + Complex B vitamin	41	2.7			x		X

*MO: Moderate Interaction; MA: Major Interaction; NI: Do Not Interact.

Source: Course Conclusion Monograph Presented at Universidade Federal de Uberlândia ⁽¹³⁾

1,537 times during the research period, through the databases Drugs[®] and Micromedex[®], which informed on the severity of the interaction and the clinical management. The calculations and statistical analyses were developed based on the total number of administrations of the drug pairs, with N= 1,537.

The database Drugs[®] showed 559 (36%) interaction possibilities, while the database Micromedex[®] presented 329 (21%) pairs of drugs with some type of medication interaction.

As regards the severity of the interaction, the database Drugs[®] found 44% of the pairs classified as moderate, 36% without interaction, 19% as major and 1% as minor. The database Micromedex[®] classified that 79% of the pairs with possible interaction do not interact, 20% are major and 1% moderate. When comparing the classifications of severity between the different databases, 72% of congruency was found between the database classifications, against 28% of discrepancies.

Table 1 highlights the frequency (%) of the possible interactions superior to 1%, according to the databases Drugs[®] and Micromedex[®] and their classifications.

Next, the most frequent interactions (superior to 1%) were grouped according to their medication classes. The classes found were Benzodiazepines + Antipsychotics, Benzodiazepines + Antihistaminic drugs and Antihistaminic drugs + Antipsychotics.

Each pair of possible interaction with frequency superior to 1% was analyzed according to the classification of the severity levels based on the databases Drugs® and Micromedex®. For the classifications considered congruent

with possible interaction, care actions were formulated based on the clinical management cited in the two databases; for the classifications considered discrepant with possible interactions, the database with the most severe classification was considered and, based on that selection, a figure with care was structured, according to actions proposed by Carpenito-Moyet (2011)⁽¹⁴⁾, constructed based on the clinical management indicated by the databases Drugs® and Micromedex® (Figure 1).

Medication classes	Medication pairs	%	Clinical management	Care
Benzodiazepine + Antipsychotic	Clonazepam + Haloperidol	1.4	Effects on Central Nervous System and/or respiratory depression.	Continuously monitor the respiratory condition, use of accessory muscles, respiratory frequency, pulse frequency and arterial pressure, level of awareness, keep the headrest raised at 30° (except if contraindicated) and monitor overall vital signs.
	Diazepam + Haloperidol	9.9		
	Diazepam + Risperidone	1.9		
	Midazolam + Haloperidol	2.7		
Benzodiazepine + Antihistaminic	Diazepam + Promethazine	9.9	Extending the QT interval can result in additive effects and greater risk of ventricular arrhythmias, including <i>torsades de pointes</i> and sudden death.	Monitor signs and symptoms of arrhythmia (palpitations, chest pain, ECG modifications, hypotension and reduced SaO ₂); start appropriate conducts depending on type of arrhythmia; administer supplementary oxygen when indicated; monitor serum electrolyte levels (sodium, potassium, calcium and magnesium).
	Clonazepam + Promethazine	1		
	Midazolam + Promethazine	2.2		
Antihistaminic and Antipsychotic	Promethazine + Haloperidol	17,7		
	Promethazine + Risperidone	1.9	Paralytic ileum, hyperthermia, insolation, anticholinergic intoxication syndrome (mydriasis, blurred vision, facial redness, fever, dry skin and mucous membranes, tachycardia, urinary retention and constipation), memory loss, disorientation, incoherence, hallucinations, psychosis, delirium, hyperactivity, spasms or spasmodic movements, stereotypy and convulsions.	Monitor intestinal functioning (intestinal noise in all quadrants), flatulence and defecation; monitor symptoms of paralytic ileum (acute and imminent pain, hiccups, nausea and vomiting, constipation and distended abdomen); investigate relation with hypovolemia; monitor the body and environment temperature; offer privacy during convulsive activity; establish an airway; aspire whenever necessary; administer oxygen through nasal catheter, grant venous access, prevent trauma using delicate movements, without restricting, after the convulsive activity, yield, place client in lateral decubitus, allow the person to sleep after the convulsive activity; monitor urinary retention, palpating and striking the suprapubic area for signs of bladder distension and, if necessary, use urinary relief catheter.

Course Conclusion Monograph presented at Universidade Federal de Uberlândia ⁽¹³⁾

Figure 1 – Main care for potential medication interactions among drugs used in psychiatric emergency care⁽¹³⁾.

Discussion

No field studies were found that verified the potential drug interactions at Mental Health services, nor studies published in scientific databases that analyzed the possible interactions and severity rankings between drugs used in psychiatric care through databases like Drugs® and Micromedex®. Nevertheless, many studies have used this type of tool to investigate drug interactions in other clinical services, besides the severity of the interactions, adverse effects and drug compatibility⁽¹⁵⁾.

In this study, 64% of interactions were found between the drug pairs administered at the same time using the database Drugs® and 21% when using the database Micromedex®. When the interaction is proven, this may entail a risk for patient safety. It is important to highlight the large number of drug interactions in mental illnesses, demanding an assessment of the risks of interactions and possible measures to reduce the unwanted effects they may cause⁽¹⁶⁾.

The databases Drugs® and Micromedex® rank the interactions found as major, moderate and minor. The potential interactions between the drug pairs found in the study were presented according to their severity. For this analysis, the most frequent pairs (superior to 1%) that were most important for clinical practice were highlighted. It was technically unfeasible to control all drugs on a prescription and their possible interactions. Therefore, the health professionals should be concerned with the drugs they frequently use at the services and know what associations can provoke an interaction⁽¹⁷⁾.

In one study, using Micromedex®, pairs of drugs used in medical clinical inpatient services were investigated, appointing that most interactions were classified as moderate (48.4%), followed by minor (37.9%) and, finally, severe (3.2%). In this study, the major interactions were significant among the drug pairs administered, emphasizing the risks of possible interactions, as they jeopardize the patient's life and can cause permanent damage. A team trained to assess and manage the interactions could minimize the health problems and risks⁽¹⁷⁾.

In other studies found in the literature, higher

frequencies were found of pairs with potential interactions classified as major. Like in the present study, Haloperidol + Promethazine (pair classified as major interaction potential) was found to be the most frequently administered pair⁽¹⁰⁾. Some studies by other authors showed that, despite presenting collateral effects, Haloperidol + Promethazine seem to be the best option to manage agitation and aggressiveness, as they allow for a lesser need for additional medication and mechanic restriction. Nevertheless, the benefit of using this combination does not exclude its risks⁽¹⁸⁻¹⁹⁾.

The database Drugs® accused several pairs of drugs administered at the same time with moderate potential interaction.

The frequency of Diazepam + Haloperidol corresponded to 9.9% of all interaction pairs administered, being used in combination in Haloperidol in emergency cases to minimize some side effects of Haloperidol, used as an anxiolytic and muscle relaxant⁽²⁰⁾. The frequency of the pair Diazepam + Promethazine corresponded to 9.9%. This association promotes the sedation of agitated patients, as Promethazine is a sedative antihistaminic that enhances the action of Diazepam⁽²¹⁾.

Amongst the drug classes, the most frequent association, totaling 15.9% of the moderate interactions, was Benzodiazepines + Antipsychotics and their concomitant use has been the standard care for agitation in emergency rooms, due to the rapid onset of its effects. Nevertheless, this approach comes with several disadvantages, as benzodiazepines can cause respiratory depression, thus requiring strict monitoring. The association of these classes can be related to the patient profile attended at the psychiatric emergency services, as it demands care related to agitation through drug barriers⁽²²⁾.

The literature appoints that the association Benzodiazepines + Antihistaminic drugs can increase the patient's sedation and serves to control agitation⁽²³⁾. Due to the need of the emergency services to rapidly obtain conditions for agitated patients to cooperate, the medical conduct requires pharmacological intervention⁽²⁴⁾. Other classes in which associations were found were Antihistaminic drugs + Antipsychotics, such as the drugs Haloperidol and Promethazine.

To devise a measure to prevent possible adverse effects when administering the medication interactions, this study emphasized the pairs with frequency levels superior to 1% that were classified as moderate and severe. Then, a tool was constructed for the safe monitoring of patients using these drugs, in order to complement and enhance care practice, minimizing the effects these possible interactions can cause for the patients. With the same intent as in this study, in his research, Secoli (2001) formulated a list with orientations for management and associated care⁽²⁵⁾.

Thus, the goal was to transform this theoretical study into practical relevance for the place of study. At the end of this research, the authors intend to present it to the hospital management and propose measures to guarantee the medication administration in Mental Health most commonly used at the place of study.

Conclusions

The administration frequency of the medication pairs with interactions according to Drugs® represent more than half of all pairs administered (1,537). This shows the large number of possible drug interactions found in psychiatric emergency care at the place of study.

The interactions classified in terms of severity as major, according to the databases investigated in the study, presented major recurrence among the possible interactions found. This is concerning in view of the permanent effect they can cause to the patient without intervention in its adverse effects.

Haloperidol and Promethazine, classified as major interaction in both databases (Drugs® and Micromedex®), demonstrated great impact on the administration frequency of pairs of possible interactions in care practice at the study hospital. This possible medication interaction represents 271 (17.7%) pairs of possible interactions administered at the same time. Despite different discussions on its administration and side effects, according to the studies found, this interaction is the best option for the pharmacological management of agitated patients in psychiatric emergency services, without excluding the need for monitoring.

The databases used in the study (Drugs® and Micromedex®) were discrepant with regard to the severity of the possible interactions, showing a lack of congruent concrete information to grant the health team safety in the prescription, administration and management of care for patients' medication interactions.

The drug classes of the predominant possible interactions were Benzodiazepines + Antipsychotics and, according to the bibliography, this can be related to the care profile in psychiatric emergency care, alerting to the need to monitor the possible side effects when drugs of these classes are administered.

The health professionals' role is to minimize the harmful risks for the patient the possible interactions cause. The care table will be relevant not only for the hospital under analysis, but for other places where risks for patient safety are detected, based on the severity ranking of potential interactions between drugs administered at the same time.

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