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Cross-sectional study of active pharmacovigilance in a private hospital of Distrito Federal during the first semester of 2021

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Abstract

Objective: To document an active pharmacovigilance search during the first semester of 2021 in a private hospital of Distrito Federal (DF) using *trigger tools* and to establish the profile of active search and adverse drug reactions (ADR) by hospital sector. **Method:** Retrospective cross-sectional observational study performed between January and June of 2021. The active search and notifications of ADR were analyzed through pharmaceutical evolutions and ADR forms filled during the period, which were stratified according to the Naranjo\Karch's and Lasagna's algorithm. The *triggers tools* investigated were vitamin K, protamine, prothrombin complex, naloxone, flumazenil and activated charcoal. Duplicated registries, voluntary notification or identified by a different method not including the *triggers tools* of interest were excluded. Descriptive statistics were used as estimates of absolute frequency, relative frequency and positive predictive value (PPV). **Results:** 83 active searches were made, with the highest number in the first two months. ADR notifications remained with an average of 2,5 per month (SD = 1,5) representing 18,1% of the searches. The amount, profile of *trigger tools* and the ADR were different between the hospital sectors. The *triggers tools* with the highest number of active search were: vitamin K, within 38 records (45,8%); protamine, within 28 records (33,7%) and naloxone, within 9 records (10,84%). Also, they were responsible for ADR identification and notification: protamine (n = 7; 46,7%); vitamin K (n = 5; 33,33%) and naloxone (n = 3; 20%). The general PPV varied greatly according to the months (0 – 0,86). The global PPV was 0,18. Naloxona showed the best performance (PPV = 0,33), followed by protamine (PPV = 0,25) and vitamin K (PPV = 0,13). **Conclusion:** The results varied according to the hospital sector. Vitamin K, protamine and naloxone showed good performance. We suggest a review of the *triggers tools* at neonatal and pediatric intensive care units due to the low performance to identify ADR with the *triggers tools* used.

Keywords: pharmacovigilance; pharmaceutical care; patient safety; adverse drug reaction.

Estudo transversal de farmacovigilância ativa em um hospital privado do Distrito Federal durante o primeiro semestre de 2021

Resumo

Objetivo: Documentar a busca ativa em Farmacovigilância no primeiro semestre de 2021 em um hospital privado do DF por meio de medicamentos gatilho e estabelecer o perfil da busca ativa e das reações adversas a medicamentos (RAM) por setor de internação hospitalar. **Método:** Estudo transversal retrospectivo realizado entre janeiro e junho de 2021. A busca ativa e as notificações de RAM foram analisadas por meio de evoluções farmacêuticas e formulários de RAM preenchidos durante o período, as quais foram estratificadas segundo o algoritmo de Naranjo\Karch e Lasagna. Os medicamentos gatilho investigados incluíram vitamina K, protamina, complexo pro-trombínico, naloxona, flumazenil e carvão ativado. Registros duplicados, notificações espontâneas (ou voluntárias) ou identificadas por outro método que não englobavam medicamentos gatilho do estudo foram excluídas. Foi realizada análise estatística descritiva com estimativas de frequências absolutas, frequências relativas e valor preditivo positivo (VPP). **Resultados:** Foram realizadas 83 buscas ativas em farmacovigilância, com maior número nos dois primeiros meses. As notificações de RAM mantiveram-se em média de 2,5 por mês (DP = 1,5), representando 18,1% do total de busca ativa. A quantidade, o perfil dos medicamentos gatilho e as RAM foram diferentes entre os setores hospitalares. Os medicamentos gatilho com maior número de busca ativa foram: vitamina K, com 38 registros (45,8%); protamina, com 28 registros (33,7%); e naloxona, com 9 registros (10,8%). Foram responsáveis pela identificação e notificação de RAM: protamina (n=7; 46,7%), vitamina K (n = 5; 33,3%) e naloxona (n = 3; 20%). O VPP geral variou bastante entre os meses (0 – 0,86). O VPP global foi de 0,18. Naloxona apresentou o melhor desempenho (VPP = 0,33), seguido de protamina (VPP = 0,25) e vitamina K (VPP = 0,13). **Conclusão:** Os resultados variaram de acordo com o setor hospitalar analisado. Vitamina K, protamina e naloxona demonstraram boa performance geral. Sugere-se uma revisão dos gatilhos utilizados nas unidades de terapia intensiva (UTI) neonatal e pediátrica devido à baixa capacidade de identificar RAM com os gatilhos utilizados.

Palavras-chave: farmacovigilância; assistência farmacêutica; segurança do paciente; farmácia clínica; eventos adversos a medicamentos

Introduction

Among the various patient care strategies in the hospital environment, one of the most effective is the use of medications, which promote health and well-being through changes in physiological functions. However, drug treatment is not exempted from causing harms. The harms resulting from its use can be caused both by risks associated with its pharmacological activity and by its inappropriate use in the medication process. Both are called Drug-Related Adverse Events (DRAEs).[1] The European Medicine Agency (EMA) defines an adverse event as any unpleasant medical occurrence in a patient who has had a medication administered and which does not necessarily have a causal relationship with this treatment.[2]

Among the DRAEs, Drug-Related Adverse Reactions (DRARs) are defined by the World Health Organization (WHO) as any harmful or undesirable and unintended response that occurs with the use of medications in doses commonly used for prophylaxis, diagnosis, treatment of diseases or modification of physiological functions.[3] The definition of DRARs carries in its genesis a causal relationship between the medication and the adverse event. This relationship is at least a possibility and, thus, cannot be discarded.[2]

DRAEs cause a series of harms, directly affecting the patients and the health system as a whole. Thus, there can be loss of trust towards the health professionals, in addition to delaying diagnosis and treatment time and increasing the time and costs related to hospitalization time.[4] A review study concluded that there was a significant difference in the hospitalization time between patients with and without DRAEs.[5] A systematic review concluded that there is an intense increase in costs in the presence of DRAEs, as well as an increase in hospitalization time, need for a specialized workforce and patient's exposure to potential harms.[6]

Patient safety has become an international priority, reinforcing awareness of the occurrence of adverse events in the health care environment.[1] Pharmacovigilance is a science that aims at detecting, assessing, understanding and preventing DRARs or any other potential problems related to medications.[7] The activity is inserted in various sectors. In the hospital setting, it is cross-sectional to various professionals that provide assistance to the patient, according to the legislation in force in each area. The physicians' duty is to prescribe medications; pharmacists are responsible for their distribution and dispensing; and the Nursing team is responsible for their preparation and administration. Finally, all the professionals involved have the responsibility of preventing and detecting DRAEs.[8]

The service must also have a continuous process of improvement strategies involving an entire chain of processes, as such events can be related to the professional practice, health products, procedures and systems, including prescription, order communication, product labeling, packaging and nomenclature, composition, dispensing, distribution, administration, education, monitoring and use.[9]

Spontaneous (or voluntary) notification is an unsolicited communication, made by a health care professional or consumer to a competent authority, describing one or more suspected adverse reactions in a patient who has received one or more medications; unlike the requested (active) notification, which has a data collection system, carried out periodically.[2] These data are indispensable for risk-benefit assessment after authorization and marketing of products and updating of diverse information as it is collected.[2,10]

Spontaneous notification is perceived as the oldest, simplest, most effective and lowest-cost method to collect information on suspected adverse events; however, it has the disadvantage of underreporting.[11] The use of trigger tools has been one of the most popular options for identifying DRAEs.[1] A Pharmacovigilance study conducted in a hospital environment observed that 71.76% of the notifications occurred through active search and 25.88% through spontaneous notification in 2015, and that the difference was 93.47% against 5.04% in the following year.[8] A similar result was found in another study, in which 90% of the reactions were detected through an active search methodology and 10% through spontaneous notification.[12] The use of trigger tools has proved to be a simple method, with greater sensitivity and specificity when compared to other methodologies and allows estimating incidence rates.[13-15] In addition, even when compared to automated DRAE-detection systems, there is a higher detection rate of these events when using the trigger tools, with the advantage of not requiring a large technological apparatus.[14,15] Nevertheless, there is a need for a qualified team, in addition to having the subjectivity bias.

A trigger is a piece of evidence in the medical chart which signals that a DRAE occurred or may have occurred. It can be a medication (antidote or reversing agent), laboratory parameters outside of the reference values, or a report of signs and symptoms that reflect the patient's health condition.[1,9] The Global Trigger Tool (GTT), developed in 2003 by the Institute for Healthcare Improvement (IHI), aims at identifying adverse events and at measuring their time variations, indicating whether or not the adjustments made by the institution are supporting improvement of the safety processes.[16]

Considering that the hospital environment is conducive to the occurrence of DRARs and, in view of the above facts, the research aimed at documenting the active search in Pharmacovigilance in the first six months of 2021.

As specific objectives, the study sought to identify the main trigger tools used in the active search in Pharmacovigilance, to map the active search in Pharmacovigilance and notifications of Drug-Related Adverse Reactions (DRARs) by sector, as well as to track and identify the main DRARs and medications involved through the trigger tools, in order to guide future actions aimed at ensuring greater patient safety. Everything was done by means of the Clinical Pharmacy service of a private hospital in *Distrito Federal* (DF).

Methods

This is a retrospective and cross-sectional study conducted in a large-size (200 beds) and high-complexity private hospital located in DF. The data were retrospectively collected from January to June 2021. The active search in Pharmacovigilance and the DRAR notifications were identified, analyzed and quantified through Pharmacovigilance pharmaceutical reports, using a report provided by Tasy® and Pharmacovigilance forms filled out from January to June 2021.

The study sample consisted of all patients hospitalized in intensive care units (neonatal, pediatric and adult) and in inpatient units in the obstetrics, pediatrics, cardiology, neurology, oncology, orthopedics and COVID-19 areas. Duplicate records were not counted and the DRAR notifications that were voluntary or identified through a means other than active search and which did not include the trigger tools included in the study design were excluded from the analysis (Figure 1).

The Pharmacovigilance service in the institution is performed by the Clinical Pharmacy team, routinely, twice a week, through the active search for prescriptions containing the following trigger tools: Vitamin K, protamine, prothrombin complex, naloxone, flumazenil and activated carbon. Investigation about the use of such medications is performed by means of diverse information contained in electronic medical records and through multiprofessional interviews. All the active searches are recorded in the medical chart as pharmaceutical records, except in cases where Vitamin K is used as prophylaxis for hemorrhage in newborns. When detected, the DRARs are filled out in a Pharmacovigilance form and stratified according to the causality criteria according to the Karch/Lasagna and Naranjo algorithms;[17,18] and are then forwarded to the institution's quality system for evaluation and subsequent notification to the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária*, ANVISA) (Figure 1).

A descriptive statistical analysis was performed with estimates of absolute and relative frequencies, which had their values expressed as percentages. The global Positive Predictive Value (PPV) for each trigger tool was calculated by dividing the number of times a trigger tool was able to identify a DRAR by the number of times the trigger tool was used in DRAR searches. The Standard Deviations (SDs) were calculated for the central tendency measures (mean values). All the data collected were transferred to an Excel® spreadsheet and processed and analyzed in the GraphPad Prism 5 software.

This study was conducted in accordance with the definitions of the Guidelines and Regulations for Research Involving Human Beings imposed by CNS Resolution 466/12 and approved by the institution's Research Ethics Committee under CAAE protocol number: 51309721.5.0000.8101.

Results

During the study period, a total of 114 Pharmacovigilance records were reported, of which 31 were not included in the data analysis because they were spontaneous notifications or were identified other than by active search and did not include the trigger tools, such as abrupt discontinuation of the medication or alterations in laboratory test results, identified through the patients' pharmacotherapy follow-up. Thus, in the first half of 2021, 83 active Pharmacovigilance searches were carried out, representing 72.8% of the total Pharmacovigilance records.

January and February were the months with the highest numbers of active search records, 27 and 23, respectively. The absolute number of records was reduced in the subsequent months: 14 in March; 7 in April; 9 in May; and 3 in June (Table 1). Despite the reduction in active search records for trigger tools, the number of notifications of adverse reactions remained between 2 and 4 per month, except for June, in which there was no record of DRARs. Thus, the mean was approximately 2.5±1.5 notifications per month, with 15 notifications in all (18.1% of the total active searches performed and 11.6% of the total Pharmacovigilance records and DRAR notifications (Table 1).

Figure 1. Stages of the method followed to conduct the study.

1. Active search in Pharmacovigilance and DRAR[1] notification	The active search service in Pharmacovigilance was carried out in intensive care units (neonatal, pediatric and adult) and inpatient units (obstetrics, pediatrics, cardiology, neurology, oncology, orthopedics and COVID-19), following the stages below: • **Stage 1:** Search for prescriptions containing the following trigger tools: Vitamin K, protamine, prothrombin complex, naloxone, flumazenil and activated carbon, through a report obtained by a computerized system. The searches were conducted twice a week from the date of the last search performed. • **Stage 2:** Investigation about the use of trigger tools by means of diverse information contained in medical records and through multiprofessional interviews. • **Stage 3:** In case of suspected DRAR, filling out of the Pharmacovigilance form with general information about the patient, brief description of what happened and characteristics of the causative medication, as well as application of the Naranjo/Karch algorithm to assess causality. • **Stage 4:** Evolution in medical chart and notification of the DRARs identified in the institution's quality system for evaluation and subsequent notification to the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária, ANVISA*). All active searches, regardless of the final result, were recorded in the medical chart as Pharmacovigilance pharmaceutical evolutions, except for the use of Vitamin K as hemorrhage prophylaxis in newborns.
2. Data collection	• Data collection through Pharmacovigilance pharmaceutical evolutions obtained through a computerized system and Pharmacovigilance forms filled out from January to June 2021.
3. Data selection	• Active search records resulting from the analysis of prescriptions containing the trigger tools used were selected. Duplicate records were excluded from the analysis, as well as voluntary Pharmacovigilance notifications or those identified by another method that did not include the trigger tools under study, as well as cases of Vitamin K use as hemorrhage prophylaxis in newborns.
4. Data analysis and treatment	• Quantification of the active search records in Pharmacovigilance and DRAR notifications through the trigger tools studied, investigation and characterization of the medications causing DRARs and analysis of the results per hospitalization sector.
5. Statistical analysis	• Descriptive statistical analysis with estimates of absolute and relative frequencies with values expressed as percentages and Positive Predictive Value (PPV), obtained by dividing the number of times a trigger tool was able to identify a DRAR by the number of times the trigger tool was used in the DRAR searches. Central tendency measures (mean values) with Standard Deviations (SDs) The Excel® and GraphPad Prism 5 software programs were used.

[1]Drug-Related Adverse Reaction

The ICU for adults was the unit with the highest number of records (49 active searches and 10 DRAR notifications), followed by the inpatient unit (18 active searches and 4 DRAR notifications). In the neonatal ICU, 10 active searches and only 1 DRAR notification were recorded. The pediatric ICU was the only unit with no DRAR notification records, with 6 active searches (Table 1).

Protamine was the trigger tool with the highest number of active search records (n=22; 44.9%) and DRAR notifications (n=6; 60%) in the ICU for adults, followed by Vitamin K, which accounted for 38.8% (n=19) of the active searches and 30% (n=3) of the DRAR notifications. Other trigger tools with active searches in the unit were prothrombin complex (n=6; 12,2%), naloxone (n=1; 2%) and activated carbon (n=1; 2%). It is to be noted that naloxone was associated with one DRAR notification (n=1; 10%) (Table 1).

Vitamin K was the trigger tool with the highest number of active searches in the other sectors, representing 80% in the neonatal ICU, 66.7% in the pediatric ICU and 38.89% in the inpatient unit. In addition to Vitamin K, active search records for prothrombin (n=2; 33.3%) in the pediatric ICU and for naloxone (n=2; 20%) in the neonatal ICU were also recorded, the latter being linked to a DRAR notification in the sector (n=1; 100%). In the inpatient unit, naloxone was the second trigger tool with the highest number of active searches (n=6; 33.3%), followed by protamine (n=4; 22.2%) and flumazenil (n=1; 5.6%). Of these, naloxone and protamine were responsible for DRAR notifications, with 1 record each (n=2; 50%). Another two notifications were linked to the active search for Vitamin K (50%; Table 1).

In general, the trigger tools with the highest numbers of active search records were as follows: Vitamin K, with 38 records (45.8%) and protamine, with 28 records (33.7%). They were followed by naloxone, with 9 records (10.8%); prothrombin complex, with 6 records (7.2%); and flumazenil and activated carbon, both with only 1 record each (1.2%) (Table 1). The trigger tools that were associated with the notification of potential DRARs were as follows: protamine (n=7; 46.7%), Vitamin K (n=5; 33.3%) and naloxone (n=3; 20%) (Table 1). No DRAR notification records were identified for flumazenil, activated carbon or prothrombin complex. The overall PPV presented a wide variation across the months (from 0 in June to 0.86 in April). The overall PPV obtained was 0.18. The naloxone trigger was the one that presented the best performance with a PPV of 0.33, followed by protamine (PPV=0.25) and by Vitamin K (PPV=0.13).

The seven DRAR notifications found through the use of protamine were related to the use of anticoagulants, six of them to the use of enoxaparin and one related to the use of enoxaparin with acetylsalicylic acid (ASA) and clopidogrel (Table 1). The five DRAR notifications found through the use of Vitamin K were also related to the use of anticoagulants, three of which were related to enoxaparin; one case related to enoxaparin together with ASA and clopidogrel; and another case related to warfarin (Table 1). Of the three DRAR notifications investigated in the use of naloxone, two were related to the use of morphine and one was associated with the use of fentanyl (Table 1). The other notifications were related to extubation procedures and there were also cases in which the medication was listed as "if necessary" for patients with difficult-to-control pain in use of opioids, being available for scheduling in case of occurrence of DRARs.

No drug administration reports were found in the active search involving flumazenil. Activated carbon was used in a case of exogenous poisoning due to attempted suicide; therefore, not being related to any DRAR within the unit.

Discussion

Active search in Pharmacovigilance has proved to be an important tool for the identification of DRARs.[8,12] This study conducted 83 active searches for DRARs, of which it was possible to identify 15, 18.1% of the total involving the search using the trigger tools chosen in the study. Other studies of Brazilian institutions with the use of triggers for the detection of DRAEs found results varying from 7.48% to 15.6%.[5,19]

The high number of active searches in the first months and its consecutive reduction in the following ones are directly related to the hospital occupancy rate during the study period. Such fact is explained by the increase in the number of hospitalizations due to the pandemic caused by the new SARS-CoV-2. Despite this, the results show that DRAR notifications did not vary much, with a mean of 2.5±1.5 reports per month, a value not very different from another study with a mean of 3.92 DRARs per month.[12]

The global PPV found was 0.18. Other studies obtained values of 0.04,[19] 0.144[5] and 0.43.[22] Comparing the performance of each trigger tool is problematic, as the result can be affected by factors such as sample size, changes in diagnostic and therapeutic practices, and temporal variation.[5]

The PPV for protamine and Vitamin K found in our study was higher than that of another survey, where the jointly evaluated PPV for Vitamin K and protamine was 0.167.[5] In the same study, differently from what was found, the benzodiazepine antagonist (flumazenil) and the opioid antagonist (naloxone) were not used in the medical records analyzed. The study by Khan et al. (2015)[23] showed PPV values of 0.33 and 0.28 for protamine and Vitamin K, respectively, showing the sensitivity and specificity of the active search for these medications and the occurrence of DRARs.

Anticoagulants were the medication class most frequently involved in DRARs, in accordance with what was found in the literature.[19-21] The main anticoagulant involved in DRARs identified by protamine and Vitamin K was enoxaparin and the notifications occurred in the ICU for adults and in the inpatient unit. This fact can be explained by the increase in the use of anticoagulants due to infection by SARS-CoV-2. Such use was intensified during the pandemic, contributing to the occurrence of DRARs due to the use of this medication.

The large number of active search records for the use of the protamine and Vitamin K trigger tools can be explained by the use of these medications in surgical and hemodynamic procedures, such as cardiopulmonary bypass and in patients on Total Parenteral Nutrition (TPN). Other causes that justified such use were coagulation disorders and bleeding due to causes other than the use of anticoagulants and electrolyte disorders, in the case of Vitamin K.

The PPV of naloxone can be underestimated since, in some active searches, the medication was listed as "if necessary" in the prescription of patients using high doses of morphine for cases of potential occurrence of DRAEs. Opioids are commonly used for pain control in cancer patients of by those where it is difficult to control pain.

Study of the use of specific trigger tools for neonatal and pediatric patients is scarce in the literature.[24] However, our data indicate that it may be a necessary strategy, due to the low number of

Table 1. Identification of drug-related adverse reactions according to the modality in which Pharmacovigilance is conducted.

Information	Total number of records and notifications N=129	Records corresponding to Pharmacovigilance and to use of trigger tools for recording[8] N=114		DRAR[2] notifications identified through active searches N=15	PPV[3]
		Without trigger tools[6] N=31	With trigger tools[1] N=83		Global PPV[3] =0.18
Notification month n (%)					
January	35 (27.1)	4 (11.4)	27 (77.1)	4 (11.4)	0.15
February	29 (22.5)	4 (13.8)	23 (79.3)	2 (6.9)	0.09
March	22 (17.1)	4 (18.2)	14 (63.6)	4 (18.2)	0.29
April	16 (12.4)	7 (43.8)	7 (43.8)	2 (12.5)	0.86
May	21 (16.3)	9 (42.9)	9 (42.9)	3 (14.3)	0.33
June	6 (4.7)	3 (50.0)	3 (50.0)	-	-
Notification hospital sector[10] n (%)					
ICU for adults	**77 (59.7)**	**18 (23.4)**	**49 (63.6)**	**10 (13.0)**	**-**
Vitamin K	22 (28.6)	-	19 (86.4)	3 (13.6)	-
Protamine	28 (36.4)	-	22 (78.6)	6 (21.4)	-
Naloxone	2 (2.6)	-	1 (50.0)	1 (50.0)	-
Prothrombin complex	6 (7.8)	-	6 (100.0)	-	-
Activated carbon	1 (1.3)	-	1 (100.0)	-	-
Without trigger tool[6]	18 (23.4)	-	-	-	
Neonatal ICU	**11 (8.5)**	-	**10 (90.9)**	**1 (9.1)**	-
Vitamin K	8 (72.7)	-	8 (100.0)	-	-
Naloxone	3 (27.3)	-	2 (66.7)	1 (33.3)	-
Pediatric ICU	**6 (4.6)**	**-**	**6 (100.0)**	**-**	-
Vitamin K	4 (66.7)	-	4 (100.0)	-	-
Protamine	2 (33.3)	-	2 (100.0)	-	-
Hospitalization unit	**35 (27.1)**	**13 (37.1)**	**18 (51.4)**	**4 (11.4)**	-
Vitamin K	9 (25.7)	-	7 (77.8)	2 (22.2)	-
Protamine	5 (14.3)	-	4 (80.0)	1 (20.0)	-
Naloxone	7 (20.0)	-	6 (85.7)	1 (14.3)	-
Flumazenil	1 (2.9)	-	1 (100.0)	-	-
Without trigger tool[6]	13 (37.1)	-	-	-	-
Tracker trigger and medications involved[7,10] n (%)					
Vitamin K	**43 (43.9)**	**-**	**38 (88.4)**	**5 (11.6)**	
Antithrombotic agents (B01A)[4]	5 (11.6)	-	-	5 (100.0)	
Enoxaparin	3 (60.0)	-	-	3 (100.0)	0.13
Enoxaparin, Clopidogrel, Acetylsalicylic Acid	1 (20.0)	-	-	1 (100.0)	
Warfarin	1 (20.0)	-	-	1 (100.0)	
Others[5]	33 (76.7)	-	33 (100.0)	-	
Identification of DRARs[9]	5 (11.6)		5 (100.0)	-	
Protamine	**35 (35.7)**	**-**	**28 (80.0)**	**7 (20.0)**	
Antithrombotic agents (B01A)[4]	7 (20.0)	-	-	7 (100,0)	
Enoxaparin	6 (85.7)	-	-	6 (100.0)	0.25
Enoxaparin, Clopidogrel, Acetylsalicylic Acid	1 (14.3)	-	-	1 (100.0)	
Others[5]	21 (60.0)	-	21 (100.0)	-	
Identification of DRARs[9]	7 (20.0)		7 (100.0)	-	
Naloxone	**12 (12.2)**	**-**	**9 (75.0)**	**3 (25.0)**	
Opioids (N02A)[4]	3 (25.0)	-	-	3 (100.0)	
Morphine	2 (66.7)	-	-	2 (100.0)	0.33
Fentanyl	1 (33.3)	-	-	1 (100.0)	
Others[5]	6 (50.0)	-	6 (100.0)	-	
Identification of DRARs[9]	3 (25.0)		3 (100.0)	-	-
Prothrombin complex	**6 (6.1)**	**-**	**6 (100.0)**	**-**	**-**
Activated carbon	**1 (1.0)**	**-**	**1 (100.0)**	**-**	**-**
Flumazenil	**1 (1.0)**	**-**	**1 (100.0)**	**-**	**-**

[1]Pharmacovigilance active search 01/2021. [2]Notification of Drug-Related Adverse Reaction. [3]PPV: Positive Predictive Value. nnnnn[4]Anatomical Therapeutic Chemical (ATC) Classification. [5]Use of trigger tools not related to DRARs. [6]Spontaneous (or voluntary) notification or other methods not involving trigger tools. [7]The results of the triggers are only presented when there was a notification associated to them. [8]Record of Pharmacovigilance pharmaceutical evolutions. [9]Use of trigger tools related to the identification of DRARs.

DRAR identification in the units (n=1) with the trigger tools used. The use of Vitamin K is particularly linked to that of TPN, due to these patients' need for caloric and protein intakes. Protamine was exclusively used in the units during surgical procedures.

As this is a retrospective study, even with a well-established protocol, its main limitation was the possible underestimated count of active search records or DRAR notifications not recorded in the pharmaceutical record or notification form. To the present day, the multiprofessional team has not reliably reported the DRARs, precluding proper analysis. In addition to that, there are variables intrinsic to the filling out the Karch/Lasagna and Naranjo algorithms.

Conclusion

This study reinforces the importance of carrying out an active search in Pharmacovigilance, which represented 72.8% of all the Pharmacovigilance records during the study period. Through the data obtained, it was possible to notice that the results presented some variations according to the sector analyzed. The ICU for adults was the unit with the highest incidence of adverse reactions, with protamine being the protagonist in the reports due to the increased use of anticoagulants in patients with COVID-19. It was also possible to characterize the profile of the trigger tools and of the medications with suspicion of causing DRARs identified by them. Due to the low number of DRARs identified in the neonatal and pediatric ICUs, a review of the trigger tools used to identify DRARs in the sectors is suggested. Studies with a greater number of notifications are still needed to strengthen the Pharmacovigilance culture in the institution and monitoring of the results.

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Collaborators

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Conflicts of interest statement

The authors declare that there is no conflict of interest regarding this article.

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