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Description of pharmaceutical activities and the use of radiopharmaceuticals in a hospital radiopharmacy of the teaching hospital in southern Brazil

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Abstract

Objective: To present the pharmacist´s activities developed in a nuclear medicine service of university hospital. **Method:** Retrospective descriptive study based on data from 2015 to 2022 and organized in productivity, logistics, and patient safety. **Results:** As for productivity, on average, 498 doses/month manipulations, 102 ^{99m}Tc-radiopharmaceuticals/month and 3.4 oral capsules/month were administered. Of the quality controls, 96.7% of the ^{99m}Tc-eluates were approved and 93.5% of the ^{99m}Tc-radiopharmaceuticals were approved for administration. Of the ready-to-use radiopharmaceuticals for diagnostic purposes, ^{18}F-FDG corresponded to 71.2% of the manipulations. As for logistics, the management of lyophilized reagents provided a reduction in losses due to expirations from 40% to 8.6%. Regarding patient safety, 03 cases of adverse drug reactions were identified after the administration of radiopharmaceuticals dextran (^{99m}Tc), sodium iodide (^{131}I) and sestamibi (^{99m}Tc), being classified as possible and probable, and 35 medications errors involving radiopharmaceuticals, being 28.6% related to sestamibi (^{99m}Tc). **Conclusion:** The pharmacist, with knowledge and expertise in drugs, can collaborate with safety and quality issues in internal processes regarding the use of radiopharmaceuticals.

Keywords: nuclear pharmacy, nuclear medicine, radiopharmaceuticals, radionuclides, patient safety

Descrição das atividades farmacêuticas e uso dos radiofármacos em radiofarmácia hospitalar de um hospital de ensino no sul do Brasil

Resumo

Objetivos: Apresentar as atividades farmacêuticas desenvolvidas em um serviço de medicina nuclear de hospital universitário. **Método:** Estudo descritivo retrospectivo com base nos dados do período de 2015 a 2022 e organizados em produtividade, logística e segurança do paciente. **Resultados:** Quanto à produtividade, em média, realizaram-se 498 manipulações de doses/mês, 102 marcações de ^{99m}Tc-radiofármacos/mês e 3,4 dispensações de cápsulas orais para terapia/mês. Dos controles de qualidades, 96,7% dos ^{99m}Tc-eluatos foram aprovados e 93,5% dos ^{99m}Tc-radiofármacos estiveram aprovados para administração. Dos radiofármacos de pronto uso para fins diagnóstico, ^{18}F-FDG correspondeu a 71,2% dos fracionamentos. Quanto à logística, o gerenciamento dos reagentes liofilizados proporcionou redução de perdas por vencimentos de 40% para 8,6%. Quanto à segurança do paciente, identificaram-se 03 casos de reações adversas após a administração dos radiofármacos dextrana (^{99m}Tc), iodeto de sódio (^{131}I) e sestamibi (^{99m}Tc), sendo classificadas como possíveis e prováveis, e 35 erros de medicação envolvendo radiofármacos, sendo 28,6% relacionados com sestamibi (^{99m}Tc). **Conclusão:** O farmacêutico, com o conhecimento e expertise em medicamentos, pode colaborar com as questões de segurança e qualidade nos processos internos no uso dos radiofármacos.

Palavras-chave: farmácia nuclear, medicina nuclear, compostos radiofarmacêuticos, radioisótopos, segurança do paciente

Introduction

Radiopharmaceuticals are defined as pharmaceutical preparations with diagnostic or therapeutic purposes that, when ready for use, contain one or more radionuclides, according to ANVISA Resolution No. 658 of March 2022. According to the World Health Organization, radiopharmaceuticals are pharmaceutical products that can be classified as ready-to-use radioactive products, radionuclide generators, non-radioactive components (lyophilized reagents) for the preparation of compounds labeled with radioactive elements, and precursors used for labeling other substances prior to patient administration[1].

Thus, a radiopharmaceutical is a combination of a radionuclide and a drug or biologically active molecule that acts as a carrier or ligand, determining the desired localization within the body[2]. The radionuclide is the main element in the composition of a radiopharmaceutical, capable of emitting different types of radioactive decay and presenting different half-lives, and is artificially produced in nuclear reactors, particle accelerators, or generators[3]. These pharmaceutical preparations, which make use of ionizing radiation, are applied in nuclear medicine, tailored to each patient, where imaging evaluates the function and physiology of various body systems with minimal adverse effects[4,5].

Radionuclides and/or radiopharmaceuticals can be produced, handled, and dispensed by different types of radiopharmacies, each with its own level of complexity. Radiopharmacies can be classified as: industrial radiopharmacy, responsible for producing radionuclides, generators, and supplies for use in centralized and hospital radiopharmacies; centralized radiopharmacy, an independent facility where manipulation and fractionation (single doses) of ready-to-use products are carried out for distribution to nuclear medicine services; hospital radiopharmacy, where management processes involving traceability of radiopharmaceutical use, receipt, labeling, fractionation, quality control, and dispensing of different radionuclides take place, and unlike other radiopharmacies, it is the one that has direct contact with patients; and research radiopharmacy, where research and development of new radionuclides for diagnostic and therapeutic purposes are conducted[3,6].

The first use of a radiopharmaceutical in humans occurred in 1927, when Blumgart and Yens measured human circulation after injecting a saline solution exposed to radon. Later, in 1938, studies by Hertz, Roberts, and Evans on thyroid function using ^{121}iodine marked the beginning of systematic use[6,7]. It is known that, of the procedures performed in nuclear medicine, about 95% are for diagnostic purposes, mostly within the specialties of oncology, cardiology, and neurology[3].

In 1960, in the United States, the concept of nuclear pharmacy or radiopharmacy emerged, and for the first time, the activities/services related to radiopharmacy and the role of the radiopharmacist in the development, preparation, quality control, and dispensing of radiopharmaceuticals were defined[8]. In Brazil, areas involving radiopharmaceuticals are regulated by radioprotection standards established by the National Nuclear Energy Commission (CNEN), such as CNEN Standard NN 3.05 of 2013, and by sanitary regulations determined by the Brazilian Health Regulatory Agency (ANVISA), such as Resolution No. 38 of 2008. Since 2008, Federal Pharmacy Council resolutions Resolution CFF No. 486 of 2008 and Resolution CFF No. 655 of 2018 have established provisions for the pharmacist's clinical role in radiopharmacy, including criteria for the professional's legal qualification in the field.

The aim of this study was to present the pharmaceutical activities carried out in a nuclear medicine service (NMS) of a university hospital regarding dose labeling and unitization (activities), quality control, logistics, and pharmacovigilance actions involving radiopharmaceuticals, as well as their implications in the routine of the service.

Methods

Study setting

A retrospective descriptive survey was conducted between 2015 and 2022 based on pharmaceutical records from a hospital radiopharmacy within the Nuclear Medicine Service (NMS) of a large public university hospital with 860 beds, located in southern Brazil. The institution's NMS performs diagnostic imaging procedures using Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography/Computed Tomography (PET/CT) for several specialties, with a primary focus on oncology. The NMS also performs therapeutic procedures, such as radioiodine therapy. Approximately 90% of the service's care is provided through the Brazilian Unified Health System (SUS), with an average of 25 examinations per day.

Data records

The records and data compilation were carried out by pharmacists working in the NMS. The pharmaceutical activities in our NMS are related to the management of radiopharmaceuticals (procurement, inventory, and storage), labeling of lyophilized reagents with sodium pertechnetate (^{99m}Tc-radiopharmaceuticals), quality control of ^{99m}Tc eluates from ^{99}Mo/^{99m}Tc generators and of ^{99m}Tc-radiopharmaceuticals, manipulation and dispensing of radiopharmaceuticals in unit doses for diagnostic purposes, such as fluorodeoxyglucose (^{18}F) (^{18}F-FDG) and ^{99m}Tc-radiopharmaceuticals. Therapeutic dose preparation and dispensing were also performed, for example, with sodium iodide (^{131}I). ANVISA Resolution No. 38 of June 2008 stipulates that pharmacovigilance, technovigilance, and hemovigilance actions must be reported and investigated when related to adverse events such as adverse drug reactions, errors in radiopharmaceutical administration, or severe cardiac and neurological events. Thus, as part of the pharmaceutical activities, pharmacovigilance in this context included reporting medication errors, product technical complaints, and adverse reactions involving radiopharmaceuticals.

The collected data were organized in Excel spreadsheets for descriptive analysis.

Data collection

For the purposes of this study, and to improve the presentation of information, the data were organized into three categories: productivity, logistics, and patient safety. Data describing the profile of examinations performed at the NMS were compiled to present the study setting.

For productivity, the following variables were considered: manipulations and dispensations performed for diagnostic and therapeutic procedures, labeling of lyophilized reagents, quality control (QC) procedures performed and approved for generator eluates and ^{99m}Tc-radiopharmaceuticals.

The collected data included: total number of fractionated doses of radiopharmaceuticals (labeled and ready-to-use), total number of lyophilized reagent labelings with ^{99m}Tc per batch, total number of therapeutic dispensations (capsules and solutions), and total number of QC procedures performed for ^{99m}Tceluates and ^{99m}Tc-radiopharmaceuticals per batch. Ready-to-use radiopharmaceuticals are supplied for direct intravenous or oral administration. These are radiopharmaceuticals with a sufficiently long half-life to allow their production in industrial radiopharmacies and, after quality control, distribution to nuclear medicine services across the country, where they may be fractionated into doses or patient-specific activities as prescribed, when necessary[9].

For cost optimization purposes, losses related to the expiration of lyophilized reagents were considered, since the shelf life of these products is relatively short and requires stricter logistical control. Losses also included preparations (manipulations) of ^{99m}Tc-radiopharmaceuticals that were dispensed but not administered for various reasons (patient absence, errors in patient preparation for the exam, cancellation by the requesting physician, or equipment operational issues). However, losses and non-administration of primary radiopharmaceuticals were not included in this study. The data collected comprised: losses due to expiration of lyophilized reagents and fractionated doses (syringes) dispensed but not administered.

For patient safety, medication errors, reports of adverse drug reactions (ADRs), and technical complaints involving radiopharmaceuticals were considered. The data collected included: radiopharmaceutical involved, reason for the suspected event, action or conduct adopted, and patient information.

The projects for data collection and use were approved by the institution's Research Ethics Committee (CAAE: 64237816700005327 and CAAE: 65615222900005327).

Results

Between 2015 and 2022, a total of 45,317 diagnostic and therapeutic procedures were performed (average of 472 procedures/month). Exceptions were observed in 2020 and 2021, the years of the Coronavirus pandemic, during which the monthly average was approximately 309, and some examinations followed different care routines. Table 1 presents the main ^{99m}Tc-radiopharmaceuticals organized by body system.

Table 2 shows data related to pharmacists' productivity, i.e., general information on dose fractionation (syringes), labeling, dispensing, quality control (QC), and total examinations performed during the period. Among the ready-to-use radiopharmaceuticals for PET/CT diagnostics, ^{18}F-FDG accounted for 3,312 (71.2%) of manipulations. For SPECT diagnostics, gallium citrate (^{67}Ga) was responsible for 176 (3.8%) manipulations, metaiodobenzylguanidine (^{131}I-MIBG) for 169 (3.6%), chromium (^{51}Cr and ^{51}Cr-EDTA) for 160 (3.4%), and thallium chloride (^{201}Tl) for 60 (1.3%), while 767 (16.5%) manipulations involved other radiopharmaceuticals. Among the ready-to-use radiopharmaceuticals for therapeutic purposes administered orally, sodium iodide (^{131}I) in oral solution form accounted for 832 (71.6%) manipulations, while in solid oral form, 326 (28%) capsules of ^{131}I were dispensed.

Regarding the QC of ^{99m}Tc eluates, performed according to the manufacturer's guidelines (IPEN – Institute for Energy and Nuclear Research), in 96.7% of the eluates all recommended QC tests (radiochemical purity, radionuclidic purity, chemical purity, and pH) were performed before labeling of the lyophilized reagents; the remaining 3.3% were not performed as they corresponded to elutions carried out for equipment testing or other reasons[4,5].

Table 1. Main diagnostic procedures using 99mTc-labeled radiopharmaceuticals according to the physiological system in the NMS (n = 39,505).

Diagnostic procedures by system	Radiopharmaceuticals	Radiopharmaceutical abbreviation	Lyophilized reagent abbreviation	Total procedures performed (%)
Cardiology	Sestamibi (99mTc)	^{99m}Tc-MIBI (MIBI)	MIBI	16471 (41.7%)
	Sodium pyrophosphate	^{99m}Tc-PIRO	PIRO	
Musculoskeletal	Medronate (99mTc)	^{99m}Tc-MDP	MDP	10995 (27.8%)
	Sodium pyrophosphate	^{99m}Tc-PIRO	PIRO	
Renal/Urinary	Succimer (99mTc)	^{99m}Tc-DMSA	DMSA	4784 (12.1%)
	Sodium pentetate (99mTc)	^{99m}Tc-DTPA	DTPA	
Pulmonary	Macrosalb	^{99m}Tc-MAA	MAA	1896 (4.8%)
	Sodium pertechnetate (99mTc)	^{99m}Tc	-	
Endocrinology	Sestamibi (99mTc)	^{99m}Tc-MIBI	MIBI	1812 (4.6%)
	Sodium pertechnetate (99mTc)	^{99m}Tc	-	
Lymphatic	Dextran (99mTc)	^{99m}Tc-DEXTRAN	DEXTRAN	1254 (3.2%)
	Sodium fitate	^{99m}Tc-FITATO	FITATO	
Hepatobiliary	Disofenin (99mTc)	^{99m}Tc-DISIDA	DISIDA	777 (2.0%)
	Sodium fitate	^{99m}Tc-FITATO	FITATO	
Gastrointestinal	Sodium pertechnetate (99mTc)	^{99m}Tc	-	522 (1.3%)
	Sodium fitate	^{99m}Tc-FITATO	FITATO	
Central nervous system	Bicisate (99mTc)	^{99m}Tc-ECD	ECD	339 (0.8%)
Others (other radiopharmaceuticals and/or procedures)				655 (1.7%)

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Table 2. Productivity data for the period 2015–2022.

Evaluated Items	2015 - 2016	2017 - 2018	2019 - 2020	2021 - 2022	Total	Mean	*SD
Total manipulations or individualized doses	16198	13722	9400	8563	47853	5981.6	1810.7
Diagnosis							
Total exams performed	14670	12859	8638	7988	44155	5519.4	1729.4
Total manipulations with ^{99m}Tc-radiopharmaceuticals	13483	11535	7707	6780	39505	4938.1	1685.2
Total manipulations of ready-to-use radiopharmaceuticals	1187	1324	931	1208	4650	581.2	151.7
Therapy							
Total exams performed	444	312	228	178	1162	145.2	59.4
Total manipulations of ready-to-use radiopharmaceuticals	310	213	172	141	836	104.5	37.9
Total dispensations of oral solid forms (capsules)	134	99	56	37	326	40.7	24.3
Lyophilized reagents labeled with ^{99m}Tc							
Total ^{99m}Tc-radiopharmaceuticals	3212	2874	2123	1634	9843	1230.4	354.2
Quality Controls Performed	2696	2808	2084	1621	9209	1151.1	295.0
Generator eluate							
Total eluations performed	1073	1096	918	869	3956	494.5	70.0
Total quality controls performed (^{99m}Tc-eluate)	994	1064	898	868	3824	478	66.4

*SD: Standard Deviation

For ^{99m}Tc-radiopharmaceuticals, QC was performed in 93.5% of the labelings, with results approved for patient administration; 6.5% were not approved for administration due to low radiochemical purity or lack of testing. Identification of batches with radiochemical purity outside the required standard occurred during the QC of the ^{99m}Tc-radiopharmaceutical; subsequently, for each batch, triplicate tests were conducted for confirmation in accordance with the manufacturer's assays (RPH). Quantitative data are presented in Table 2.

Among the ^{99m}Tc-radiopharmaceuticals most frequently used in the radiopharmacy for diagnostic purposes (n ≈ 9,700 vials of lyophilized reagents), the following were prominent: ^{99m}Tc-MDP accounted for 2,623 (27%) labelings, ^{99m}Tc-MIBI for 2,474 (25.5%), ^{99m}Tc-DTPA for 1,448 (14.9%), ^{99m}Tc-MAA for 1,118 (11.5%), ^{99m}Tc-DEXTRAN for 742 (7.6%), ^{99m}Tc-PHYTATE for 457 (4.7%), ^{99m}Tc-DMSA for 409 (4.2%), ^{99m}Tc-ECD for 340 (3.5%), and others for 529 (5.4%).

Regarding radiopharmaceutical logistics, cost optimization data were characterized by losses due to expiration of lyophilized reagents and fractionated doses of ^{99m}Tc-radiopharmaceuticals that were dispensed but not administered. During the study period, 197 vials of lyophilized reagents were lost (average of 24.6 vials per year). Among the lyophilized reagents, losses included 68 (34.5%) vials of DISIDA, 34 (17.2%) of PIRO, 33 (16.7%) of PHYTATE, 22 (11.2%) of ECD, 21 (10.7%) of DMSA, and 16 (8.1%) of others. Figure 1 shows the total variation in losses due to expiration of lyophilized reagent vials during the period.

As for dose losses, 3,084 doses (syringes) were fractionated and dispensed but not administered (average of 32.1 per month; corresponding to 5–7% of manipulations). Among the fractionated radiopharmaceuticals, 1,471 (47.7%) corresponded to ^{99m}Tc-MIBI preparations, mainly for cardiac scintigraphy; 767 (24.9%) to ^{99m}Tc-MDP for bone scintigraphy; 242 (7.8%) to ^{99m}Tc-DMSA for static renal scintigraphy; 154 (4.9%) to ^{99m}Tc-DTPA for dynamic renal scintigraphy; 143 (4.6%) to ^{99m}Tc-MAA for lung perfusion scintigraphy; 79 (2.6%) to ^{99m}Tc-DEXTRAN for lymphatic system scintigraphy; and 228 (7.4%) to others. Figure 2 shows the losses of prepared doses (n ≈ 47,800 syringes) and those not administered (n ≈ 3,084 syringes) over the period.

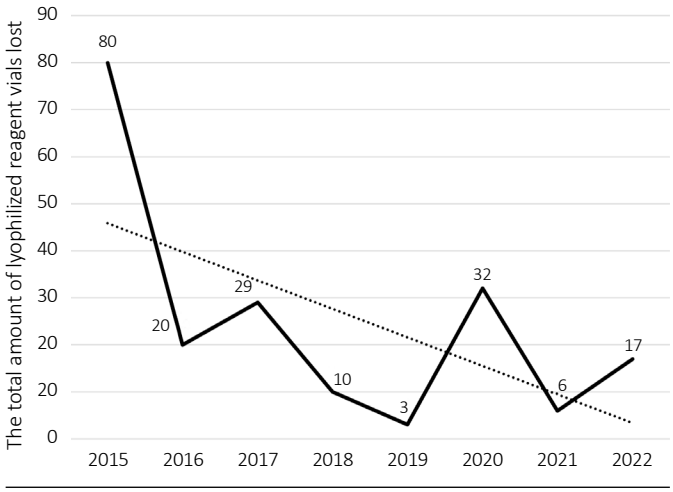
With regard to ADRs, the NMS observed, following administration of 3 radiopharmaceuticals (incidence of 0.006%)- ^{99m}Tc-DEXTRAN, ^{99m}Tc-sestamibi (MIBI), and sodium iodide (^{131}I) - the onset of nausea, vomiting, hypertension, and pain episodes. The events were classified according to causality using the algorithm of Naranjo et al. (1981) as possible ADRs (nausea, vomiting, and hypertension with ^{99m}Tc-DEXTRAN; nausea and vomiting with ^{131}I) and probable ADRs (nausea, vomiting, and pain with ^{99m}Tc-MIBI) [11]. The ADRs were recorded as radiological occurrences of the NMS; since they were mild ADRs already well described in the literature and in the product package inserts, they were not reported to manufacturers and/or ANVISA.

As for product technical complaints, two radiopharmaceuticals, MIBI and DMSA, were reported internally and to manufacturers due to QC problems in certain batches. In both products, radiochemical purity remained below 90%, and the manufacturers replaced the affected batches. No technical complaint was reported to ANVISA.

Regarding medication errors, classified according to the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP), 35 errors were identified during the study period (rate of 0.08%). Of these reports, 16 cases (45.7%) were related to preparation/handling in the radiopharmacy, and 9 cases (25.7%) were associated with the administration of radiopharmaceuticals. Most error notifications were linked to ^{99m}Tc-MIBI, accounting for 10 cases (28.6%).

Table 3 presents a summary of pharmaceutical activities related to productivity, logistics, and patient safety. Tables 2 and 3 jointly illustrate the pharmaceutical activities carried out in the hospital radiopharmacy of the Nuclear Medicine Service (NMS) at the study site.

Figure 1 . Total Losses of Lyophilized Reagent Vials Due to Expiration During the Period (n = 197)



Discussion

Pharmacists play a pivotal role in radiopharmacies, whether in production, quality control, preparation, dispensing, or in clinical activities involving radiopharmaceuticals, as well as in ensuring process safety and quality assurance[11]. In hospital-based NMS, radiopharmacies present specific challenges and complexities in the scope of pharmaceutical activities performed.

Pharmaceutical productivity in the hospital radiopharmacy can be represented by labeling, fractionation, quality control, and dispensing of radiopharmaceuticals. Pozzo et al. (2023), covering the period from 2015 to 2021, reported a steady increase in PET procedures in Brazil, even during the pandemic[12]. PET relies on short half-life radiopharmaceuticals, either produced in particle accelerators (cyclotrons) and delivered ready-to-use, such as ^{18}F-FDG, or obtained from radionuclide generators for local labeling, such as gallium-68 (^{68}Ga). These radiopharmaceuticals, often produced by private companies, were not significantly affected by transportation or supply issues during the pandemic.

Figure 2 . Total Fractionated and Unadministered Doses (Syringes) from 2015 to 2022.

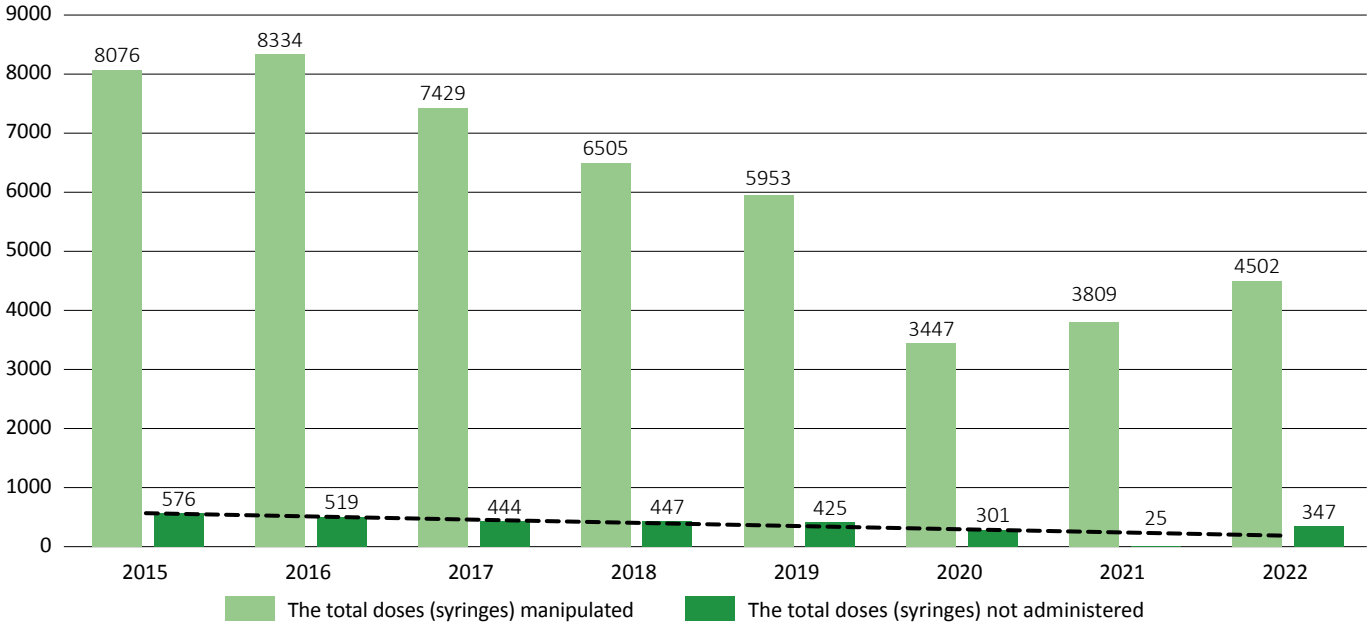


Table 3. Evaluated Items: Productivity, Logistics, and Patient Safety, 2015 to 2022.

From the Study	Evaluated Items – Pharmaceutical Activities at the Study Site	Total (monthly average)
Productivity	Manipulation or fractionation of radiopharmaceuticals	47.853 (498.5)
	Dispensation of oral solid forms	326 (3.4)
	Labeling of lyophilized reagents with 99mTc	9.843 (102.5)
	Quality control of 99mTc-radiopharmaceuticals	9.209 (95.9)
	Quality control of 99mTc eluates	3.824 (39.8)
Logistics	Loss of lyophilized reagents due to expiration	197 (2.0)
	Unit-dose syringes dispensed but not administered	3.084 (32.1)
Patient Safety	Medication errors	35 (0.4)
	Adverse drug reactions (ADRs)	04 (0.04)
	Technical complaints	02 (0.02)

Although they provide high diagnostic accuracy and clinical effectiveness, not all PET procedures are reimbursed by the Brazilian Unified Health System (SUS), and they involve high costs[12,13]. Bertoldi et al. (2022), in a descriptive study conducted in 2020 at the same NMS as the present study, reported that 74% of oncological PET/CT scans with ^{18}F-FDG were reimbursed by SUS, while 10.8% were covered by private insurance, with most cases (55%) performed for the diagnosis of non-Hodgkin's lymphoma[14]. The expansion of PET diagnostic procedures for treatment evaluation, staging, and diagnostic investigation is reflected in the total number of examinations performed during the study period, accounting for 71% of procedures, corresponding to more than 3,300 PET scans.

In our NMS, more than 90% of diagnostic examinations involved the preparation of ^{99m}Tc-radiopharmaceuticals, averaging 24 exams per day. Quality controls of both the ^{99m}Tc-eluate and ^{99m}Tc-radiopharmaceuticals were systematically performed prior to patient administration, in compliance with ANVISA Resolution No. 38 of June 2008. Pozzo et al. (2023) also highlighted that conventional diagnostic procedures, such as stress/rest myocardial scintigraphy, used to assess ventricular dysfunction, ischemia, and myocardial viability, and bone scintigraphy, used to detect bone metastases- remain among the most frequently performed procedures under SUS, representing 80.1% and 85.2% of exams, respectively. These findings are consistent with the results of our study, in which myocardial and bone scintigraphy were among the most requested procedures[12].

The generator quality control approval rate of 96.7% was deemed acceptable, although ideally 100% of elutions should undergo testing. Required assays for ^{99m}Tc-eluate release include chemical, radionuclidic, and radiochemical purity tests, along with pH and visual inspection[4]. In certain generator batches, deviations were observed in chemical purity, indicating an excess of alumina/aluminum (Al_2O_3) in the eluate (>5 ppm). The presence of Al^{3+} ions is associated with reduced stability of ^{99m}Tc-DTPA increasing free technetium content and compromising product quality, altered biodistribution of ^{99m}Tc-MDP with abnormal hepatic and splenic uptake, and interference with the particle size of ^{99m}Tc-MAA, leading to higher pulmonary concentration of the radiopharmaceutical, among other adverse effects[15].

Of the ^{99m}Tc-radiopharmaceuticals, 93.5% were approved in their quality control tests (pH, radiochemical purity, and visual appearance of the solution). In some batches of ^{99m}Tc-MIBI and ^{99m}Tc-DMSA, we identified deviations in radiochemical purity, which fell below 90% as indicated by the manufacturer; these cases were reported both internally and to the manufacturer, with the affected batches subsequently replaced.

In this study, the logistics of lyophilized reagents, together with cost optimization, were directly related to the management of radiopharmaceuticals, encompassing the handling of activities and radiopharmaceuticals ordered from IPEN (Institute of Energy and Nuclear Research), the total volume of ^{99m}Tc-radiopharmaceuticals, and the scheduling of patients, all of which directly impact costs by reducing waste. In this context, special attention was given to losses resulting from the expiration of lyophilized reagents, as these products have a relatively short shelf life due to the properties of their components, which are highly sensitive to moisture and oxygen[3]. Initially, it was observed that the monthly orders of lyophilized reagents from manufacturers significantly exceeded the service's consumption, leading to unused stock and expiration. To address this, orders were subsequently adjusted based on the average monthly consumption, thereby reducing losses and positively impacting the area's costs. Losses of lyophilized reagent vials varied over the years but showed a significant reduction from the beginning to the end of the monitoring period, decreasing from 40% (80 vials) to 8% (17 vials).

As for the fractionated doses that were dispensed but not administered, whenever possible, these were reassigned for use in other cases within the radiopharmaceutical's validity period. It was observed that approximately 6.4% of doses were not administered, highlighting the need for improved dispensing planning by the radiopharmacy. One illustrative example was ^{99m}Tc-MIBI, a radiopharmaceutical used in cardiac scintigraphy, which requires patient preparation 24 hours prior to the examination, including restrictions on certain foods, beverages, and medicines, as well as a fasting period. Due mainly to lack of adherence to dietary instructions, many patients were unable to undergo the exam because of inadequate pre-exam preparation. To mitigate this issue, illustrated educational materials with patient instructions were developed to facilitate comprehension, particularly regarding prohibited foods and beverages, and to emphasize the importance of correctly following the guidelines for an accurate evaluation of myocardial perfusion, thereby reducing the number of unadministered doses.

Pharmacovigilance actions are essential to detect problems, monitor, and prevent adverse events related to radiopharmaceuticals, since such events may compromise care during the procedure or patient safety through potential harm. Patient safety involves identifying the event, reporting it, and implementing preventive or corrective measures that reduce risks or harm while also fostering process improvements with an educational approach for healthcare professionals.

Actions that enable the identification of problems or deviations in radiopharmaceutical quality are highly relevant, as such deviations can compromise the quality of imaging examinations by interfering with the biodistribution of the radiopharmaceutical in the body[16]. Regarding adverse drug reactions (ADRs), the incidence related to radiopharmaceuticals is considered low when compared with other classes of medicines, given that the administered doses involve low levels of radioactivity and, in most cases, consist of a single administration per patient[17]. The most commonly reported ADRs with radiopharmaceuticals include nausea, dyspnea, bradycardia, hypotension, flushing, urticaria, and bronchospasm; no reports are associated with the radiation itself[17].

Santos-Oliveira and Machado (2011), when analyzing studies related to ADRs, observed that the prevalence of ADRs with radiopharmaceuticals ranged from zero to 25 cases per 100,000 administrations, most of them classified as mild[18]. Schreuder et al. (2019) analyzed 2,447 ADRs involving radiopharmaceuticals and found that 84.4% of the events, mostly classified as mild, were related to radiopharmaceuticals used for diagnostic purposes (mean of 1.63/100,000 administrations), with cutaneous reactions accounting for 26.6% of the events[19]. An American study conducted between 2007 and 2011 reported that, during this period, 1,010,977 diagnostic examinations (20.5% PET and 79.5% SPECT) and 13,200 therapeutic procedures were performed, finding an ADR prevalence of 2.3/100,000 administrations[20].

As observed in our service, the number of ADRs identified and reported was low, and most were classified as possible, potentially attributable to different causes. These are well described in the literature and are generally easy to manage[17,19].

However, studies evaluating quality of life and the impact of potential late ADRs have shown that the prevalence of ADRs after radiopharmaceutical administration, both for diagnostic and therapeutic purposes, may be higher than reported[21,22]. Schreuder et al. (2021) assessed ADR frequency from the patient's perspective and concluded that 2.8% of cases reported experiencing some ADR following diagnostic radiopharmaceutical administration, with 80% of events occurring shortly after administration and 20% within one week after injection in the nuclear medicine setting[21].

Medication errors in hospital service processes may occur; however, identifying these events enables the development of corrective and improvement actions to prevent recurrence. All such actions should carry an educational component for those involved and other professionals.

Studies conducted in nuclear medicine services (NMS) have shown error rates above 20% across different stages of the processes[17,23]. Despite the low error rate (0.08%) found in our study, this finding is consistent with data reported in the literature regarding injectable medication preparation errors in hospitals across different regions, where rates can range from 0.1% to 73%[24]. Kearney and Denham (2016) evaluated 570 incidents reported to the Australian Medicines Agency involving radiopharmaceuticals and found that 73.2% of errors were related to incorrect preparation and administration, with 7.2% linked to incorrect dosing and 36.4% to radiopharmaceutical substitution during administration[25]. Kasalak et al. (2020) evaluated incidents in the nuclear medicine service of a tertiary hospital in the Netherlands, where, among 147 identified events, 24.5% were associated with radiopharmaceuticals (including substitution, incorrect dose, improper preparation, and inadequate administration route), and 19% with administration incidents, mostly patient mix-ups. Importantly, in 98.6% of identified errors, no harm to patients was reported[5]. The low rates observed in pharmacovigilance activities in our study, including ADRs, medication errors, and product-related technical complaints, may indicate good internal process control and safety.

With regard to occupational radiation exposure rates, these were not considered in this study. For radiological protection purposes, pharmacist shifts in the radiopharmacy area must be rotated. For diagnostic radiopharmaceuticals, the main differences for professionals in the field are related to exposure, penetration, and the energy released by the compounds: while ^{99m}Tc-radiopharmaceuticals emit electromagnetic radiation in the form of gamma photons at 140 keV, ^{18}F-FDG emits positron photons at 511 keV.

It is important to acknowledge the limitations of this study. There are currently many novel radiopharmaceuticals available for diagnostic and therapeutic purposes in nuclear medicine; however, their high cost hinders routine incorporation, leaving classical radiopharmaceuticals in use at some public institutions. The complexity of radiopharmaceuticals in NMS impacts both pharmaceutical activities and radiological exposure rates. In this study, pharmacists' dosimetry in relation to individual activities was not assessed. Additionally, regarding logistics, losses of primary radiopharmaceuticals were not considered, nor were cost variations over time.

Conclusion

This study contextualized the pharmaceutical activities carried out by the radiopharmacy in a NMS of a public teaching institution. The activities were presented with respect to productivity, patient safety, and logistics. The radiopharmaceuticals involved in each activity were described, along with a brief discussion of their implications for service routines. In summary, the study highlights that pharmacists, with their knowledge and expertise in medications, acting as members of a multidisciplinary team, can contribute significantly to process safety and quality in the use of radiopharmaceuticals.

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Contributors

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Conflict of interest

The authors declare no conflicts of interest related to this article.

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