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Adverse Reactions to Contrast Media in Patients Seen at the International Clinic, San Borja Headquarters

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Abstract:
This paper aimed to determine the adverse reactions related to contrast media used in patients treated in the imaging unit of the International Clinic, San Borja headquarters, from January to December 2019. The study methodology was of a basic descriptive-retrospective type, with a non-experimental cross-sectional design. The study sample consisted of medical indications from the treating physician obtained in the imaging area. The data collection sheets of the patients who presented adverse reactions were used as an instrument to measure the study variables. The research identified that the adverse reactions in patients were of dermatological (79.6%, 41) and respiratory (4.5%, 3) nature. The highest incidence was observed in females (63.6%, 28). Adults (29 to 49 years) formed the most frequent age group, comprising 70.5% (31). Skin rash and pruritus with 36.4% and 15.9% of cases were the most frequent adverse reactions related to contrast media used in patients treated in the imaging area of the International Clinic, San Borja headquarters.

Keywords: adverse reactions, contrast media, incidence, severity.

在圣博尔哈总部国际诊所就诊的患者对造影剂的不良反应

摘要:
本文旨在确定 2019 年 1 月至 2019 年 12 月在圣博尔哈总部国际诊所成像部门接受治疗的患者中使用的造影剂相关的不良反应。研究方法为基本的描述性回顾性研究，非-
实验横截面设计。研究样本包括在成像区域获得的治疗医师的医学适应症。出现不良反应的患者的数据收集表被用作测量研究变量的工具。研究发现，患者的不良反应具有皮肤（79. 6%，41）和呼吸（4. 5%，3）性质。女性的发病率最高（63. 6%，28）。 成年人（29 至 49 岁）是最常见的年龄组，占 70. 5% （31）.

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36. 4%和15. 9%的皮疹和瘙痒是在圣博尔哈总部国际诊所成像区接受治疗的患者中使用的造影剂最常见的不良反应。

关键词：不良反应、造影剂、发生率、严重程度。

1. Introduction

This study follows the Norbert Wiener University Academic School of Pharmacy and Biochemistry research lines (Huarcaya Mayta, 2018), whose main objective is to determine the adverse reactions related to the use of contrast media used in patients treated in the imaging area of the Clinic International, San Borja headquarters from January to December 2019.

The importance of this research lies in providing information since all drugs can produce unwanted effects, and the notification of suspicion in serious cases is mandatory for all health professionals (WHO, 2017).

This research presents four chapters divided into the following content: The first chapter introduces the statement of the problem, the formulation of the problem, objectives, and justification. The second chapter is devoted to the methodology; it includes the type and design of the study, the selection and size of the sample, the operational definition of the variables, the data collection procedures, the instruments applied to the sample, the analysis of data, and ethical aspects. The investigation results, presented in tables and figures are discussed further. The fourth chapter presents the research conclusions.

2. Methodology

2.1. Research Method

The researchers applied the descriptive method for their study.

2.2. Investigative Approach

For this study, a quantitative approach was used: the data from the medical records were collected, and statistical data were applied (Biored Sur, 2017; Digemid, 2014).

2.3. Research Design

A non-experimental and cross-sectional review of the medical records presented adverse reactions to contrast media in compliance with (Alfonso, 2015; Alvarado, 2018; Cultraro, 1994; García, et al., 2011; Garrido et al., 2020).

2.4. Population, Sample, and Sampling

2.4.1. Population

The patients were seen in the imaging unit during the investigation period. The sample population included 20.000 patients.

2.4.2. Shows

All the patients who presented adverse reactions during the investigation were seen in the imaging unit and totaled 44 patients.

$$n = \frac{Z^2\ p\ q\ N}{E^2\ (N-1) + Z^2\ p\ q}$$

where:
N – population;
n - sample size;
Z - 95% confidence level (standardized value of 1.96);
p - estimated prevalence. It is assumed p = 50% (0.5) to maximize the sample size because the population parameter is unknown (Investigator's Impartiality Criterion) q = 1 - p E = Precision or error magnitude of 0.05. This value is considered a magnitude of error because we consider a confidence level of 0.95 (95%).

$$n = \frac{Z^2\ p\ q\ N}{E^2\ (N-1) + Z^2\ p\ q}$$

$$\boldsymbol{n = \frac{1.96^2 x\ 0.5 x (1-0.5) x 54}{0.05^2 (54-1) + 1.96^2 x\ 0.5 x (1-0.5)}}$$

$$\boldsymbol{n = 44}$$

where:
N – population;
n - sample size;
Z - 95% confidence level (standardized value of 1.96);
p - estimated prevalence. P = 50% (0.5) is assumed, to maximize the sample size because the population parameter is unknown (Investigator's Impartiality Criterion) q = 1 - p;
E - precision or error magnitude of 0.05. This value is considered a magnitude of error because we consider a confidence level of 0.95 (95%).

2.5. Operational Variables

Characteristics of the patients treated in the imaging areas were used as independent variables (Castillo, 2014).

Adverse reactions to contrast media were dependent variables (Bottinor, et al., 2013; Montoro De Franscisco, 2016).

2.6. Data Collection Techniques and Instruments

2.6.1. Technique

The technique involved the use of records of all the data collected, and it consisted of 4 parts (Ardusso, et al., 2012; Sartori, et al., 2013):

- Evaluation and registration of the contrast media used.
- Identification of the patient (sex and age)

• Classification of ADR and severity
• Evolution of the ADR (outcome presented by the ADR).

2.6.2. Validation

For the validation of the instrument, in this research work, the judgment test of 3 experts was carried out. The opinion of teachers and professionals with extensive experience and professional trajectory in public health was used, giving a conformity value of 95%.

Table 1. The criterion of expert judges

Profesionales	Congruencia	Amplitud	Redacción	Claridad	Pertinencia	Resultado
Mg. Rodríguez Arizábal Julio	95%	95%	96%	94%	95%	95%
QF. Huamán Alcántara Severo	95%	95%	96%	95%	95%	95%
QF. Idelfonso Quispe Clarisa	95%	95%	96%	95%	95%	95%
						Total 95%

2.7. Data Processing and Analysis Plan

After collecting the required information, it was grouped according to the indicators and/or measurable characteristics in the context of the proposed objectives.

The data were analyzed according to the results obtained by the statistical program (SPSS), version 25, to determine the frequency, percentage, and frequency of interest, based on the type of data to be measured.

2.8. Ethical Aspects

The corresponding permits were requested from the authorities of the International Clinic. The personal data of the patients was reserved.

The information collected was used for academic purposes only.

3. Findings and Discussion

Table 2 and Figure 1 show that 370 ml Iopramide (93.2% of the cases) was the most used contrast medium in the patients in the imaging area of the International Clinic, San Borja 2019 headquarters. Gadoteric Acid 0.05 mmol was used only in 4.5% of the cases, and in the rest, Gadobutrol 1 mmol 2.3% was used.

Table 2. Distribution of contrast media used in patients in the imaging area of the International Clinic, San Borja 2019 headquarters

Contrast medium	Frequency	Percentage
Gadoteric acid 0.05 mmol	2	4.5
Gadobutrol 1 mmol	1	2.3
Iopromide 370 ml	41	93.2
Total	44	100.0

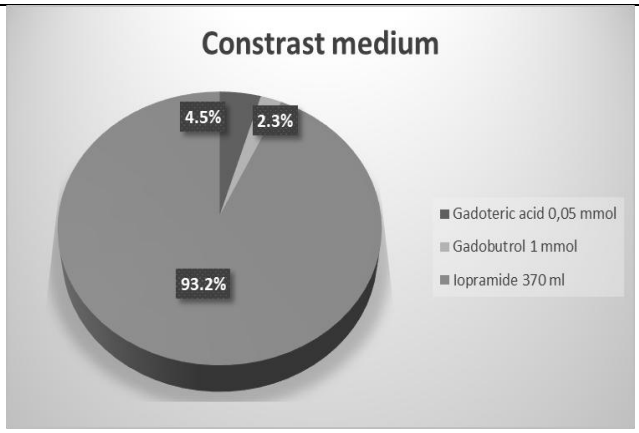

Figure 1. Distribution of contrast media used in patients in the imaging area of the International Clinic, San Borja 2019 headquarters

Table 3 shows that the majority of patients treated in the imaging area of the international Clinic were women in 63.6%, the most frequent age group was adults (29 to 49 years) in 70.5% in line with (Astargo, 2016). Weight of the patients was 51 to 70 kg in most cases 56.8%. These results can be visualized in Figure 2.

Table 3. Distribution of patients treated in the imaging area of the International Clinic, San Borja 2019 headquarters, according to sex, age and weight

Indicators		Frequency	Percentage
Sex	Male	16	36.4
	Female	28	63.6
Age	Young	10	22.7
	Adult	31	70.5
	Older Adult	3	6.8
Weight Kg	30-50 Kg	5	13.5
	51-70 Kg	21	56.8
	71-95-Kg	11	29.7
	Total	37	100.0
	Lost	7	15.9
Total		44	100.0

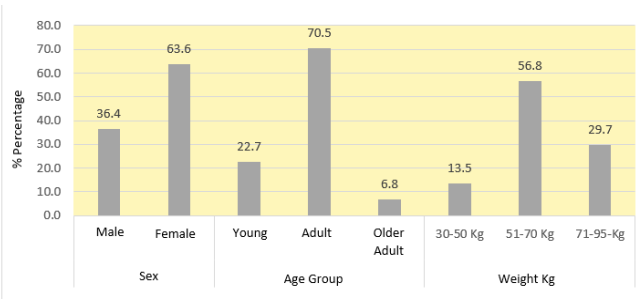

Figure 2. Distribution of patients treated in the imaging area of the International Clinic, San Borja 2019 headquarters, according to sex, age and weight

Table 4 and Figure 3 show the total of adverse reactions, of which 88.6% were classified as mild severity, while the remaining 11.4% corresponded to moderate severity adverse reactions (Huarcaya Mayta, 2018; Segovia Medina, 2015; Sigcho Jácome & Velalcázar Oñate, 2017). According to the contrast medium, it was observed that there were no reactions of moderate severity with gadoteric acid 0.05 mmol and Gadobutrol 1 mmol. For Iopramide 370 ml, this type of reaction was observed in 12.5% of patients, and the

remaining 87.8% corresponded to mild adverse reactions.

Table 4. Distribution of adverse reactions to the use of contrast media according to severity

Contrast medium		Severity		Total
		Slight	Moderate	
Gadoteric acid 0.05 mmol	N	2	0	2
	%	100.0	0.0	100.0
Gadobutrol 1 mmol	N	1	0	1
	%	100.0	0.0	100.0
Iopromide 370 ml	N	36	5	41
	%	87.8	12.2	100.0
Total	N	39	5	44
	%	88.6	11.4	100.0
The interval for percentage at 95% confidence interval	Li	79.3	2.0	---
	Ls	98.0	20.7	---

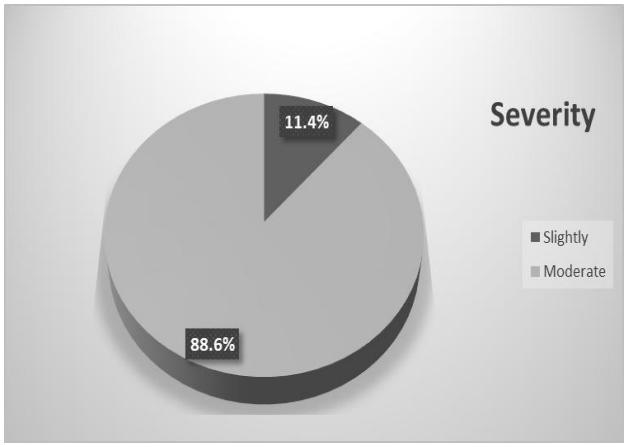

Figure 3. Distribution of adverse reactions to the use of contrast

Table 5 and figure 4 show the adverse reactions related to the contrast media analyzed (Gadoteric acid 0.05 mmol, Gadobutrol 1 mmol, and Iopromide 370 ml). Skin rash with 36, 4% was the most common adverse reaction in skin disorders, followed by pruritus (15.9%), while in respiratory disorders, breathing difficulties occurred in 4.5% relative to all adverse reactions (Guiop Shapiama, 2018).

Table 5. Distribution of adverse reactions related to contrast media in patients in the imaging area of the International Clinic, San Borja 2019 headquarters

Adverse Reactions		Frequency	Percentage
Skins disorders	Rashes	16	36.4
	Itching	7	15.9
	Erythema	6	13.6
	Rash	6	13.6
	Skin Rash	5	11.4
	Urticaria	1	2.3
	Total	41	93.2
Respiratory Disorders	Difficulty breathing	2	4.5
	Dysphonia	1	2.3
	Total	3	7
Total		44	100.0

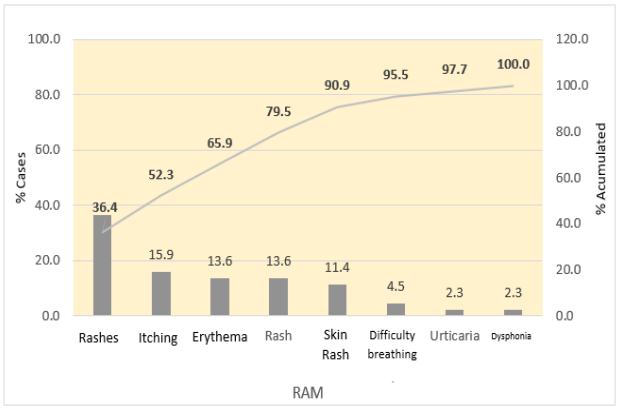

Figure 4. Distribution of adverse reactions related to contrast media in patients in the imaging area of the International Clinic, San Borja 2019 headquarters

Table 6 and Figure 5 indicate that the most frequently affected organ and system was skin disorder with 93.2%, while the remaining 6.8% corresponded to respiratory disorders (Huitron, 2018).

When analyzing each contrast media, we observed that in the case of gadoteric acid 0.05 mmol and Gadobutrol 1 mmol, the affected systems correspond 100% to skin disorders. In the case of 370 ml Iopromide, this percentage drops to 92.7%, and respiratory disorders appear with 7.3%.

Table 6. Distribution of adverse reactions to contrast media according to the affected organ

Contrast medium		Organ and system affected.		Total
		Skin disorder	Respiratory disorder	
Gadoteric acid 0.05 mmol	N	2	0	2
	%	100.0	0.0	100.0
Gadobutrol 1 mmol	N	1	0	1
	%	100.0	0.0	100.0
Iopromide 370 ml	N	38	3	41
	%	92.7	7.3	100.0
Total	N	41	3	44
	%	93.2	6.8	100.0
Interval for the percentage media according to severity	Li	85.7	0.0	---
	Ls	100.0	14.3	---

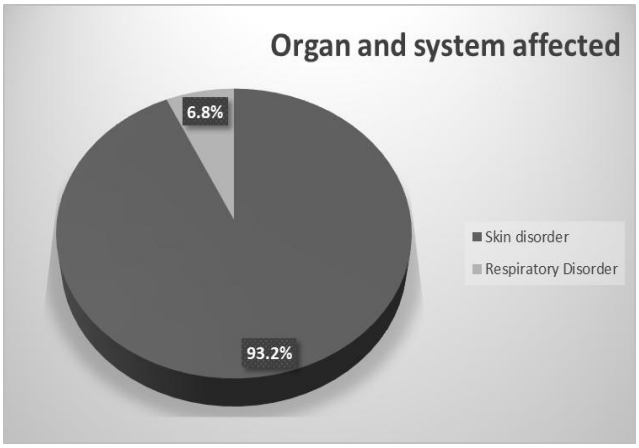

Figure 5. Distribution of adverse reactions according to the organ they affect

Table 7 and Figure 6 show that type A adverse reactions were the most common, observed in 86.4% of cases, while type B was observed in 9.1% of cases. The remaining 4 5% corresponded to type C. For gadoteric acid 0.05 mmol, 100% of the adverse reactions were of type A, while in the case of Gadobutrol 1 mmol, 100% of type E interactions were observed. Finally, for Iopramide, 370 ml, 87.8% of cases correspond to type A adverse reactions.

Table 7. Distribution of adverse reactions to the use of contrast media according to type A, B, C, D, E, F

		Type			
Contrast medium		**Type A**	**Type B**	**Type E**	**Total**
	N	2	0	0	2
Gadoteric Acid 0.05 mmol	%	100.0	0.0	0.0	100.0
	N	0	0	1	1
Gadobutrol 1 mmol	%	0.0	0.0	100.0	100.0
	N	36	4	1	41
Iopromide 370 ml	%	87.8	9.8	2.4	100.0
	N	38	4	2	44
Total	%	86.4	9.1	4.5	100.0
Interval for percentage at	Li	76.2	0.6	0.0	100.0
95% confidence interval	Ls	96.5	17.6	10.7	100.0

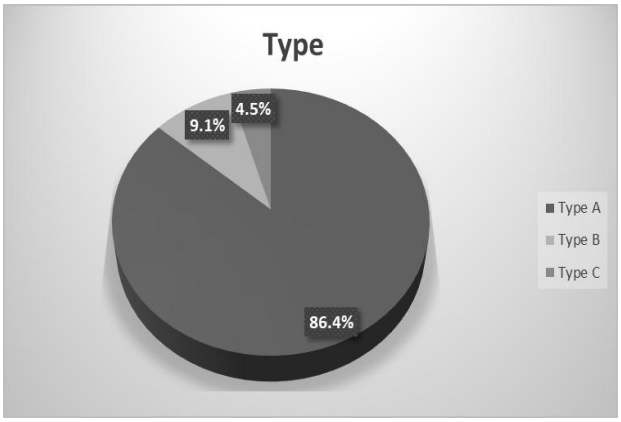

Figure 6. Distribution of adverse reactions according to type A, B, C, D, E, F

Table 8 and Figure 7 show the adverse reactions according to the causality algorithm, and they were classified as adverse reactions of probable category 47.7%, followed by the defined category 34.1%. At the same time, the remaining cases were distributed among unlikely 9.1%, conditional 6.8%, and possible with 2.3%. The adverse reactions produced by Gadoteric Acid 0.05 mmol corresponded to the probable category 50% and defined 50%. For Gadobutrol 1mmol, the only reaction observed was a probable category, with Iopromide 370 ml 46.3% of the reactions were classified as probable category followed by definite with 34.1%.

Table 8. Distribution of adverse reactions to the use of contrast media according to the causality algorithm

			Causation category.					Total
			Unlikely	Conditional	Possible	Likely	Defined	
Contrast medium	Gadoteric acid 0.05 mmol	n	0	0	0	1	1	2
		%	0,0	0,0	0,0	50,0	50,0	100,0
	Gadobutrol 1 mmol	n	0	0	0	1	0	1
		%	0,0	0,0	0,0	100,0	0,0	100,0
	Iopramide 370 ml	n	4	3	1	19	14	41
		%	9,8	7,3	2,4	46,3	34,1	100,0
Total		n	4	3	1	21	15	44
		%	9,1	6,8	2,3	47,7	34,1	100,0
Interval for percentage at 95% confidence interval		Li	0,6	0,0	0,0	33,0	20,1	---
		Ls	17,6	14,3	6,7	62,5	48,1	---

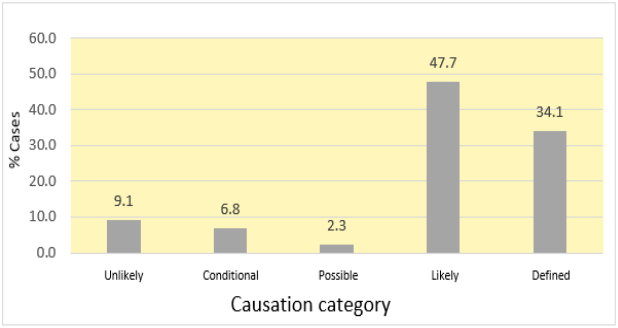

Figure 7. Distribution of adverse reactions according to the causality algorithm

4. Conclusion

Iopromide 370 ml was the contrast medium with the highest prevalence of adverse reactions. This contrast medium was responsible for 93.2% of the ADR occurrences.

It was determined that the females presented a higher incidence of adverse reactions to contrast media (63.6% - 28 cases) in contrast to the males, who only presented 36.4% (16). The most frequent age group was adults (29 to 49 years) with 70.5% (31). The results showed that 11.4% of the drug reactions related to the use of contrast media were moderate in severity, while the remaining 88.6% were mild in severity.

The most frequent adverse reactions related to contrast media used in patients treated in the imaging area of the International Clinic, San Borja headquarters were skin rash and pruritus with 36.4% and 15.9% of cases.

The skin was the most affected organ by adverse reactions related to contrast media, with a 93.2% prevalence.

The research revealed that 11.4% of the drug reactions related to contrast media were moderate in severity, while the remaining 88.6% were mild in severity.

At the same time, 47.7% of the drug reactions related to the use of contrast media were of probable causality, 34.1% of definite causality, 9.1% unlikely, 6.8% conditional, and 2.3% remaining of possible causality.

Concerning the ADR typology, 86.4% of the drug reactions related to contrast media referred to category A, followed by category B and C with 9.1% and 4.5%.

5. Limitations and Further Study

Regarding that the research scope is health, and we are in the process of a pandemic to collect the information of the chosen sample, it had to face the protocols for pandemic since people feared contagion because the Clinic had staff to follow-up in the care of its patients and its collaborators. However, with empathy, it was possible to overcome this difficulty.

Acknowledgments

First of all, we are thankful to the International Clinic of San Borja, which allowed us to collect the information despite the pandemic. We are also thankful to the authors, for example, to Dr. Ambrocio Esteves, for the follow-up and concern for completing the work and the members belonging to the investigation that showed commitment to compile and process the research ending in a publication. We also thank the Journal for giving us space to publish the investigation. Furthermore, we thank the moral contribution of all the participants, each in their respective investigative space.

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