Utilization of inhalers in pediatric population attending a public hospital in Santiago de Chile

Giovanni Cortés Ayala¹, Patricia Carrasco Sánchez², Elena Vega¹ 1: Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile Sergio Livingstone 1007, Independencia, Santiago, Chile. 2: Area of Pharmacy, Hospital Dr. Exequiel González Cortés, San Miguel, Santiago, Chile emvega@cig.uchile.cl

Abstract-Introduction: The pharmacy in Dr. Exequiel González Cortés hospital dispenses metered dose inhalers (MDI) to pediatric patients suffering from chronic respiratory diseases such as asthma, chronic obstructive pulmonary disease or cystic fibrosis. The fact of knowing data associated with the dispensing of MDI would optimize their use, from a logistical perspective. Objective: To evaluate the use of inhalers and to identify their consumption trends in the outpatient pediatric population of Exequiel González Cortés Hospital. Methodology: Based on the records of ambulatory pharmacy and the national health fund, a database was created, where the necessary information for this work was analyzed, using as a time period from June 01, 2015 to May 31, 2016, both dates inclusive. Results: In the period studied, the most dispensed medication was fluticasone 250 mcg, and less than five MDI were delivered per patient, with the peak of dispensation located between April and May 2016. In addition, it was evidenced that about two thirds of the patients were dispensed less drug than theoretically corresponded to them. Conclusion: The population using drugs was dispensed less inhalers than they would need, which would should indicate lack of adherencet.

Keywords— Metered dose inhalers; pediatrics; respiratory tract diseases; organization and administration.

I. INTRODUCTION

In Chile, the phenomenon of chronic respiratory diseases would have an impact in population, despite of the outdated data about prevalence of diseases as asthma, chronic obstructive pulmonary disease (COPD) or cystic fibrosis (CF). As an example, an increase in the hospitalization rate for asthma was observed between 2001 and 2014 in paediatric patients [1]. In addition, COPD was the eighth cause of death during 2017 [2], reason why is of vital importance to have efficient health policies to deal with these diseases.

In this context, the Chilean Ministry of Health through the law 19.966 [3], provides health benefits based on the clinical evidence, using the healthcare network, with the aim of guarantee to population, both prompt diagnosis and treatment of these diseases.

The Hospital Dr. Exequiel González Cortés (HEGC), located on the municipality of San Miguel, is

a highly complex paediatric healthcare center of reference, attending patients from eleven areas of the metropolitan region.

This hospital, through its outpatient pharmacy, delivers pharmacotherapies to patients for various diseases. For the treatment of respiratory diseases as asthma, CF or COPD, inhaled corticosteroids (IC) are used. The corticosteroids as a single therapy, or associated to a long-acting adrenergic beta 2 agonist [4-6]. As rescue therapies, salbutamol (albuterol) and ipratropium bromide are prescribed. All these drugs, in metered doses inhalers (MDI) are part of HEGC's formulary system.

These drugs are usually dispensed in this healthcare center in schedules of 1 dose (puff) each 12 hours (1-1), 2 doses in the morning and 1 dose in the night (2-1), or 2 doses each 12 hours (2-2). Each MDI contains 120 doses. Therefore, if the total dose of each inhaler is divided by the prescribed daily dose amount, an MDI should last approximately 60, 40 y 30 days respectively, so patients should attend to take a new device at intervals of time similar to those mentioned, in the outpatient pharmacy.

Despite all the above, the HEGC has not an information system, which is reflected in the fact that the pharmacy team do not know about the consumption trends of these medicines over time. They also do not know who are the patients needing this therapy, or where they come from, which in turn impairs knowing if patients take their therapies in time. Therefore, the access to these data, will allow to pharmacy unit, to optimize the logistical and financial resources associated to the supply of these medicines.

For this reason, the objective of this work was to evaluate the utilization of MDI and to identify their consumption trends in the outpatient paediatric population of the HEGC.

II. MATERIAL AND METHODS

The analyzed data included number of patients, ages, places of residence, date of MDI dispensing, types of drugs and number of inhalers. Summing the outpatient-pharmacy prescription records and the database of the national health fund, a second database was created. All the information entered and assessed belonged to the study period, from June 1, 2015, to May 31, 2016, both dates inclusive.

The sensitive information of patients was coded to avoid their individualization. The information obtained

in previous sections was analyzed using dynamic tables made in Microsoft Excel®. The categorization of patients by age was based and adapted from the paediatric classification proposed by UNICEF (United Nations Children's Emergency Fund) [7]. All the patients whose age was equal or less to 1 year 11 months, were grouped as "neonates and infants".

The Ethics Committee of the South Metropolitan Health Service of Santiago, Chile (Memorandum 469/2016) authorized this study.

III. RESULTS

In the time period studied (one year), 2084 patients were dispensed with at least one inhaler, of which 57% were male. The detail of the provenance of patients is shown in Figure 1.

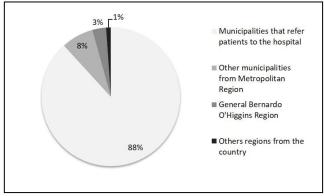


Fig. 1. Distribution of patients according to place of residence

On the other hand, it was found that de average age of users was 6.5 ± 4.7 years. The Table 1 shows that more than 40% of patients were children in scholar age.

TABLE 1.	DISTRIBUTION	OF	PATIENTS	WHO	WITHDREW					
INHALERS ACCORDING TO AGE GROUP.										

Group	Age	Percentage (%)		
Neonates and infants	Until 2 years	15.2		
Pre-school child	2 years - 4 years 11 months	25.8		
School child	5 years - 11 years 11 months	41.8		
Adolescents	12 years - 17 years 11 months	15.9		
Adults	From 18 years	1.3		
Total		100		

Meanwhile, Figure 2 presents the quantity of inhalers dispensed per month, highlighting that May, April and November were the time when most devices were distributed.

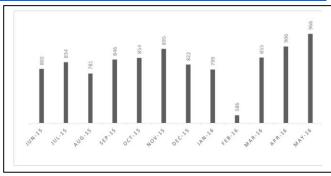


Fig. 2. Total number of inhalers dispensed per month

Along the year studied, 9946 MDI were dispensed from the outpatient pharmacy, with an average of 829 inhalers dispensed per month, and 38 per day, respectively.

Table 2 shows the amount of inhalers dispensed per year, noting that the most of patients (67.5%) took up to five MDI per year.

TABLE 2.	NUM	BER	OF	PAT	ΓIEN	TS	(OR	CAREGIVERS)
ACCORDING	G TO	THE	NUM	BER	OF	INH	ALERS	S WITHDRAWN
PER YEAR								

Number of MDI in a year	Number of patients/caregivers	Percentage (%)				
1 a 5	1407	67.5				
6 a 12	557	26.7				
13 a 24	109	5.2				
More than 24	11	0.5				
Total	2084	99.9				
MDI: Metered dose inhaler						

The most widely used drug was propionate fluticasone (FP), in number of dispensed units, both as single and associated therapy (Table 3). Furthermore, it was the most widely used active ingredient in children up to 4 years old. From 5 years on, the combination propionate fluticasone with salmeterol (FS) was the most extensively dispensed medicine.

Each patient was dispensed an average of 4.6 ± 4.3 inhalers, marking 1 MDI withdrawal every 2 months approximately, considering both, rescue and maintenance therapies. Without rescue therapies, the number drops to 4.3 ± 3.7 devices per patient.

TABLE 3. NUMBER OF INHALERS DISPENSED IN THE OUTPATIENT PHARMACY BY DRUG AND AGE GROUP OF PATIENTS

	ipratropium bromide 20 mcg	budesonide 200 mcg	budesonide/formotero I 160/4,5 mcg	fluticasone 125 mcg	nasal fluticasone 50 mcg	fluticasone/ salmeterol 125/25 mcg	salbutamol 200 mcg	Total
Neonates and infants	30	9	5	677	7	105	116	949
Preschool child	26	7	166	1467	247	937	244	3094
School child	48	32	132	1100	883	1431	331	3957
Adolescent s	2	14	87	337	427	718	173	1758
Adults	13	0	11	7	36	59	62	188
Total	119	62	401	3588	1600	3250	926	9946

IV. DISCUSSION

Among the strengths of this work, stands out the fact that the annual behavior of drugs dispensed in an outpatient pharmacy could be reflected, as well as the distribution and the origin of the patients who accesses these medicines. This analysis showed an apparent low adherence in paediatric patients with respiratory diseases. Although these data are imprecise and requires further analysis, they also indicate that to define health interventions aimed to improve this aspect is necessary.

Among the limitations of this work, the lack of dose individualization for each patient hindered obtaining a more accurate estimation of adherence to pharmacotherapy. The actual medical diagnosis for each MDI use is also unknown. Likewise, the transcription of information from the paper prescription to pharmacy records is done manually, which could cause errors in the quantities of drugs entered, therefore, an erroneous calculation of annual consumption of MDI.

The majority of the patients using MDI in this hospital service, were scholar-age children. No results were found in the literature to contrast this observation. However, it can be assumed that patients, as they grow and are controlled, are referred to less complex healthcare centers. As an important point, it should be noted that the pathologies suffered by each patient remain unknown, so the prescription of these medicines have any justification for use as such.

Analyzing the information from the El Bosque Quality Air Monitoring Station, it is observed that for several air pollutants (ozone, nitrogen oxides, carbon and particulate matter < 10) the maximum concentration value lasts from April to June, which coincides with the observed peak of drug dispensing8. This coincidence may not be complete, since, as the quality air worsens, exposure to physical activities outdoors decreases, decreasing, also, the number of consultations to medium and high complexity healthcare services, and therefore, drug dispensing.

Prescribed maintenance inhalers usually contain 120 doses, with a use of 2 daily doses, with an approximate duration of 2 months at best, needing 6 devices to cover one year of treatment.

These results indicate that patients accessed an average of 4.6 inhalers. This could be explained because patients, for different reasons, cannot pick up their inhalers at the pharmacy obtaining the medication by other means, for instance, purchasing. Furthermore, this data could indicate lack of adherence to treatment, which in turn could cause an increase in frequency and intensity of exacerbations, an increasing use of emergency services and subsequent hospitalization in highly complex facilities [9, 10].

It was observed that in maintenance therapies for all age groups in general, the active ingredient most widely used was Fluticasone Propionate (PF) over Budesonide (BD). This can be explained in part to the pharmacodynamics characteristics; PF has greater potency than BD over the glucocorticoid receptor [11]. Furthermore, PF has an oral bioavailability near to 0%, and a practically complete topical bioavailability [12]. While BD has an oral bioavailability close to 9% [13], and a topical bioavailability close to 40% [14]. The above mentioned implies a decrease in the dose of inhaled corticosteroids and in the potential adverse effects produced by the prolonged use of these drugs, both topically and systemically [15].

In children younger than 5 years, an increased use of PF was observed as single therapy. Meanwhile in children of 5 years and older, fluticasone with salmeterol was preferred. However, there is no clear explanation for this phenomenon. In the case of asthmatic patients, the National Guideline of bronchial asthma in children under 15 years old [4], mentioned that PF and BD are on the second step of treatment, while the combinations of fluticasone/salmeterol and budesonide/formoterol are in the third step [16]. From this point of view, it could be assumed that as patient grows up, it occurs an impairment of chronic respiratory pathologies.

In the case of COPD and CF, it is difficult to explain the point in the previous paragraph, since these drugs do not intervene in the course of these pathologies, and their use is limited to prophylaxis to decrease the amount and intensity of exacerbations [17, 18].

V. CONCLUSION

In light of the results, it was observed that the most patients' users of MDI, were school-age children, they were given fluticasone as maintenance therapy for their chronic respiratory pathologies, and they were dispensed less medication than they might need. This last point requires a deeper analysis to evaluate the cause of this phenomenon. Knowing this information the hospital pharmacy would optimize the drug supply management of MDI for the outpatient paediatric population.

REFERENCES

- A. Herrera, G. Cavada, J. Mañalich, "Pediatric asthma hospitalization in Chile: 2001-2014. Hospitalizaciones por asma infantil en Chile: 2001-2014", Rev. Chil. Pediatr, vol. 88, pp. 602-607, 2017.
- [2] R. Rojas L. Biagini, F. Fuentealba. "Economic evaluation of three therapies for chronic obstructive pulmonary disease in Chile. Cost-utility analysis. Evaluación económica de tres terapias para la enfermedad pulmonar obstructiva crónica en Chile. Análisis de costo utilidad", Value in health, vol. 18, pp. A841, 2015.
- [3] Law N°19.966, "Establishes a health guarantee regime. Establece un régimen de garantías en salud", National Congress, Chile, August 25, 2004.
- [4] Clinical Guideline AUGE, "Moderate and severe bronchial asthma in children under 15 years of age. Guía clínica AUGE. Asma bronquial moderada y grave en menores de 15 años", Santiago de Chile: Ministry of Health, 2006.
- [5] Ministry of Health, "National Cystic Fibrosis Program. Programmatic technical guidelines for diagnosis and treatment. Programa nacional de fibrosis quística. Orientaciones técnicas programáticas para diagnóstico y tratamiento", Santiago de Chile: Ministry of Health, 2012.
- [6] Clinical Guideline AUGE, "Chronic obstructive pulmonary disease (COPD). Enfermedad pulmonar obstructiva crónica (EPOC)", Santiago de Chile: Ministry of Health, 2012.
- UNICEF, "Supplies and logistics. Dispersible tablets. Suministros y logística. Comprimidos dispersables". [Internet] c12/03/2010. [cited 12 August 2020] Available at: https://www.unicef.org/spanish/supply/index_5357 1.html
- [8] El Bosque Station, "Air quality national information system. Sistema nacional de información de la calidad del aire", [Internet]: Santiago, Chile: RC Ingeniería; c2009-2015 [cited 01 july 2020]. Available at: https://sinca.mma.gob.cl/index.php/estacion/index/ key/D17
- [9] M. Pérez, R. Puig-Peiró, S. Paz, L. Lizán, "direct cost of chronic obstructive pulmonary disease associated with variations in adherence and persistence. Coste directo de la enfermedad pulmonar obstructiva crónica asociado a

variaciones en adherencia y persistencia", Rev. Patol. Respir, vol. 18, pp. 49-56, 2015.

- [10] C. Melero-Moreno, N. Rodríguez-Meleán, R. Díaz-Campos. "Adherence to treatment in asthma. Current situation. Adherencia al tratamiento en asma. Situación actual", Rev. Asma, vol. 2, pp. 13-22, 2017.
- [11] N. Adams, T. Lasserson, C. Cates, P. Jones, "Fluticasone versus beclomethasone or budesonide for chronic asthma in adults and children", Cochrane Database Syst Rev, vol. 17, CD002310, 2007.
- [12] Product Information: Flovent[™] HFA inhalation aerosol, fluticasone propionate inhalation aerosol. GlaxoSmithKline, Research Triangle Park, NC, [Internet] 2006 [cited 25 October 2019]. Available at: https://www.accessdata. fda.gov/drugsatfda_docs/label/2006/021433s006lb l.pdf
- [13] G. Greenberg, B. Feagan, F. Martin, L. Sutherland, A. Thomson, N. Williams et al, "Oral budesonide for active crohn's disease", N. Engl. J. Med, vol. 331, pp. 836-841, 1994.
- [14] Product Information: Pulmicort Flexhaler™ inhalation powder, budesonide inhalation powder. AstraZeneca, LP. [Internet] Wilmington, DE. 2008 [cited 25 October 2019]. Available at: ca/content/dam/azhttps://www.astrazeneca. ca/downloads/product information/pulmicortturbuhaler-product-monograph-en.pdf
- [15] E. Hossny, N. Rosario, B. Lee, M. Singh, D. El-Ghoneimy, J. Soh, P. Le Souef, "The use of inhaled corticosteroids in pediatric asthma: update", World Allergy Organ J, vol. 9, pp. 26, 2016.
- [16] Global initiative for asthma. Global strategy for asthma management and prevention, [Internet]. GINA 2018 [cited 09 February 2020]. Available at: https://ginasthma.org/ 2018-gina-report-globalstrategy-for-asthma-management-and-prevention/
- [17] M. Miravitlles, J. Soler-Cataluña, M. Calle, J. Molina, P. Almagro, J. Quintano, et al. "Spanish Guidelines for Management of Chronic Obstructive Pulmonary Disease (GesEPOC) 2017. Pharmacological Treatment of Stable Phase", Arch Bronconeumol, vol. 53, pp. 324-335, 2017.
- [18] I. Balfour-Lynn, K. Welch, S. Smith, "Inhaled corticosteroids for cystic fibrosis", Cochrane Database Syst Rev, vol. 7, CD001915, 2019.