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Drug Use Evaluation of Intravenous Immunoglobulin (IVIG) in a Hospital in Iran

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ABSTRACT

Intravenous Immunoglobulin (IVIG) is extracted from the donation plasma of 1000 to 10000 healthy individuals. The results of DUR observations are essential to inform the physician to improve drug prescribing principles. Therefore, studying the pattern of use of IVIG due to its role in the treatment and control of diseases, its high cost, and lack of access to it are considered as an important research topic. In this regard, we aimed to evaluate the pattern of IVIG use in Baqiyatallah Alazam Hospital. This descriptive cross-sectional study was conducted with a prospective direction in Baqiyatallah Alazam hospital from January to March 2019. All patients who received IVIG in hospital wards were included and data were gathered according to the designed form. Finally, all data were compared and analyzed by SPSS version 16. 52 patients with a mean age of 44.2 years old were enrolled. All the prescription was matched to the mentioned indication in the designed form. The highest amount of IVIGs was assigned to the FDA-approved indications with 42.8% (the total amount of IVIG consumed in the patients during admission was 3367.5 gr). Primary immunodeficiency, Guillain-Barre syndrome, malignant migrating focal epilepsy, and stimulus provoked non-epileptic were the most causes of IVIG prescription respectively in all FDA categories. The presence of a clinical pharmacist in the treatment team not only improves the quality of medication but also plays an important role in reducing the cost of treatment for patients and the health system.

Keywords: *IVIG, Consumption Model Modification, Drug use evaluation, Drug Utilization Review, Medication Use Evaluation.*

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INTRODUCTION

Intravenous Immunoglobulin (IVIG) is a biological product derived from human blood and extracted from the donation plasma of approximately 1000 to 10000 healthy individuals. The full spectrum of antibodies produced by this large population will be included in the final product. It contains 5-8 g/dl of protein, of which 90% is IgG [1]. This drug was first introduced in 1980 to treat immunodeficiency states. Since then, its use has been extended to other fields such as neurology, hematology, and rheumatology [2].

Drug Utilization Review (DURs), in addition to drug use patterns, are used to diagnose drug problems in different fields, requiring further studies. In addition, to determine the relationship between logical and correct use of drug therapy and degree of morbidity, the result of treatment (effect in clinical and economics) and its quality are applicable [3, 4]. The results of the DUR observations are essential to inform the physician of the illogical use of the drug for

advice and recommendations to improve drug prescribing principles [5, 6].

Due to its high-quality production problems and increasing indications, it has led to problems such as the global shortage of this product and increased costs [2, 7]. Therefore, studying the pattern of use of IVIG due to its prominent role in the treatment and control of many diseases, its high cost, and lack of access to it are considered important research topics [8]. In this regard, we aimed to evaluate the pattern of IVIG use in Baqiyatallah Alazam Hospital.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted with a prospective direction in Baqiyatallah Alazam hospital from January to March 2019. All patients who received intravenous immunoglobulin in all hospital wards were included in the study. The patient's demographic information (age, sex), prescribing physician, diagnosis, and other forms of information collected from the case patients were collected and recorded. All patients receiving IVIG for any reason were included in the study. To evaluate the concordance of IVIG indications with the standard and rational prescribing guidelines, we sub-categorized the identified indications of IVIG into three main categories:

(a) FDA labeled indications, (b) off-labeled with support (strong evidence suggests its efficacy), and (c) off-labeled with no support (there is not any, or sufficient evidence to justify its usage). In our study, IVIG indications in categories, A and B were flagged as appropriate, whereas category C indications were considered inappropriate.

Data Analysis

Statistical analysis was carried out using Microsoft excel 2017 for windows release and SPSS 16.

RESULTS AND DISCUSSION

Among patients admitted in different parts of Baqiyatallah Alazam hospital, 52 patients were included in the study to examine the pattern of IVIG drug use, of which 63.4% were male (N=33) and 36.6% were female (N=19). The mean age of the patients was almost 44.2 years old. As **Table 2** shows, IVIG was prescribed for 13 different diagnoses.

Indicators of IVIG drug use based on the international standard guidelines in this study were categorized in three general categories: FDA approved, Off-labeled with support, and Off-labeled without support, so that the highest amount of IVIGs was assigned to the FDA approved indications with 42.8%. IVIG consumptions for the Off-labeled with support and Off-labeled without support indications were 24.8% and 32.4%, respectively.

In the FDA-approved indications, the primary immunodeficiency disorders (PID) (70.9%), idiopathic thrombocytopenic purpura (ITP) (19%), Kawasaki disease (KD) (8.8%), and passive immunity (1.3%), the causes of prescriptions were included. Guillain-Barre syndrome (GBS) (44.85%), rejection of cardiac and renal transplantation by antibody (31%), myasthenia gravis (13.8%), recurrent dermatomyositis/polymyositis, autoimmune hemolytic anemia (AIHA), and neonatal hemochromatosis (each with 3.45%) were the causes of IVIG administration in the Off-labeled with support category. Two types of intractable childhood epilepsy (malignant migrating focal epilepsy and stimulus provoked non-epileptic) (66.7%), treatment infertility in women (22.2%) and icterus treated with exchange transfusion (11.1%), as the reasons prescribing this drug were concerned with Off-labeled without support category.

The total amount of IVIG consumed in the patients during admission was 3367.5 gr, of which 1441 gr was for FDA approved indications, 835 gr was for off-labeled with support indications, and ultimately, for off-labeled without support indications, it was consumed at 1091 gr.

Most of the prescriptions were for the neurology section and 2091 gr of 3367.5 (62.1%) of drugs were consumed in this segment. Afterward, the internal and pediatrics ward took more drugs.

Utilization of IVIG by indication and evidence category in this study is based on **Table 1**:

Table 1. Indication categories for use of IVIG

A- FDA labeled
• Chronic inflammatory demyelinating polyneuropathy (CIDP)
• Prevention of bacterial infection in patients with hypogammaglobinemia and/or recurrent bacterial infections with B-cell chronic lymphocytic leukemia (CLL)
• Treatment of immune thrombocytopenia purpura (ITP)
• Treatment of primary humoral immunodeficiency syndromes (PID)
• Kawasaki syndrome
• Multifocal motor neuropathy (MMN)
• Passive immunity
B- Off-labeled with support
• Secondary to malignant acquired hypogammaglobulinemia (CLL, MM, Non-Hodgkin Lymphoma) to prevent infection
• Rejection of cardiac and renal transplantation by antibody
• Recurrent dermatomyositis/polymyositis
• Guillain-Barré syndrome
• HIV-related thrombocytopenia
• Myasthenia gravis
• MS relapse
• *Lambert–Eaton myasthenic syndrome*
• Treatment of Clostridium difficile infection
• Prevention of bacterial infection in the association of blood cells with severe hypogammaglobulinemia
• *Stiff person* syndrome
• Neonatal hemochromatosis
• Autoimmune hemolytic anemia
• Systemic necrotizing vasculitis with anti-neutrophil cytoplasmic antibody (ANCA-positive)
• Autoimmune blistering diseases (pemphigus vulgaris, annular pemphigoid, etc.)
• Acute disseminated encephalomyelitis
• Allogeneic hematopoietic cell transplantation for primary immune deficiency diseases
• Fetal and neonatal alloimmune thrombocytopenia
• Hemolytic disease of the fetus and newborn
• Post-transfusion purpura
• Treatment of secondary hemorrhagic immunodeficiency
C- Off-labeled without support
Indications that do not place into any of the above categories.

Table 2. Indications for IVIG administration

Indications	FDA approved (a)	Off-labeled with support (b)	Off-labeled without support (c)	Amount of IVIG (%)
Primary immunodeficiency disorders	a			1021 gr (70.9%)
Idiopathic thrombocytopenic purpura	a			274 gr (19%)
Kawasaki disease	a			127 gr (8.8%)
Passive immunity	a			19 gr (1.3%)
Guillain-Barre syndrome		b		374.5 gr (44.85%)
Rejection of cardiac and renal transplantation by antibody		b		259 gr (31%)
Myasthenia gravis		b		115.5 gr (13.8%)
Recurrent dermatomyositis/polymyositis		b		28.6 gr (3.45%)
Autoimmune hemolytic anemia		b		28.6 gr (3.45%)

Neonatal hemochromatosis		b		28.6 gr (3.45%)
Malignant migrating focal epilepsy and stimulus provoked non-epileptic			c	728 gr (66.7%)
Treatment infertility in women			c	242 gr (22.2%)
Icterus treated with exchange transfusion			c	121 gr (11.1%)
Total	1441 gr (42.8%)	835 gr (24.8%)	1091 gr (32.4%)	3367.5 gr

Understanding the factors affecting the misuse of medications will enable the health providers in the implanting program to prevent inappropriate use of them, and medication use evaluation (MUE) is the cornerstone in this manner [9]. Limited worldwide availability of IVIG, increasing the demands for unlicensed use, and escalating costs, in addition to possible adverse reactions and inadequate information for IVIG use, especially in the Middle East, has been remained the evaluation of IVIG misuse as one of the priorities of MUE for several years [10-12]. Therefore, this study was designed to describe the use of IVIG in one of the largest academic tertiary referral hospitals in a developing country in the Middle East.

Studying the pattern of use of IVIG due to its prominent role in the treatment and control of many diseases, its high cost, and lack of access to it are considered important research topics [8]. In this study, conducted in Baqiyatallah Alazam Hospital on IVIG recipients over 2 months, the most common cause of PID (47.8%) agreed with what was found by Lin *et al.* in two educational hospitals in Sydney [11].

In our study, the most commonly used IVIGs after PID was ITP (12.8%), GBS (11.1%), intractable childhood epilepsy (9.4%), Kawasaki disease (6%), and icterus due to ABO incompatibility (3.4%). The study by Dawoud showed that IVIG consumed for appropriate and inappropriate indications were 39% and 61% respectively [12]. While in the present study the most courses' IVIG administration was for FDA-approved indications.

In the present study, most IVIGs prescribers were neurologists (62.1%). In other studies, according to the indications, different prescribing services have been reported. For example, in the study by Foster *et al.* in ICU, approximately 40% of IVIG prescriptions were administrated by the special care team; other specialists include plastic surgeons (16%), oncologists/hematologists (14%), neurologists (13%) and infectious specialists (9%) [13].

In the 2 month interval of this study, about 6810 million Rials of IVIG were consumed in this center, of which 32.4 percent were devoted to the indications of use not accepted by the FDA.

CONCLUSION

Owing to different studies and costs and financial burden on the health system, it is better to provide a regional guideline for IVIG prescribing and sufficient monitoring of the need for it. Owing to limited information on its effect in many cases, high prices, and problems, prescribers should be more careful about prescribing it [14]. On the other hand, the presence of a clinical pharmacist in the treatment team not only improves the quality of medication but also plays an important role in reducing the cost of treatment for patients and the health system [15].

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ETHICS STATEMENT: The project was found to be in accordance to the ethical principles and the national norms and standards for conducting Medical Research in Iran.

This research was approved by Research Ethics Committees of Baqiyatallah University of Medical Sciences and registered with the code: IR.BMSU.REC.1397.301.

All the participants signed written informed consent forms.

REFERENCES

1. Looney RJ, Huggins J. Use of intravenous immunoglobulin G (IVIG). Best Pract Res Clin Haematol. 2006;19(1):3-25.
2. Villanueva G, de Jong JL, McNeer JL. Intravenous Immunoglobulin in the Treatment of Hematologic Disorders in Pediatrics. Pediatr Ann. 2017;46(1):e13-e8.
3. Wettermark B, Elseviers M, Almarsdóttir AB, Andersen M, Benko R, Bennie M, et al. Introduction to drug utilization research. Drug Util Res: Methods Appl. 2016:1-12.
4. Ammann EM, Haskins CB, Fillman KM, Ritter RL, Gu X, Winiecki SK, et al. Intravenous immune globulin and thromboembolic adverse events: A systematic review and meta-analysis of RCTs. Am J Hematol. 2016;91(6):594-605.
5. Rocchio MA, Schurr JW, Hussey AP, Szumita PM. Intravenous Immune Globulin Stewardship Program at a Tertiary Academic Medical Center. Ann Pharmacother. 2017;51(2):135-9.
6. Davis S, Rungruangphol PD, Gibson CM. Maximizing benefits with the medication use evaluation process. Hosp Pharm. 2018;53:284–5.
7. Perez EE, Orange JS, Bonilla F, Chinen J, Chinn IK, Dorsey M, et al. Update on the use of immunoglobulin in human disease: a review of evidence. J Allergy Clin Immunol. 2017;139(3):S1-S46.
8. Dashti-Khavidaki S, Khalili H, Farshadi F, Aghamohammadi A, Movahedi M, Hajibabaei M. Inpatient paediatric use of intravenous immunoglobulin at an academic medical centre. Singapore Med J. 2008;49(2):147.
9. Sohrevardi S, Shafiei A, Mirzania S. Intravenous Immunoglobulin: A Drug Utilization Review at Shahid Sadoughi Hospital in Yazd. J Pharm Care. 2015;2(4):170-6.
10. Oguz EG, Okyay GU, Akoglu H, Merhametsiz O, Yildirim T, Canbakan B, et al. Efficacy of combined plasmapheresis and intravenous immunoglobulin therapy in kidney transplant patients with chronic antibody-mediated rejection. Iran J Kidney Dis. 2016;10:151-5.
11. Fakhari Z, Farsaei S, Sabzghabaee AM. Predicting Factors for the Pattern of Intravenous Immunoglobulin Utilization in a Middle Eastern University Hospital. J Res Pharm Pract. 2018;7(4):188-94. doi:10.4103/jrpp.JRPP_18_73
12. Dawoud T. A utilization review of intravenous immunoglobulin in a tertiary care hospital in United Arab Emirates.: 40e. Pharmacother: J Hum Pharmacol Drug Ther. 2013;33(5):e59.
13. Cherin P, Marie I, Michallet M, Pelus E, Dantal J, Crave JC, et al. Management of adverse events in the treatment of patients with immunoglobulin therapy: A review of evidence. Autoimmun Rev. 2016;15(1):71-81.
14. Yang L, Wu EY, Tarrant TK. Immune Gamma Globulin Therapeutic Indications in Immune Deficiency and Autoimmunity. Curr Allergy Asthma Rep. 2016;16(8):55.
15. Moradi M, Moti T. Drug use evaluation of human intravenous immunoglobulin (ivig) in a teaching hospital in East of Iran. J Pharm Care. 2016;4:70-4.