Journal of Pharmaceutical Care
jpc.tums.ac.ir

Intravenous Immunoglobulin: A Drug Utilization Review at Shahid Sadoughi Hospital in Yazd

Seyed Mojtaba Sohrevardi [1], Alireza Shafiei [2], Shima Sadat Mirzania [3*]

[1] Associate Professor of Clinical Pharmacy, Department of Pharmaceutics, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran.
[2] Assistant Professor of Asthma, Allergy and Clinical Immunology, Department of Pediatrics, Tehran University of Medical Sciences, Tehran, Iran.
[3] Pharmacy Student, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran.

ARTICLE INFO

Article type:
Original article

Keywords:
Drug Utilization Review
Intravenous Immunoglobulins
Hospital

ABSTRACT

Background: Drug use evaluation (DUE) aims at improving the patients' care. Studying the administration pattern of intravenous immunoglobulin (IVIG) is an important research topic due to its significant role in the treatment and controlling of many disorders, high prices, and limited availability of this drug.

Methods: This observational cross-sectional study was conducted at Shahid Sadoughi Hospital in Yazd, central Iran, from May to September 2014. The orders of different wards in the hospital for IVIG given to the hospital central pharmacy were surveyed. Also, a special form developed for evaluation the method of administration. The related physician and nurse were consulted on drug complications and the causes. Finally, the gleaned data were compared to the available standards on the prescription and administration of IVIG.

Results: A total of 75 patients received IVIG during this study. 58.7% of the prescriptions belonged to the cases approved by Food and Drug Administration (FDA). The most frequent cause of the use of IVIG was idiopathic thrombocytopenic purpura (ITP). The rate and dose of administration was suitable in most of the patients, yet, the measurement of laboratory parameters required for IVIG were observed in only a few cases. Complications occurred in 26.7% of the patients receiving it, which was mostly related to infusion-related reactions. On the whole, 3922 g IVIG was used during this study of which 1848 g belonged to the cases approved by FDA.

Conclusion: Regarding the high costs of IVIG, complications, and limited information on the quality of the effect of this drug in the treatment of many cases, physicians should be cautious enough with its appropriate use. Besides, the presence of a clinical pharmacist in the health-care team not only improves the quality of drug therapy and treatment results, but also plays an important part in decreasing the treatment costs for the patients.

J Pharm Care 2014; 2 (4): 170-176.

► Please cite this paper as:
Sohrevardi M, Shafiei A, Mirzania S. Intravenous Immunoglobulin: A Drug Utilization Review at Shahid Sadoughi Hospital in Yazd. J Pharm Care 2014; 2(4): 170-176.

Introduction

Intravenous immunoglobulin (IVIG) is a biologic product derived from human blood and extracted from the donated plasma of 1000-10000 individuals. The whole spectrum of antibodies produced by this huge population is manifested in the final product. IVIG contains about 5-8 g/dL protein of which about 90% is IgG (1). IVIG is used in immunodeficiency patients to protect against infections by creating a suitable concentration of antibody

* *Corresponding Author*: Shima Sadat Mirzania
Address: Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran, Tel:+983538203419, Fax:+983538203418.
Email: shimamirzania@ymail.com

against a wide range of pathogens. It is also used in treating autoimmune disorders as an anti-inflammatory agent and an immunomodulator (2). Drug use evaluations (DUE) focus on measuring the quality improvement of drug use (3). These studies help us understand the method of performance of current treatment interventions. They were not only lead to the promoted effectiveness of treatment, but also decrease the costs and prevent the pharmaceutics complications (4). Studying the drug use pattern of IVIG is considered as an important research topic due to its significant role in the treatment and control of many diseases, high cost, and limited access to it (5). This observational cross-sectional study was conducted at Shahid Sadoughi Hospital in Yazd, central Iran, to investigate the prescription and administration pattern of IVIG.

Patients and Methods

The present observational cross-sectional research was carried out at Shahid Sadoughi Hospital in Yazd, central Iran, during May to September 2014 to study the prescription and administration pattern of IVIG. All the patients receiving IVIG at Shahid Sadoughi Hospital in Yazd, Iran, were investigated during the course of the study. To do so, the related information was culled daily from the hospital wards that had ordered this drug to the central pharmacy of the hospital. Additionally, the researcher attended the patients' bedside during the use of the drug by patients and surveyed the patients' paraclinical findings there. Moreover, a special form developed by the Advisory Council on Hospital Pharmaceutics on the method of prescription and administration of drugs (administration protocol) was separately completed for each patient. Additionally, during the course of drug use by the patients, the attending physician and nurse were consulted on the incidence of complications of this drug and its causes, the prescribed dose, the length of treatment in each administration of the drug, round of drug administration by the patient, drug indications, performance of preventive measures, and simultaneous taking or not taking the immunosuppressant drugs by the patient. The gleaned data were recorded. The patients receiving IVIG were separately studied to see whether the required criteria for the administration of this drug had been observed and if so, to what degree they have been observed. Finally, the collected data were compared to the present criteria for IVIG use pattern (6). The textbook of American Hospital Formulary System (AHFS) (7) was used as the reference of indications of the prescribed drug and its dosage.

Data were entered in 17 SPSS software. Independent sample T-test and Chi square test were used to compare quantitative and qualitative variables, respectively. Data were expressed as mean ± SD or percentage. P-value less than 0.05 was considered as statistically significant difference.

Results

A total of 75 patients received IVIG (Intratect® made with Biotest company in UK, each ml contains 50 mg human normal immunoglobulin (purity of at least 96% IgG) during study period. 39 patients (52%) were male and 36 patients (48%) were female. The age of the patients ranged from 1 day to 80 years with a mean age of 24.6±0.3 years and a median of 17 years. IVIG was prescribed for 18 indications given in details in Table 1.

In 44 patients (58.7%) IVIG was used for indication which were approved by FDA and in the remaining (41.3%) not approved by FDA. On the whole, 3922 g IVIG was used during this study of which 1848 g was used for the cases approved by FDA and 2074 g for cases not approved by FDA. The Pediatrics Ward (36%) and then Neurosurgery Ward (24%) accounted for the greatest part of the orders for this drug. Also, the frequency of IVIG use in wards were as follows: Internal Ward (13.3%), Neonatal intensive care unit (10.7%), Surgery (4%), Infections (4%), intensive care unit (ICU) (2.7%), Gynecology (2.7%), Pediatric ICU (2.7%),. Hydration was performed with 500 ml infusion of dextrose 3.33% & sodium chloride 0.3% for 58.8% of the IVIG receivers. Furthermore, 25 patients (33.3%) received this drug for the first time while other patients had a previous history of the use of this drug. The infusion of this drug began for 42 patients (56%) with the minimum rate and the rate of infusion increased gradually. Also, 16 patients (21.3%) receiving IVIG, used immunosuppressant drugs simultaneously. The weight of the patients varied from 700 g to 85 kg with a mean of 40±2.8 kg and a median of 49 kg. During the course of this study, 63 patients (84%) went through just one treatment cycle and 12 patients (16%) underwent more than one treatment cycle. The mean value of daily administration of this drug and the total administration of that cycle was calculated for patients who underwent one treatment cycle. However, for the patients who underwent more than one treatment cycle, the mean value of daily administration of this drug and the total administration of the cycle was calculated for the first cycle that occurred during the course of this study. The results of these calculations are presented in Table 2.

The shortest treatment length at this hospital was 1 day and the longest one was 9.5 days with a mean of 2.4±1.7 days and a median of 2 days. The lowest rate of infusion was 0.01 ml/kg/min and the highest rate was 3.4 ml/kg/min with a mean of 0.4±0.6 and a median of 0.1. Additionally, seven patients (9.33%) underwent two treatment cycles, one patient (1.3%) three treatment cycles, two patients (2.7%) four treatment cycles, one patient (1.3%) five treatment cycles, and one patient (1.3%) underwent eight treatment cycles.

Among the receivers of IVIG, 5 patients (6.7%) were

Table1. Indications of IVIG administration.

Indication	FDA approved	Percentage	Frequency
Idiopathic Thrombocytopenic Purpura	Yes	37.3	28
Primary immunodeficiency	Yes	6.7	5
Secondary immunodeficiency	Yes	6.7	5
Lupus erythematus systemic	No	1.3	1
Neuromuscular disorders	No	1.3	1
Transverse myelitis	No	2.7	2
Encephalitis	No	6.7	5
Progressive epilepsy	No	1.3	1
Multiple sclerosis	No	4	3
Chronic Inflammatory Demyelinating Polyneuropathy (*CIDP*)	Yes	8	6
Polymyositis	No	1.3	1
Acute polyneuropathy	No	1.3	1
Myasthenia gravis	No	4	3
Neonatal icter	No	5.3	4
Guillain-Barre syndrome	No	5.3	4
Premature neonates with sepsis	No	4	3
Diabetic plexopathy	No	1.3	1
Myelopathy and HTLV	No	1.3	1

HTLV: Human T-lymphotropic virus

Table 2. The mean value of daily administration of IVIG and the total administration of one treatment cycle.

Indication	Daily administration	Total administration of one treatment cycle
Idiopathic Thrombocytopenic Purpura	0.5	1.1
Primary immunodeficiency	0.5	0.7
Secondary immunodeficiency	0.3	0.4
Lupus erythematus systemic	0.3	0.3
Neuromuscular disorders	0.4	1.7
Transverse myelitis	0.4	2.4
Encephalitis	0.5	2
Progressive epilepsy	0.5	2
Multiple sclerosis	0.5	3.1
Chronic Inflammatory Demyelinating Polyneuropathy *(*CIDP*)*	0.4	0.8
Polymyositis	0.5	2
Acute polyneuropathy	0.4	1.3
Myasthenia gravis	0.7	1.2
Neonatal icter	1.4	1.4
Guillain-Barre syndrome	0.4	1.2
Premature neonates with sepsis	1.5	1.5
Diabetic plexopathy	0.4	2
Myelopathy and HTLV	0.4	1.2

HTLV: Human T-lymphotropic virus

elderly (65+ years), 7 patients (9.3%) had infections, and 2 patients (2.7%) were affected by diabetes mellitus for whom some precautions had to be taken. Moreover, 20 (26.7%) of the participants suffered from complications of whom 18 patients suffered from just one complication while 2 patients showed more than one complication. Complications are presented in Table 4.

From 20 patients (26.7%) who developed complications, 15 patients (75%) were treated. Of 20 patients with complications, 11 patients (55%) had a high rate of initial infusion. The treatment monitoring parameters were measured only for 13 patients (17%) and were performed as measurement of renal function including Blood Urea Nitrogen (BUN), serum creatinine, and urinary output.

Discussion

Intravenous immunoglobulin is a biologic product derived from human blood and extracted from the plasma donated by 1000 to 10000 humans (1). It is used for immunodeficiency patients to protect against infections by creating an appropriate concentration of antibodies against a wide range of pathogens and in treating autoimmune diseases as an anti-inflammatory agent and immunomodulator (2). FDA has approved the use of IVIG for the following cases: primary immunodeficiency, secondary immunodeficiency in patients with chronic lymphocytic leukemia (CLL) and hypogammaglobulinemia, Kawasaki disease, Idiopathic Thrombocytopenic Purpura (ITP), HIV infection in pediatric patients, graft-versus-host disease (GVHD), and chronic inflammatory demyelinating polyneuropathy (CIDP) (8). Nonetheless, more than half of the cases of the uses of IVIG are related to the cases not approved by FDA among them are: hemolytic disorders of neonates not responding to phototherapy, AIDS-related thrombocytopenia, multiple myeloma associated with hypogammaglobulinemia, Guillain-Barre' syndrome, dermatomyositis, multiple motor neuropathy (MMN), neonates born with a weight less than 2500 g to prevent the incidence of nosocomial infections in them, multiple sclerosis (MS), Myasthenia gravis, autoimmune hemolytic anemia, solid organ transplantation, and necrotizing fasciitis. Some comprehensive criteria have been developed for a number of these cases indicating that the use of this drug is out-of-date even for the many cases approved by FDA as it is not cost-effective (9). IVIG can also be used as an adjunct treatment in cases of sepsis. Of course, clinical studies indicate low rate of its effectiveness in this regard (10). A study carried out in the US demonstrated that the most frequent cases of the use of IVIG were not approved by FDA included: multiple sclerosis (MS), prevention of anti-phospholipids syndrome in spontaneous abortion, Guillain-Barre' syndrome, and the progression of HIV after delivery. Except for the frequent abortions and sepsis in premature neonates, the use of IVIG was associated with positive results in other cases (6). In a study conducted in Japan, 197 patients with Kawasaki disease underwent treatment by IVIG and 22 patients did not respond to treatment (11).

Drug use evaluation (DUE) studies aim at improving the results of patient care (3). The physicians need take special precautions in using this drug properly due to high costs, complications, and limited information on the quality of the efficacy of this drug (6). The findings of this study can help decision-makers of the health-care system to reduce the costs and enable physicians to promote the quality of treatment of patients (4). In this study, conducted on patients receiving IVIG at "Shahid Sadoughi" Hospital in Yazd during a 4-month period, the most frequent cause of IVIG was ITP (37.3%) which is consistent with the findings of the study by Mohammadzadeh et al., carried out at "Amir Kala" Hospital in Babol, northern Iran (12). A study conducted in Canada revealed that the treatment of ITP with either Prednisolone or IVIG induced a quick and considerable increase in the blood platelet count which was slightly higher for IVIG. Yet, this mild difference in platelet count cannot justify the higher costs and potential risk of the use of this drug (13). In our study, the following disorders had the highest percentage of infusion after ITP: CIDP (8%), primary immunodeficiency (6.7%), secondary immunodeficiency (6.7%), encephalitis (6.7%), Guillain-Barre syndrome (5.3%), neonatal icterus (5.3%), premature neonates with sepsis (4%), myasthenia gravis (4%), and multiple sclerosis (4%). Regarding the study conducted in Canada, information such as the distributed quantity of IVIG in gram, administration indications, specificity of physicians' prescription, and the number of patients who used the drug for a therapeutic indication were determined during a one-year period. It was shown that IVIG was prescribed for 90 different indications. 47% and 62% of the use of IVIG in adults and children, respectively, related to the approved indications. Although 53% and 38% of IVIG use in disapproved cases were in adults and children, respectively, most cases of its use (about 89% of both populations) were rendered as appropriate against the present standards. Hematologists and neurologists accounted for most prescriptions of IVIG (14). In our study, 58.7% of the patients received this drug for the cases approved by FDA, yet, more than 50% of the cases of prescription of IVIG belonged to the indications not approved by FDA in the Neurosurgery Ward, NICU, and Infectious disease Ward. Also, 26.7% of the 75 patients in this study developed complications. Of these, 4 patients (5%) experienced the infusion for the first time. Furthermore, 4 patients (5.3%) of the patients suffered from fever and chills, 3 patients (4%) developed headaches, 1 patient (1.3%) developed nausea, 4 patients (5.3%) developed allergic reaction, 1 patient (1.3%) suffered from shortness of breath (dyspnea), 4 patients (5.3%) developed hypertension, 1 patient (1.3%)

Table 3. The IVIG received by patients with frequent doses during the study.

	Mean	Max	Min	Median	SD
2th treatment cycle	1.5*	4.5	0.1	1.1	1.3
3th treatment cycle	1.5	4.6	5.0	0.7	1.8
4th treatment cycle	1	2.3	0.4	0.7	0.9
5th treatment cycle	2.7	2.7	2.7	-	-
6th treatment cycle	1.7	1.7	1.7	-	-
7th treatment cycle	2.3	2.3	2.3	-	-
8th treatment cycle	1	1	1	-	-

* g/kg

Table 4. Complications were observed during IVIG administration.

Complications	Percentage	Frequency
Fever and chills	5.3	4
Headaches	4	3
Nausea	1.3	1
Allergic reaction	5.3	4
Dyspnea	1.3	1
Hypertension	5.3	4
Hypotension	1.3	1
Generalized edema	1.3	1
Skin rashes	5.3	4

developed hypotension, and 1 patient (1.3%) suffered from generalized edema. Also, 4 patients (5.3%) showed complications as hives. The highest percentage of reactions related to mild reactions. In the study by Bjokander et al., carried out on 49 patients receiving IVIG, only 4.7% of them manifested the complications. Most reactions were mild including fever and chills, nausea, slight backache, and headache (15). Infusion reactions may occur in those patients who experienced it for the first time or in the patients who used a different commercial product compared to the previous times. These reactions occur 3 min to 1 h after the onset of infusion and include facial redness or flush, dyspnea or shortness of breath, shivering and chills, fever, dizziness, nausea, vomiting, hypotension, hypertension, and diaphoresis or profuse sweating (7). The influential factors triggering the incidence of these complications include presence of infection, high speed of infusion, changing the commercial product used, and the first time infusion (16). Mild reactions usually follow the infection and quick infusion of IVIG (17). In our study, 55% of the patients with quick infusion of IVIG developed complications. The probability of incidence of complications is lowered when parenteral hydration is performed and IVIG is infused with a logical and acceptable rate (19). The patients should be completely hydrated before receiving IVIG. Hydration is obligatory before infusion in patients with a history of deficiency in renal functioning, diabetes mellitus, elderly patients over 65 years, cardiovascular patients, and patients who use nephrotoxic drugs to prevent complications that induce the incidence of thrombolytic accidents and renal problems due to IVIG infusion (20). In this study, hydration was performed before the onset of infusion in 58.7% of the patients receiving IVIG. On the contrary, hydration before infusion was not performed for 55% of the patients who developed complications. Additionally, 9.5% of the study patients had infection, 2.7% were affected by diabetes mellitus, and 6.7% of the patients were elderly for whom some precautions had to be taken. In the study by Brennan, 41% of the cases of peripheral reactions related to patients for whom the precautions had to be taken (21). Because of potential increased risk of thrombosis it is necessary to consider baseline assessment of blood viscosity in patients at risk for hyperviscosity (e.g., those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols [triglycerides], or monoclonal

gammopathies). If transfusion-related acute lung injury is suspected it is necessary to perform appropriate tests for the presence of antineutrophil antibodies in both the product and patient serum. IGIV has been reported to be associated with renal dysfunction and it is necessary to close monitoring of renal function (urine output, serum creatinine, and blood urea nitrogen) (7). In our study the monitoring parameters were measured only in 13 patients (17%) as the measurement of renal functioning including BUN, serum creatinine, and urinary output. It is better to start the IVIG infusion with a rate of 0.01 ml/kg/min and in the case of patient's compatibility, this rate may be doubled every 20-30 min while controlling for the patient's vital signs, ultimately reaching the rate of 0.08 ml/kg/min (18). The drug infusion began with a slow rate in 56% of the patients and was speeded up in the case of patient's tolerance. The mean rate of infusion in the Neurosurgery Ward, Internal Medicine Ward 1 and 2, Ward of Surgery, and Gynecology Ward was considered to be consistent with the standards; however, this rate was recommended higher than the permissible limit in the Pediatrics Ward, Pediatric ICU, Ward of Infectious disease, and NICU. Also, 16 patients (21.3%) used immunosuppressant concurrent with IVIG. Furthermore, 10 patients with ITP, 2 patients with myasthenia gravis, and 1 patient out of the patients with secondary immunodeficiency, autoimmune disorder, multiple sclerosis, and CIDP received immunosuppressant, simultaneously. The mean values of received IVIG for each IVIG-receiving patient with one treatment cycle during the study were 1.2 g/kg in the Neurosurgery Ward, 1.4 g/kg in the Pediatrics Ward, 0.9 g/kg in the Internal Medicine Ward 1, 0.3 g/kg in the Internal Medicine Ward 2, 1.4 g/kg in the NICU, 0.4 g/kg in the Ward of Surgery, 0.3 g/kg in the Gynecology Ward, 1 g/kg in the ICU, 1.3 g/kg in the Pediatric ICU, and 1.3 g/kg in the Infection Ward. Lower doses of IVIG are used in immunodeficiency patients. The initial dose is usually 0.3 to 0.5 g/kg every 3-4 weeks. Of course, 0.8 g/kg doses are also used in the cases in which the treatment of infection is necessary. Some patients may need higher doses or more frequent doses to be safe from acute infections, and to control chronic infections or maintaining the IgG level that is required as the goal of treatment. Higher doses (1-2 g/kg) are also prescribed to create anti-inflammatory and immunomodulatory effects of IVIG (2).

The findings of our study demonstrated that the most frequent cause of IVIG use was ITP in this hospital. This drug was prescribed with suitable dose and rate of infusion for patients who received it; however, the laboratory and clinical parameters required for the infusion of IVIG were observed in only a few cases. Complications occurred in 26.7% of the patients receiving this drug which was higher than the rate reported by similar studies. Hence, nurses and practitioners are required to pay more attention to the infusion of this drug. Since most complications were of the mild types which occur as a function of the rate of infusion, they may be reduced by paying more attention o the rate of infusion. Moreover, physicians can prevent the incidence of these complications by taking appropriate preventive measures such as sufficient hydration of the patient and improving the quality of the drug. On the whole, 3922 g of this drug was used during this study of which 1848 g was used for the cases approved by FDA and 2074 g for the cases disproved by FDA. This imposes considerable costs on the health-care system. In the study conducted in the US, the price of 1 g of IVIG was speculated to be $US 30 in 2011 (20). During the 4-month period of this study, using the governmental subsidies for drugs, about 5700 million Rials of IVIG was used in this hospital of which 2970 million Rials devoted to the cases of use not approved by FDA. Due to the limited information on the quality of the effect of this drug in many cases, high costs, and complications of IVIG, practitioners must take special care in its use and avoid its improper administration (21). Besides, the presence of a clinical pharmacist in the health-care team not only improves the quality of drug therapy and treatment results, but also plays an important role in decreasing the treatment costs for the patients and society in general (22). Nurses are not always knowledgeable regarding the administration techniques, rates and schedules of administration. We have lack of presence of a pharmacist in the most of the hospitals in Iran. The ideas that the pharmacists must have personal contact with the patients, and she/he can play a role in training nursing staff, are new and not accepted by the Iranian medical community. Involvement of pharmacy department in drug preparation, instead of drug admixtures by the nurses, can help to improve quality of drug therapy by decreasing the medication errors and adverse drug events (23).

References

1. Looney RJ, Huggins J. Use of Intravenous Immunoglobulin G (IVIG). Best Pract Res Clin Haematol 2006;19(1):3-25.
2. Lucas M, Lee M, Lortan J, Lopez-Granados E, Misbah S, Chapel H. Infection outcomes in patients with common variable immunodeficiency disorders: relationship to immunoglobulin therapy over 22 years. J Allergy Clin Immunol 2010;125(6): 1354-1360.e4.
3. American Society of Health-System Pharmacists. ASHP guidelines on medication-use evaluation. Am J Health-Syst Pharm 1996; 53:1953–5.
4. 4. Mohammadi M, Mirrahimi B, Mousavi S, Moradi M. Drug Use Evaluation of Three Widely Prescribed Antibiotics in a Teaching Hospital in East of Iran. J Pharm Care 2013;1(3):100-3.
5. Dashti-Khavidaki S, Khalili H, Farshadi F, Aghamohammadi A, Movahedi M, Hajibabaei M. Inpatient pediatric use of intravenous immunoglobulin at an academic medical centre. Singapore Med J 2008;49(2):147-9.
6. Orange JS, Hossny EM, Weiler CR, et al. Use of intravenous immunoglobulin in human disease: a review of evidence

by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. J Allergy Clin Immunol 2006;117(4):S525-53.
7. McEvoy GK. AHFS drug information. American Society of Health-System Pharmacists; 2010:3330-43.
8. Gelfand EW. Intravenous immune globulin in autoimmune and inflammatory diseases. N Engl J Med 2012;367(21):2015-25.
9. Darabi K, Abdel-Wahab O, Dzik WH. Current usage of intravenous immune globulin and the rationale behind it: the Massachusetts General Hospital data and a review of the literature. Transfusion 2006;46(5):741-53.
10. Di Rosa R, Pietrosanti M, Luzi G, Salemi S, D'Amelio R. Polyclonal intravenous immunoglobulin: an important additional strategy in sepsis. Eur J Intern Med 2014;25(6):511-6.
11. Yanagimoto K, Nomura Y, Masuda K, et al. Immunoglobulin G values before treatment are correlated with the responsiveness to initial intravenous immunoglobulin therapy for Kawasaki disease. Int Arch Allergy Immunol 2014;164(2):83-8.
12. Mohammadzadeh I, Tamaddoni A, Atar Zadeh SH, Arzani A. Assessment of IVIG treatment in children and its complications, Babol, 1999-2004. Journal of Babol University of Medical Sciences 2006; 8(30): 32-5.
13. Ancona KG, Parker RI, Atlas MP, Prakash D. Randomized trial of high-dose methylprednisolone versus intravenous immunoglobulin for the treatment of acute idiopathic thrombocytopenic purpura in children. J Pediatr Hematol Oncol 2002;24(7):540-4.
14. Hanna K, Poulin-Costello M, Preston M, Maresky N. Intravenous immune globulin use in Canada. Can J Clin Pharmacol 2003;10(1):11-6.
15. Bjorkander J, Wadsworth C, Hanson LA. 1040 prophylactic infusions with an unmodified intravenous immunoglobulin product causing few side-effects in patients with antibody deficiency syndromes. Infection 1985;13(3):102-10.
16. Dashti-Khavidaki S, Aghamohammadi A, Farshadi F, et al. Adverse reactions of prophylactic intravenous immunoglobulin; a 13-year experience with 3004 infusions in Iranian patients with primary immunodeficiency diseases. J Investig Allergol Clin Immunol 2009;19(2):139-45.
17. Kahwaji J, Barker E, Pepkowitz S, et al. Acute hemolysis after high-dose intravenous immunoglobulin therapy in highly HLA sensitized patients. Clin J Am Soc Nephrol 2009;4(12):1993-7.
18. Daw Z, Padmore R, Neurath D, et al. Hemolytic transfusion reactions after administration of intravenous immune (gamma) globulin: a case series analysis. Transfusion 2008;48(8):1598-601.
19. Brennan VM, Salome-Bentley NJ, Chapel HM. Prospective audit of adverse reactions occurring in 459 primary antibody-deficient patients receiving intravenous immunoglobulin. Clin Exp Immunol 2003;133(2):247-51.
20. Winters JL, Brown D, Hazard E, Chainani A, Andrzejewski C Jr. Cost-minimization analysis of the direct costs of TPE and IVIg in the treatment of Guillain-Barre syndrome. BMC Health Serv Res 2011;11:101.
21. Leong H, Stachnik J, Bonk ME, Matuszewski KA. Unlabeled uses of intravenous immune globulin. Am J Health Syst Pharm 2008;65(19):1815-24.
22. Dashti-Khavidaki S, Khalili H, Hamishekar H, Shahverdi S. Clinical pharmacy services in an Iranian teaching hospital: a descriptive study. Pharm World Sci 2009;31(6):696-700.
23. Sohrevardi SM, Mirjalili MR, Jarrahzadeh MH, Mirjalili M, Mirzaei E. Evaluating the Frequency of Errors in Preparation and Administration of Intravenous Medications in the Intensive Care Unit of Shahid-Sadoughi Hospital in Yazd. J Pharm Care 2014; 2 (3): 114-19.