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Research Article

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Adverse Effects of Intravenous Immunoglobulin: A Case in Pediatrics with Kawasaki Disease

L Torissi[1*], A Soulaymani[1], A Mokhtari[1], A Dibi[3], A Thimou Izgua Amal[3], A Mdaghri Alaoui[3], R Soulaymani[2] and R Benkirane[2]

[1]Laboratoire de Génétique et Biométrie, Faculté des Sciences, Université Ibn Tofail, Kénitra, Maroc
[2]Centre Antipoison et de Pharmacovigilance du Maroc CAPM, Ministère de la Santé, Rabat, Maroc
[3]Hôpital d'Enfants de Rabat HER, Centre Hospitalier Ibn Sina CHU, Rabat, Maroc

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ABSTRACT

Intravenous immunoglobulin IVIg is an essential treatment for many neurological, immunological and haematological conditions. However, the severity of its rare adverse effects is often underrecognised. We report a case of a child receiving IVIg for Kawasaki Disease who developed severe skin reactions and cyanosis. Kawasaki disease is an acute, self-limited vasculitis of unknown etiology that occurs predominantly in infants and children. If not treated early with high-dose intravenous immunoglobulin, 1 in 5 children develop coronary artery aneurysms; this risk is reduced 5-fold if intravenous immunoglobulin is administered within 10 days of fever onset 1. Immunoglobulins are a plasma-derived drug, which have been initially used as a replacement therapy for patients with antibody deficiency. Since 1980 they have also been used for their anti-inflammatory and immunomodulating efficacy in auto-immune diseases. In Kawasaki disease Intravenous Immunoglobulins IVIgs still modulate the synthesis and the release of cytokines and chemokines, in combination with neutralization of the suspected bacterial superantigen activity 2.

Keywords: Pediatric; Adverse drug reaction; Immunoglobulins; Kawasaki disease

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INTRODUCTION

Children are more vulnerable to Adverse Drug Reactions ADRs, and this susceptibility is compounded due to hospitalization. The objective of the study is to make health professionals aware of the importance of the notification to avoid serious consequences on the health of the pediatric population and to propose preventive strategies and encourage regulatory authorities to carry out corrective actions.

EXPERIMENTAL SECTION

The prevention of adverse effects is based on spontaneous reports on pharmacovigilance and the case presented in this article is part of a study authorized by the Ministry of Health in Morocco concerning adverse effects in pediatrics. A prospective observational study about adverse drug event in children was conducted for 6 months at Children's Hospital of Rabat HER between February and June 2013. The population included in this study was hospitalized patients in the various pediatric services of the hospital having an adverse drug event which was the subject to consultation or hospitalization. The study was authorized by the Ministry of Health and presented to the members of the hospital committee with the sensitization of the health professionals concerned with regard to the importance of spontaneous notification of cases of adverse reactions occurring during the duration of the study. Post-medication adverse reaction reports were completed by notifies prescribers, pharmacists, etc. and these reports were sent to the poison and pharmacovigilance center. Centre Antipoison et de Pharmacovigilance à Rabat for the purpose of assessing accountability and relationship cause-effect according to the French method.

RESULTS

The case notified by Nephrology Department was a child E. A male with Kawasaki disease present clinical and para-clinical description of adverse event with a febrile spike, mottled skin, chills and cyanosis. The drug was taken on the 20/05/2013: the dosis of 2 g/kg in slow infusion of "Immunoglobuline Normale IV LFB 50 mg/ml", the time to onset of the adverse event after taking the drug was 30 minutes, the differential diagnosis eliminated was the outbreak of disease. The conduct adopted was the discontinuation of the drug and hospitalization, the corrective treatment was medication with antipyretics and change of immunoglobulins by anotherimmunoglobulin TEGELINE. The evolution was favorable.
The accountability "imputability" of the effect of IVIgs according to the French method revealed that the time of onset of the adverse reaction is compatible, the course of the adverse effect is suggestive because regression at a standstill. On the semiological level: the semiology is questionable because other non-pharmacological explanations are possible.

The French Method is Based on
Intrinsic accountability imputabilité intrinsèque relies on seven criteria divided into two groups: chronological criteria and semiological criteria. The Intrinsic accountability is made from patient observation data, establishes the cause-and-effect relationship between each medication taken by a given patient and the occurrence of a clinical or para-clinical event determined, it must be established independently for every medicine taken by the patient before the occurrence of the event and is not influenced by the degree of accountability of the associated drugs. The chronological criteria are based on the time of occurrence of the adverse event in relation to taking the drug, the evolution of the adverse event after discontinuation of the drug and the re-administration of the drug. The time of occurrence of the event may be: very suggestive, incompatible or compatible. The evolution of the event after discontinuation of the drug may be a suggestive evolution, a non-conclusive evolution, or non-suggestive evolution. Extrinsic accountability: relate to the bibliographic references like: Drug Dictionary, Vidal, Martindale Meyler's Side Effect.

DISCUSSION

The dosage and method of administration of the drug for Kawasaki Disease is [1] 1,6 à 2,0 g/kg ou 2 g/kg in several doses over 2 to 5 days or in a single dose with a combination treatment Acetylsalicylic Acid. The Side effects IVIG administration are more common in patients with primary immunodeficiencies like chills-hyperthermia-like reactions sometimes accompanied by headache, nausea, vomiting, allergic manifestations, elevated or decreased blood pressure, arthralgias and mild lumbago may occur occasionally. The risk of anaphylaxis is higher in case of rapid intravenous infusion in patients with IgA-deficient agammaglobulinemic or hypogammaglobulinemic patients who have never received immunoglobulins or whose last IVIG therapy was more than 8 weeks. Rapid flow may even be responsible for arterial and venous thrombotic events, particularly in patients with vascular risk. Rare cases of hypotension and anaphylactic shock have been reported, even in patients who have not had hypersensitivity reactions in previous injections. Rare cases of isolated hypertensive outbreaks have been reported in patients receiving IVIG. Very rare cases of transient lower extremity pain have been observed. As with other IVIg, rare cases of cutaneous reactions especially eczematous, regressive, rare cases of hemolytic anemia and/or regressive hemolysis and cases of elevated serum creatinine and/or acute renal failure and severe rare cases of transient transaminase increase have been reported. Cases of aseptic meningeal reaction, particularly in patients with idiopathic thrombocytopenic purpura, have been reported with IVIg. This meningeal involvement is reversible in a few days after stopping treatment. A rare case of thrombosis has been reported with IVIG in the majority of elderly patients as well as in patients at risk of cerebral or cardiac ischemia, overweight or with severe hypovolemia [2,3].

CONCLUSION

To ensure the safety of treatment, preparation recommendations, administration initial velocity and duration of infusion to be respected and IVIG monitoring must be strictly adhered to in pediatrics. The results of this type of reports are to promote spontaneous ADRs reporting. Pharmacovigilance have an important impact for increase health professional's role in the spontaneous notification of ADRs especially in pediatrics for the pediatric population.

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REFERENCES

[1] JW Newburger; AB Masato Takahashi; C Jane Burns. Kawasaki Disease. **2016**, 67, 14.
[2] B Chaigneab; L Mouthonab. Mechanisms of action of intravenous immunoglobulin. *Transfusion and Apheresis Science*. **2017**, 56(1), 45-49.
[3] ANSM Agence Nationale de Sécurité du Médicament et des produits de santé. *Summary of Product Characteristics.* **2018**.