



Short Communication

Continuous increase of immunoglobulin therapy in Iceland

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ABSTRACT

Background: The use of immunoglobulin treatment has been increasing for various indications. The objective of this study was to evaluate clinical use of immunoglobulin therapy in Iceland, estimate off-label usage and describe possible changes in this treatment option.

Methods: All prescriptions for intravenous or subcutaneous immunoglobulin treatment require authorisation from Landspítali University Hospital. Patient information is registered and was retrieved for the period 2010 to 2019.

Results: A total of 921 patients received immunoglobulin treatment in the study period, intravenous therapy was given in 895 (97.2%) of the cases. Registered indications were 667, off-label indications were 245 and uncertain were nine. The total annual number of patients receiving immunoglobulin treatment increased from 87 in 2010 to 392 in 2019. The increase in immunoglobulin usage was both for registered and off-label indications, 61 to 309 and 26 to 83, respectively.

Conclusion: Continually increasing demand and global shortage dictates careful consideration of indications before initiating or continuing treatment with immunoglobulins.

Key Message: With global shortage of immunoglobulins, careful consideration and patient selection is important.

Capsule Summary: Increasing immunoglobulin usage improves treatment for many patients. However, immunoglobulins are a limited resource and prudent use is imperative.

Introduction

Use of immunoglobulin therapy, given intravenously (IVIG) or subcutaneously (ScIG), is continually expanding and is now indicated as treatment for several immunodeficiencies and immune mediated diseases [1–4]. It is retrieved from human blood-donors, is a limited resource and is expensive. The increasing global use can be partly explained by several emerging indications for off-label usage as well as new registered indications [4–6]. This has, in light of the expensive and time-consuming manufacturing process of the drug, brought more expenses for health care systems [7–9]. In addition, the current global shortage of the drug is of grave concern [9]. It is therefore important to recognize changes in immunoglobulin use and indications. The objective of this study was to evaluate clinical use of immunoglobulin therapy in Iceland, estimate off-label usage, describe changes in use and compare national use to an earlier period 2005–2009 [10].

Methods

The administration of immunoglobulin therapy in Iceland is centralised through the Landspítali University hospital and is exclusively licensed for subcutaneous home treatment or hospital based intravenous treatment. IVIG is only administered in two medical centres in Iceland. The treatment must be prescribed by specialists in critical care, haematology, immunology, neurology, oncology, and pulmonology and all individual prescriptions for IVIG and ScIG require authorisation from The Drug and therapeutic committee of Landspítali University Hospital. The hospital's pharmacy registry contains information on all ScIG and IVIG treatments in Iceland, including dosing, indications, and detailed clinical history of the patients. Using these registries, we conducted a retrospective, observational study on individuals who received immunoglobulin therapy in Iceland from 2010 to 2019. Demographic information on individuals receiving treatment was collected and indications categorized according to the 10th edition of the International Classification of Diseases (ICD). Individuals who were prescribed immunoglobulins without clear indications despite review of medical files, were categorised as having uncertain indications. Indications were categorised as registered or off-label based on the European Medicines Agency and Food

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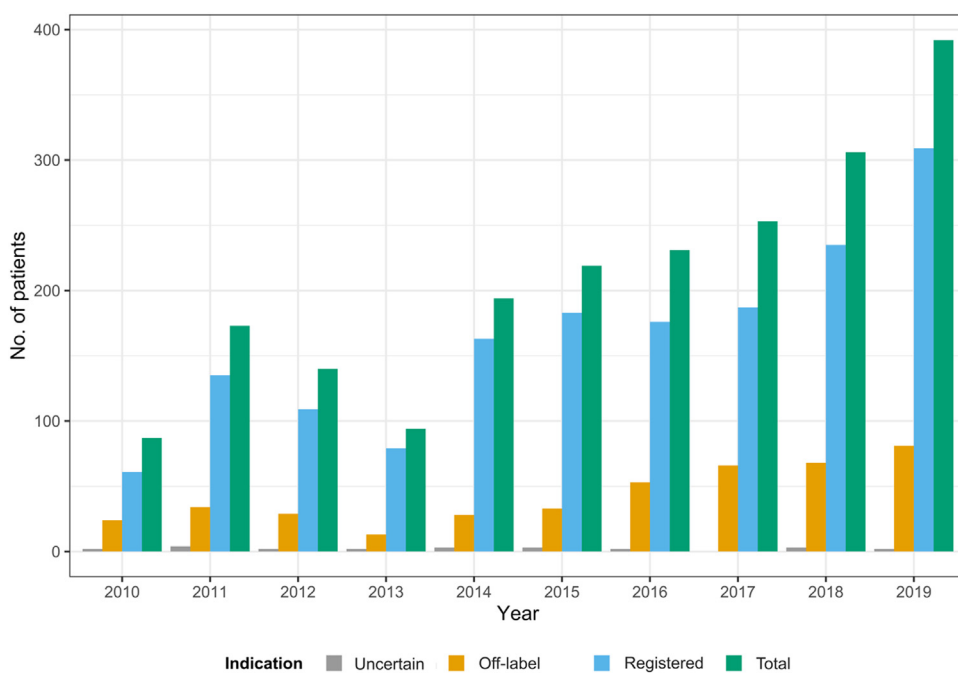


Fig. 1. Number of granted applications for immunoglobulin treatment in patients in Iceland during 2010–2019 ($n = 921$). The figure shows the number of individuals with a granted application for immunoglobulin treatment per year during the study period and whether the treatment was given based on a registered indication, off-label, or unclear indication according to guidelines of the European Medicines Agency and/or the Food and drug administration of the United States. Each individual is only counted once per year but can be counted on more than one year.

Table 1

Most frequent registered indications for immunoglobulin treatment in Iceland 2010–2019.

Registered indication	Patients
Nonfamilial hypogammaglobulinemia (D80.1)	214
Selective deficiency of immunoglobulin G [IgG] subclasses (D80.3)	74
Inflammatory polyneuropathies (G61.8), (G61.9), (G80.0)	52
Multiple myeloma (C90.0)	44
Chronic lymphocytic leukaemia of B-cell type (C91.1)	34
Idiopathic thrombocytopenic purpura (D69.3) and Thrombocytopenia (D69.6), (P61.0)	33
Guillain-Barré syndrome (G61.0)	30
Off-label indication	Patients
Myasthenia gravis (G70.0)	29
Encephalitis, myelitis, and encephalomyelitis (G04), (G04.0), (G04.8), (G04.9), (G05), (G05.8)	27
Asthma (J45), (J45.1), (J45.9)	19
Polyneuropathies (G62), (G62.8), (G62.9)	17

Only indications with more than 15 patients are included in the table (573/912), other groups were smaller and diverse (339/912). Related indications are counted together.

Each patient receiving treatment was assigned one main indication for treatment. For patients who had a granted application for treatment for more than one related condition, the most frequent, specific and recent indication was chosen. Patients who received treatment based on an unclear indication or more than one unrelated indication are not included in this table.

and Drug Administration guidelines [1, 2]. Data on the route of administration was also collected, i.e. IVIG or ScIG.

The study was approved by the Hospital Scientific Ethical Committee and the Data protection Authorities (Ref: 50/2019) in Iceland, and the Hospital Scientific Research Committee (Dec. 2019/16).

Results and discussion

The study included 921 individuals; median age at first treatment was 58 (+/- 18,8), females were 526 (57%). IVIG was given in 895 (97%) of cases. Registered indications were 667, off-label 245 and uncertain 9. Of those, 214 had hypogammaglobulinaemia, 5 had transient hypogammaglobulinaemia of infancy and none had total agammaglobulinaemia. Total number of patients receiving immunoglobulins increased from 87 in 2010 to 392 in 2019. The increase in registered and off-label indications were 61 to 309 and 26 to 83 respectively (Fig. 1). The most common registered indication for immunoglobulin treatment was non-familial hypogammaglobulinemia followed by immunoglobulin G subclass deficiency whereas for off-label indications, myasthenia gravis, encephalitis, myelitis, and encephalomyelitis were most common (table 1).

It is evident that immunoglobulin usage increased during the study period, for registered as well as off-label indications. This reiterates the continuous increase described previously from 2005 to 2009 [10]. The continuous increase in immunoglobulin usage is thought provoking as well as the expanding use for off-label indications. This may reflect increasing experience of the beneficial effect of intravenous immunoglobulins in high doses for several autoimmune disorders and neurological diseases but can also be attributed to inappropriate use and incomplete registration. More prudent use of immunoglobulins is imperative, especially in view of limited availability of blood/plasma donors, cost for health care systems and the increasing demand.

Declaration of Competing Interest

The authors have no conflict of interest to report regarding to this study

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