Differences in clinical outcome in patients with Common Variable Immunodeficiency treated with Ig replacement therapy: Results from the ESID Database

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Abstract

Rationale

- The most frequent primary immunodeficiency diagnosis in the ESID Database is common variable immunodeficiency (CVID; n=2401). The primary treatment is immunoglobulin (Ig) replacement therapy by intravenous (IV) or subcutaneous (SC) administration. We retrospectively assessed the clinical outcome with Ig therapy in patients with CVID by country and route of administration.

Methods

- Data were provided for patients with CVID who were treated with Ig therapy. Four health parameters were evaluated by country and by route of administration. The number of patients with available data varied from 417 to 645 between the four parameters.

Results

- There was a highly significant variation between countries in the four outcomes (median occurrence per year, p<0.001). The number of days unable to perform daily duties was highest in Poland (22.5) and Netherlands (7.0), and lowest in the UK (1.1). The number of days in hospital due to the immunodeficiency was highest in Poland (18.3) and Turkey (10.7). The overall number of infections was lowest in Russia and Sweden (both 1.0) and highest in Turkey (6.0). Turkey also had the highest number of serious bacterial infections (2.0). In contrast, the differences observed in these clinical outcomes between IVIg versus SCIg therapy were relatively small.

Conclusions

- These results appear to show a wide regional variation, whereas the differences observed between IV and SC administration were relatively small. Further research into the confounding factors such as the socio-economic impact of sick-leave, available treatment options in the respective countries and existing local CVID management protocols, should be conducted.

Introduction

- Common variable immunodeficiency (CVID) is a primary immunodeficiency disease (PID) characterised by low levels of serum immunoglobulins (Ig) and increased susceptibility to infections.
- Ig replacement therapy is the current treatment of choice for CVID. It can be administered either intravenously (IVIg) or subcutaneously (SCIg).
- The European Society for Immunodeficiencies (ESID) maintains an internet-based database for clinical and research data on patients with PID.
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- Data from the ESID Database were used to assess the clinical outcomes of Ig replacement therapy in patients with CVID by country, by route of administration and in patients who switched from IVIg to SCIg.

Methods

Study design

- Data collected by the ESID Database between 2004 and 2010 were retrospectively analysed. Patients were included in the cohort based on the availability of the necessary data items. A total of 691 patients were analysed. Patients of all ages were included.
- Data were obtained for patients with CVID treated with Ig therapy. Four health parameters were chosen to assess the clinical outcomes of treatment in these patients:
  - Days unable to perform daily duties
  - Days in hospital (due to immunodeficiency, excluding out-patient clinic visits)
  - Number of infections
  - Number of serious bacterial infections
- Differences in the four health parameters were assessed:
  - By country
  - By route of administration (IVIg only, SCIg only and in patients who had received both IVIg and SCIg in their lifetime)
  - In patients who switched from IVIg to SCIg treatment (patients were assessed before and after the switch)

Statistical methods

- All health parameter data were converted into the relative unit of occurrences per year.
- Patients who had data recorded over time periods <1 month were excluded from the analysis.
- In the preparation for this poster, countries that provided ≤10 valid data values for the 'by country' analysis were excluded because their data could not be regarded as representative.
- Out of the 166 patients who received both IVIg and SCIg in their lifetime, only 24 patients had data on clinical outcomes recorded for both routes and could be used in the analysis of the outcomes before and after the switch.
- Statistical significance was defined as p<0.05.

Results

Health parameters by country

- The occurrence of all four health parameters varied significantly between the countries (days unable to perform daily duties, p<0.002; all other outcomes, p<0.001). By country data are presented in Figure 1.

Health parameters in patients who received IVIg only, SCIg only or treatment by both routes

- Although median values for number of days in hospital and number of serious bacterial infections were zero for patients in the IVIg and SCIg groups, a statistically significant difference between treatment routes was observed in the inter-quartile range (IQR) in terms of number of days in hospital (p=0.01) and serious bacterial infections (p=0.04) [Figure 2].
- In patients who had received both IVIg and SCIg in their lifetime, the median (IQR) number of days unable to perform daily duties was 3.7 (0.0, 14.8) days per year and the median number of infections per year was 3.3 (1.4, 5.3) [Figure 2].

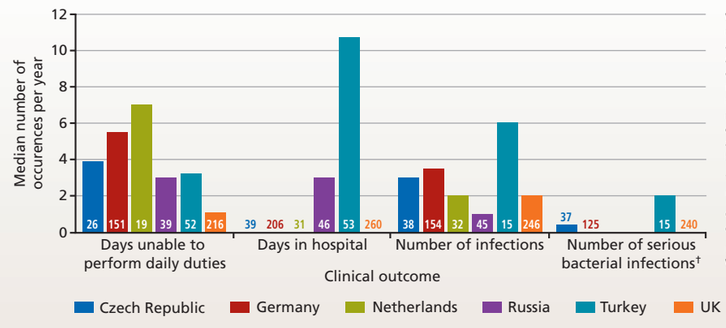
Health parameters before and after the switch from IVIg to SCIg

- The median and IQR number of days unable to perform daily duties, number of infections and number of serious bacterial infections did not vary between administration routes in patients who switched from IVIg to SCIg (Figure 3).
- Although the median number of days in hospital was zero for both routes, there was a statistically significant difference between treatment groups in the IQR with patients spending more time in hospital when receiving IVIg compared with SCIg (p=0.04) [Figure 3].

Conclusions

- The results show a wide regional variation in the clinical outcomes observed in patients with CVID treated with Ig replacement therapy.
- Further research into confounding factors such as the socio-economic impact of sick-leave, available treatment options in the respective countries and existing local CVID management protocols should be conducted.
- In addition, there may also be differences in clinical outcomes depending on the age of patients. In our analysis, the Turkish cohort consisted mainly of children, while the German and UK cohorts consisted mainly of adults.
- Patients on IVIg presented with more days in hospital and serious bacterial infections than the SCIg group, and patients who switched from IVIg to SCIg spent fewer days in hospital after the switch.

Figure 1. Clinical outcomes for each country



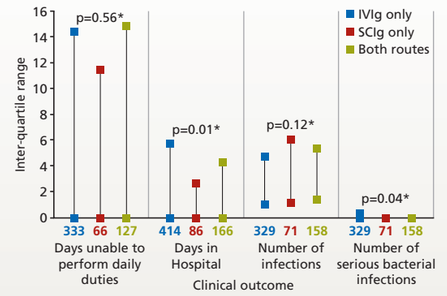
White numbers at base of each column represent to the number of patients assessed in each country for the associated clinical outcome; the number of patients assessed for serious bacterial infections is colour-coded for the Czech Republic. For countries that reported a median occurrence of zero for a specific clinical outcome, the number of patients assessed for that outcome is colour-coded by country.

†No data were analysed in the Netherlands and Russia.

Countries providing ≤10 data values were excluded from this analysis.

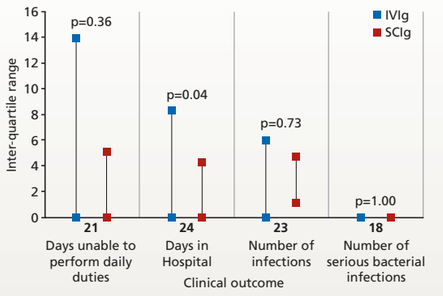
Data were compared using the Kruskal-Wallis test.

Figure 2. Clinical outcomes in patients who received IVIg only, SCIg only or treatment by both routes (inter-quartile ranges)



IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin.
*p-value for comparison of IVIg only and SCIg only routes. Colour-coded numbers at base of the x-axis represent the number of patients assessed by that treatment route for the associated clinical outcome. For all treatment routes, the median number of days in hospital and number of serious infections was 0.0. For patients on IVIg only and SCIg only, the median number of days unable to perform daily duties was 3.0 and 3.8, respectively; the median number of infections was 2.0 and 2.9, respectively. Data were compared using the Mann-Whitney test. The Czech Republic, Egypt, Germany, the Netherlands, Poland, Russia, Sweden, Turkey and the UK provided data for all outcomes. Additionally: France contributed data for days unable to perform daily duties and days in hospital; Ireland contributed data for days in hospital, number of infections and number of serious infections.

Figure 3. Clinical outcomes in patients who switched from IVIg to SCIg (inter-quartile ranges)



IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin.
Black numbers at base of the x-axis represents the number of patients assessed for the associated clinical outcome. For both treatment routes, the median number of days unable to perform daily duties, days in hospital and serious bacterial infections was 0.0. The median number of infections was 1.6 for patients on IVIg and 2.8 for patients on SCIg. Data were analysed using the Wilcoxon matched-pairs test.
Outcomes data were provided by Germany and the UK.

- These results indicate that there may be differences in the clinical outcome depending on the route of Ig administration. It must be noted that the differences we observed were restricted to the IQR.
- We intend to collect more data on clinical outcomes and run this analysis again on a larger cohort to see if the trends we identified will be confirmed.
- Furthermore, the outcomes of Ig patients should be compared with a control cohort of healthy individuals in order to determine the overall effect of Ig replacement on improving the health of patients with CVID.

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