Incidence and prevalence rate estimation of GH treatment exposure in Piedmont pediatric population in the years 2002-2004: Data from the GH Registry

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ABSTRACT. Objective: The aim of this study is to estimate the annual incidence and prevalence rate of the GH treatment exposure in patients under the age of 18 treated for hypopituitarism or isolated GH deficiency (GHD) in Piedmont, during the period January 1, 2002 to December 31, 2004. Methods: The selection criteria for recombinant human GH (rhGH) treatment in childhood were approved by the Ministry of Health in Italy in the yr 1998. The present analysis is based on data from the Registry of subjects receiving GH therapy (GH Registry) made up of the 918 pediatric patients (age <18 yr) with a diagnosis of GHD (excluding Prader-Willi and Turner syndromes and other conditions), diagnosed in the period January 1, 2002 - December 31, 2004. The case series has been described as regards the number of cases per year of diagnosis; the prevalence and incidence rates, calculated per 10,000 (%/ooo) inhabitants, are given for each year of the study period. Results: The prevalence rate increases slightly from 8.62%/ooo in 2002 to 9.44%/ooo in 2004 and the incidence rates estimated were 2.49%/ooo, 1.86%/ooo and 1.97%/ooo in the yr 2002, 2003 and 2004, respectively. Conclusion: The Piedmont GH Registry represents the first database available in Italy and could set an example for the other Italian regions as well.


INTRODUCTION

GH replacement therapy (GHRX) has been offered to GH-deficient children for more than 30 yr. Before 1985, GH was extracted from human pituitary gland and, in relation to the relative paucity of the product, was limited only to children with severe forms of GH deficiency (GHD). The introduction of recombinant human GH (rhGH) increased the drug availability and made it possible to treat a greater number of patients even with less severe forms of GHD. Moreover, in the last years, GHRX was also proposed for adult patients with GHD, with onset either in pediatric age or in adulthood (1, 2), because of the important somatotrophic effect on body composition, structure function, muscle strength and metabolic effects in general.

As a matter of fact, the aim of the substitute therapy differs between children and adult patients: an improvement in height and height velocity in children and an enhancement of the metabolic effects in the others. Although rare, this disorder has recently attracted more attention from the scientific community. Numerous studies in the literature describe the characteristics of GHD and the risk factors associated with it (3-5). Many studies describe the characteristics of patients with GHD, the effects of the therapy with rhGH both in pediatric and in adult population, but in contrast, few studies offer a reliable estimate of its
Incidence and prevalence in the population (6, 7). It is necessary to underline that the incidence and prevalence of GHD depend on the inclusion criteria considered: auxological criteria, hormonal test performed and normal value considered. In childhood, the Kabi International Growth Study (KIGS), which enrolled a large group of patients followed for at least 10 yr, reported an incidence of GHD of around 1/5000 (8). Parkin (9) indicated an incidence of 1 in every 30,000 births, about half having idiopathic deficiency and half having deficiency secondary to cranial disease. Other authors indicated in a Scottish study a prevalence of severe GHD in about 1/4000 children and another study confirmed the same proportion studying a pediatric population in Utah (USA) (10). A recent report from the files of children candidates for rhGH treatment in Belgium indicated the prevalence of childhood GHD of 1/5600 (11). In adulthood, fewer studies are available and the most recent and updated was the one of Regal et al. (12), who reported the results in the population of north-western Spain (Galicia) and the estimated prevalence and incidence of hypopituitarism and GHD in adults.

The difficulty in obtaining data on incidence and prevalence rate of GHD is probably due to the rarity of regional and national structured databases. As far as the European experience goes, we should mention the national French Registry, which made it possible to describe the situation of GHD in France (13). Within the framework of a regional project for the control and monitoring of GH treatment in Piedmont, a Registry of subjects receiving GH therapy (GH Registry) has been activated since January 2000. Information on patients receiving GH therapy in the 12 authorized centers for the diagnosis and treatment of GHD was gathered using a structured computerized data collection form; the coordinating centre (Department of Public Health and Microbiology, University of Turin) took care of data-management, data-cleaning and data-analysis. The Registry provides a continuous update of the database, regarding information about new patients beginning treatment and those already in therapy, so that the information can be accessed for various types of analysis.

Presently, after 5 yr since the activation of the GH Registry, the database is robust enough to offer reliable data for a primary analysis of the situation in Piedmont.

Objectives
The aim of this study is to estimate the annual incidence and prevalence rate of the GH treatment exposure in patients under the age of 18 treated for hypopituitarism or isolated GHD in Piedmont, during the period January 1, 2002 to December 31, 2004. The study focused on this period because, during these years, data were considered reliable enough, after the first years of settlement of the Piedmont Register.

MATERIALS AND METHODS

Registry structure
Since January 1, 2000, the Piedmont Region activated and authorized 12 different centres for the diagnosis and therapy of GHD. Seven centers for the city of Turin and its districts, two in the city of Alessandria, two in the city of Cuneo, one in the district of Novara and one in the district of Verbania. All the authorized centers have a dedicated on-line access and protected login as well as password, to allow a daily update of the data base. The Registry is managed by the Department of Public Health and Microbiology of the University of Turin with a specific Regional Health System mandate. The latter is in charge for data management and statistical analysis.

All patients diagnosed as GH deficient, in each of the authorised centers, are entered into the Registry. Every 6 months, since the baseline intake, a follow-up visit provides additional clinical information. The database includes demographic information, such as sex, date of birth and province of residence, and precise clinical and auxological data (diagnosis, type of GHD, height, weight, height velocity, pubertal development stages, skeletal maturation, GH stimulation test and related response peak, spontaneous nocturnal GH secretion, IGF-I levels and rhGH substitutive dose). The patients’ data found to contain errors or missing information are systematically reported to the respective center by the coordinating center, then corrected or completed by physicians. Every 6 months all data are processed for statistical analysis.

Criteria for selecting patients: Diagnosis of growth hormone deficiency
The selection criteria for rhGH treatment in childhood were approved by the Ministry of Health in Italy in the yr 1998 [Nota 39 (14)] and defined the following criteria:
1) pituitary GHD, when the child fails to show GH peak ≥10 μg/l in response to two classical provocative tests (ie, physical exercise, ITT, clonidine, glucagon, arginine, l-dopa test) or ≥20 μg/l in response to GHRH+arginine or pyridostigmine test;
2) GH insufficiency due to neurosecretory dysfunction, when the child has a low spontaneous 24 or 12 h mean GH concentration in spite of a normal response to provocative tests;
3) GH insufficiency due to peripheral GH bioinactivity, when the child has a normal spontaneous 24 or 12 h mean GH concentration, a normal GH response to provocative tests but low IGF-I levels.

In November 2005, a new edition of theNota 39 was approved (18) which defined new diagnostic criteria.

Database
The present analysis is based on data from the GH Registry made up of the 918 pediatric patients (age <18 yr) with a diagnosis of GHD (excluding Prader-Willi and Turner syndromes and other conditions), diagnosed in the period January 1, 2002 - December