A Comprehensive Literature Review of the Burden of Gaucher Disease

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Abstract

The Epidemiology of GD

• Gaucher Disease (GD) is an inherited, autosomal recessive disorder, and is the most common lysosomal storage disease (LSD). GD results from the absence of glucocerebrosidase (GLC3), known also as acid β-glucosidase, to cleave glucosylceramide into free glucose and ceramide.

• GD is a lifelong, progressive disease characterized by accumulation of glucosylceramide in mononuclear leukocytes in the liver, spleen, bone, brain, and other tissues, leading to severe complications if left untreated.

• GD is rare in the general population (global prevalence: 1 case per 100,000-150,000 people; but increased frequency of Jewish Ashkenazi descent), where prevalence is estimated at 1-2 per 100,000.

• Type 1 GD (non-neuropathic) affects 80% of all GD patients, while type 2 (acute neuropathic) and type 3 (subacute/chronic neuropathic) affect the nervous system as well, with differing ages of onset and disease progression. All three types require enzyme replacement therapy (ERT).

• The majority of GD require clinical examination, and magnetic resonance imaging (MRI) for markers of neurodegeneration or neuroimaging (PET or SPECT) to detect early stage PD.

• GD treatment has revolutionized quality of life with the introduction of enzyme replacement therapy (ERT) and substrate reduction therapy (SRT) to decrease glucocerebroside loads in the liver, spleen, and other organs.

• GD impacts hematologic levels and platelet counts, decrease spleen and liver size, resolve symptoms of bone disease, and improve overall health-related quality of life (HRQOL).

• Severe GD patients may require additional treatment options including analgesics for bone pain, blood transfusions, orthopedic surgery, and early splenectomy or bone marrow transplantation.

A literature review was conducted to better understand the epidemiology, clinical, and natural course of GD.

Methods

• MEDLINE, EMBASE, CENTRAL, and “grey” literature were searched to identify English-language studies using PubMed, Cochrane Library, and manually retrieved studies.

• Prevalence of GD by Country and Publication Year

• Data on clinical manifestations and comorbidities were from genetic, hospital, or tertiary care databases. A total of 177 relevant studies were summarized.

• A preliminary analysis of 97 eligible studies is presented here (a number of studies reported overlapping outcomes: epidemiology [22 studies]; mortality data [13 studies]; and assessments of health economic burden [657].

• Inclusion criteria were studies reporting prevalence, incidence, clinical manifestations, complications, and economic burden of GD (exclusions were for hematologic manifestations).

• Studies were included if they reported outcomes in GD patients; exclusion criteria were for hematologic manifestations.

• The standardized incidence and prevalence of GD in the general population varies from 0.30 to 5.80 per 100,000 population.

• Common manifestations of GD such as anemia, thrombocytopenia, splenomegaly, hepatomegaly, and bone disease were reported across studies.

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Results

Results (continued)

• Involvement of GD also varied among geographic/glutocerebrosidase studies in Europe, Asia, and Canada, ranging from 0.10 to 40.40 per 100,000 population (Figure 3).

• The highest GD incidence across the general population was in Asia (8.80 per 100,000).

• For 177 relevant studies, incidence of GD was reported in the general population. A meta-analysis of these studies reported an initial incidence of 0.30 per 100,000 in the general population.

• GD being diagnosed in this population than might ordinarily have been the case with purely clinical studies.

• Several studies have suggested that ERT improved HRQOL in patients with type 1 GD, with post-treatment improvements in physical function and QOL.