Parental Needs and QoL in Children with Pompe Disease

Subjects: Health Care Sciences & Services

Contributor: Loredana Benedetto , Olimpia Musumeci , Annunziata Giordano , Mattia Porcino , Massimo Ingrassia

Pompe disease (PD) is a rare metabolic disorder with progressive neuromuscular consequences that negatively impact a child's development and quality of life (QoL). Despite an improved prognosis with treatment, the risk for early death due cardiorespiratory crisis remains. Parents not only face physical fatigue and family distress in coping with the child's special needs but also experience emotions, worries, and unexpressed needs (a "humanistic burden") that require supportive interventions.

childhood rare diseases Pompe disease quality of life parental needs

1. Introduction

Rare diseases are defined by their low prevalence within the population, yet their psychological impact is devastating. Pompe disease (PD or glycogen storage disease type II, GSD II) is a rare inherited metabolic disorder characterized by a deficiency of the enzyme acid alpha-glucosidase (GAA), which induces an accumulation of glycogen mainly in skeletal muscle, leading to slowly progressive muscle weakness, resulting in walking disability and reduced respiratory function.

Generally, children with infantile-onset Pompe disease (IOPD) present cardiomyopathy, heart failure, marked hypotonia, and respiratory failure, leading if untreated to a grim prognosis due to cardiorespiratory complications [1]. The current treatment for PD at all ages is enzyme replacement therapy (ERT), which reduces the risk of early death [2][3]. Early identification through newborn screening (NBS) is essential for early treatment and to improve the prognosis [4][5].

2. Health-Related Quality of Life in Infantile PD

Respiratory distress and feeding difficulties are commonly observed in infantile PD, and they can require continuous and/or invasive supports, such as ventilation, nasogastric tubes, or percutaneous endoscopic gastrostomy (PEG) [6].

The clinical condition associated with infantile PD interferes significantly with children's quality of life (QoL), that is, the physical, emotional, and social functioning related to their health state [7][8]. Speech/feeding problems or the decline in motor functions limit children's daily activities, with restricted participation in social and physical activity (mainly due to fatigue in sport practice) [9]. Nevertheless, the early initiation of ERT seems to have a good impact

on QoL, facilitating earlier independent walking and/or reducing the need for ventilation [10][11]. Furthermore, learning problems and attention deficits observed in children with PD in comparison with peers, together with negative mood symptoms, may have a negative impact on QoL [12]. However, studies assessing QoL in infantile PD are scarce.

3. Caring and Parental Burden

Due to the progressive functional impairment in PD, parents undergo significant distress in managing day-to-day living. They live on high alert for their child's health, particularly for cardiorespiratory crises, and frequently describe their experience as both exhausting and totally involving [13]. The continuous provision of support at home (i.e., managing motor disability/feeding problems) along with ensuring treatments (like ERT twice a month) place an overload of caregiving responsibilities on them. This overload has adverse effects on both the physical and psychological health of parents. In the psychological literature, these consequences are defined as the "burden of care", a condition experienced by family members caring for a child or relative with a chronic/disabling disease. Caregiver burden encompasses objective changes in the various aspects of life (such as time devoted to care and economic costs) as well as subjective consequences (like emotional strain and familial or social challenges) associated with providing daily care [14][15]. Kanters et al. [16] found higher levels of burden and worse health outcomes among primary caregivers, typically parents (94%), of children with PD compared to caregivers of adults. Higher burden levels were linked to more intense daily care responsibilities, including the time-consuming ERT, the child's personal care, and social activities. In prioritizing the child's needs, parents also face difficulties in balancing family life (including marital and sibling relationships) and fulfilling work obligations, with an increase in stress and conflicts [13][17].

4. The Humanistic Burden

However, the caregiver's experience is often studded with emotions, worries, and unexpressed needs that extend beyond the negative impact of the clinical and practical consequences of diseases. In a review by Schoser et al. [18], the term "humanistic burden" was introduced to encapsulate the overall implications of PD in both the patient's and the caregiver's adjustment. This emphasizes the necessity for a comprehensive understanding of the emotional strain, suffering, and relational and existential needs arising from a rare and disabling disease. However, the authors noted a critical gap in the literature, stating "complete absence of data on the humanistic burden of the IOPD" ([18] p. 12), highlighting a significant void in the literature. Consequently, this study seeks to delve into the unexpressed psychological needs and challenges that contribute to the burden on parents caring for a child with PD.

4.1. Living in Uncertainty

A study by Pruniski et al. [19] delved into the psychological consequences experienced by parents who received an early diagnosis of PD following NBS. All parents reported heightened anxiety and fears about the future coupled with a sense of living with uncertainty. Three primary sources of uncertainty emerged: uncertainty about the

diagnosis (such as the differences between IOPD and late-onset Pompe disease [LOPD] or the hope for a false-positive NBS), uncertainty about effective treatment ("who to contact? When to start it?"), and concerns about the future, encompassing both the child's development and family dynamics. Notably, the lack of knowledge about and resources to cope with their baby's diagnosis was associated with greater anxiety and fear, particularly in cases of early LOPD diagnosis. LOPD is experienced as a "waiting condition", marked by hypervigilance of the child's symptoms, an intensified search for assistance (i.e., increased medical consultations or hospitalizations), and worse psychosocial consequences for parents (including emotional strain, cessation of work, and/or financial burden).

4.2. The Unspoken Fears

Early identification and ERT have significantly enhanced the prognosis of IOPD. However, despite the treatment, the mortality rate of children from respiratory and cardiac failure remains high [20][21]. The apprehension of sudden death stands out as one of the biggest sources of suffering that parents experience, compounded by the necessity to talk about the child's illness with the child's siblings [11].

In numerous instances, parents became "experts" on the rare condition [13][22]. Interestingly, they often exhibit a level of awareness and knowledge surpassing that of professionals (e.g., pediatricians and rehabilitation therapists) regarding recent research or treatments. This reversed parent–professional role may be associated with an increased sense of responsibility in parents. This heightened responsibility manifests in decisions related to treatments and in the exhausting pursuit ("odyssey") of specialized centers offering more advanced therapeutic interventions [10][22].

Moreover, given that PD is genetically inherited, parents harbor concerns about the potential transmission of the disorder to their other children. This concern can lead to guilt in one of the parents, who may perceive themselves as the cause of the condition [13]. The siblings, in turn, may feel anxious, fearing the onset of similar symptoms. They often experience a sense of isolation and neglect as the illness demands the involvement of their parents, thereby causing siblings to shoulder added responsibilities within the family [23]. Families confronting rare genetic disorders encounter numerous challenges that comprise a condition of burden and uncertainty due to the management of medical complexities, grief, and worries regarding present and future generations [10][24].

5. Protective Factors and Resilience

Research has investigated the protective factors that enhance parents' adjustment to a rare condition, facilitating the development of positive aspects (such as personal growth, a sense of coherence, and appreciation of life), even while experiencing suffering and the burden of care [13]. Focusing on daily tasks, actively seeking support, and acknowledging the positive aspects of caring for a child with a rare disease were identified as coping strategies linked to a reduced parental burden [25]. Furthermore, parents who possess flexibility, optimism, inner strength and

self-efficacy, acceptance, and family cohesiveness are more resilient; they experience better adaptation outcomes and meanings despite their child's health problems [19][22].

References

1. Felice, T. Pompe Disease, a Storage Cardiomyopathy. Cardiogenetics 2017, 7, 6857.
2. van der Meijden, J.C.; Kruijshaar, M.E.; Harlaar, L.; Rizopoulos, D.; van der Beek, N.A.M.E.; van der Ploeg, A.T. Long-term follow-up of 17 patients with childhood Pompe disease treated with enzyme replacement therapy. J. Inherit. Metab. Dis. 2018, 41, 1205–1214.
3. Chen, M.; Zhang, L.; Quan, S. Enzyme replacement therapy for infantile-onset Pompe disease. Cochrane Database Syst. Rev. 2017, 11, CD011539.
4. Chien, Y.-H.; Lee, N.-C.; Thurberg, B.L.; Chiang, S.-C.; Zhang, X.K.; Keutzer, J.; Huang, A.-C.; Wu, M.-H.; Huang, P.-H.; Tsai, F.-J.; et al. Pompe Disease in Infants: Improving the Prognosis by Newborn Screening and Early Treatment. Pediatrics 2009, 124, e1116–e1125.
5. Gragnaniello, V.; Pijnappel, P.W.W.M.; Burlina, A.P.; In't Groen, S.L.M.; Gueraldi, D.; Cazzorla, C.; Mainesf, E.; Polo, G.; Salviati, L.; Di Salvo, G.; et al. Newborn screening for Pompe disease in Italy: Long-term results and future challenges. Mol. Gen. Met. Rep. 2022, 33, 100929.
6. Marques, J.S. The Clinical Management of Pompe Disease: A Pediatric Perspective. Children 2022, 9, 1404.
7. Varni, J.W.; Limbers, C.A.; Burwinkle, T.M. Parent proxy-report of their children's health-related quality of life: An analysis of 13,878 parents' reliability and validity across age subgroups using the PedsQL 4.0 Generic Core Scales. Health Qual. Life Outcomes 2007, 5, 2.
8. Varmi, J.W.; Seid, M.; Kurtin, P. PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in healthy and patient populations. Med. Care 2001, 39, 800–812.
9. Scheffers, L.E.; Helbing, W.A.; Utens, E.M.W.J.; Dieleman, G.C.; Dulfer, K.; Noske, J.; van den Broek, W.A.; Walet, S.; Olieman, J.F.; Eschner, J.C.; et al. Study Protocol of the Exercise Study: Unraveling Limitations for Physical Activity in Children with Chronic Diseases in Order to Target Them with Tailored Interventions—A Randomized Cross Over Trial. Front. Pediatr. 2022, 9, 791701.
10. Prakash, S.; Penn, J.D.; Jackson, K.E.; Dean, L.W. Newborn screening for Pompe disease: Parental experiences and follow-up care for a late-onset diagnosis. J. Genet. Couns. 2022, 31, 1404–1420.

11. Hahn, A.; Schänzer, A. Long-term outcome and unmet needs in infantile-onset Pompe disease. Ann. Transl. Med. 2019, 7, 283.
12. Korlimarla, A.; Spiridigliozzi, G.A.; Stefanescu, M.; Austin, S.L.; Kishnani, P.S. Behavioral, social and school functioning in children with Pompe disease. Mol. Genet. Metab. Rep. 2020, 25, 100635.
13. von der Lippe, C.; Neteland, I.; Feragen, K.B. Children with a rare congenital genetic disorder: A systematic review of parent experiences. Orphanet J. Rare Dis. 2022, 17, 375.
14. Chou, K.-R. Caregiver burden: A concept Analysis. Int. Ped. Nurs. 2000, 15, 398–407.
15. Novak, M.; Guest, C. Application of a multidimensional caregiver burden inventory. Gerontologist 1989, 29, 798–803.
16. Kanters, T.A.; van der Ploeg, A.T.; Brouwer, W.B.; Hakkaart, L. The impact of informal care for patients with Pompe disease: An application of the CarerQol instrument. Mol. Genet. Metab. 2013, 110, 281–286.
17. Belzer, L.T.; Wright, S.M.; Goodwin, E.J.; Singh, M.N.; Carter, B.S. Psychosocial Considerations for the Child with Rare Disease: A Review with Recommendations and Calls to Action. Children 2022, 9, 933.
18. Schoser, B.; Bilder, D.A.; Dimmock, D.; Gupta, D.; James, E.S.; Prasad, S. The humanistic burden of Pompe disease: Are there still unmet needs? A systematic review. BMC Neurol. 2017, 17, 202.
19. Pruniski, B.; Lisi, E.; Ali, N. Newborn screening for Pompe disease: Impact on families. J. Inherit. Metab. Dis. 2018, 41, 1189–1203.
20. Chakrapani, A.; Vellodi, A.; Robinson, P.; Jones, S.; Wraith, J.E. Treatment of infantile Pompe disease with alglucosidase alpha: The UK experience. J. Inherit. Metab. Dis. 2010, 33, 747–750.
21. Tardieu, M.; Cudejko, C.; Cano, A.; Hoebeke, C.; Bernoux, D.; Goetz, V.; Pichard, S.; Brassier, A.; Schiff, M.; Feillet, F.; et al. Long-term follow-up of 64 children with classical infantile onset Pompe disease since 2004: A French real-life observational study. Eur. J. Neurol. 2023, 30, 2828–2837.
22. Cardinali, P.; Migliorini, L.; Rania, N. The Caregiving Experiences of Fathers and Mothers of Children with Rare Diseases in Italy: Challenges and Social Support Perceptions. Front. Psychol. 2019, 10, 1780.
23. Haukeland, Y.B.; Vatne, T.M.; Mossige, S.; Fjermestad, K.W. Psychosocial Functioning in Siblings of Children with Rare Disorders Compared to Controls. Yale J. Biol. Med. 2021, 94, 537–544.
24. Metcalfe, A.; Plumridge, G.; Coad, J.; Shanks, A.; Gill, P. Parents' and children's communication about genetic risk: A qualitative study, learning from families' experiences. Eur. J. Hum. Gen. 2011, 19, 640–646.

25. Picci, R.L.; Oliva, F.; Trivelli, F.; Carezana, C.; Zuffranieri, M.; Ostacoli, L.; Furlan, P.M.; Lala, R. Emotional Burden and Coping Strategies of Parents of Children with Rare Diseases. J. Child. Fam. Stud. 2015, 24, 514–522.