ISSN: 2395-6429

INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

IJCMPR

Available Online at http://www.journalcmpr.com

DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20170035

REVIEW ARTICLE

POMPE'S DISEASE: A REVIEW ARTICLE

Amal Sebastian., Ahammed Fuwad C H., Muhammed Ashique K and Ren Joy Mathew

Pharm D interns, Krupanidhi College of pharmacy, Chikka Bellandur, Carmelaram Post, Bangalore-35

ARTICLE INFO

Article History:

Received 10th January, 2017
Received in revised form 28th February, 2017
Accepted 15th March, 2017
Published online 28th April, 2017

Key words:

Accumulation, GAA, electrolyte therapy

ABSTRACT

Pompe disease is an inherited disorder caused by the buildup of a complex sugar called glycogen in the body's cells. The accumulation of glycogen in certain organs and tissues, especially muscles, impairs their ability to function normally. Mutations in the GAA gene cause Pompe disease. Current estimates for Pompe disease put the overall disease incidence at approximately 1 in 40,000 live births The muscle biopsy and GAA enzyme levels are monitored for the diagnosis of pompe disease. Pompe disease include respiratory, cardiac and movement problems. There is no cure for pompe disease. Usually electrolyte replacement therapy is done to treat pompe disease.

INTRODUCTION

Pompe disease is an enzyme defect which causes the accumulation of complex sugar called glycogen. The accumulation occurs in certain tissues and organs, especially in muscles that ultimately causes the impairment of the function [(1)]. The signs and symptoms of pompe disease may emerge from any age infancy to late adulthood. Pompe disease is progressive and symptoms get worsen over time [(2)].

When the symptoms appear in children and adults the rate of progression is less compared to infants. The signs and symptoms in infants include breathing difficulties, trouble feeding, failure to meet developmental mile stones such as rolling over and sitting up. The X - rays in infants shows enlarged heart [(2)]. Variety of symptoms are observed in Children and adults including weakness of the leg and hip muscles, leading to difficulties with mobilities aswellas breathing difficulties[(2)]. A cure for pompe disease does not exist. However the introduction of enzyme replacement therapy is a major therapeutic advantage [(3)]. Current estimates for Pompe disease put the overall disease incidence at approximately 1 in 40,000 live births[(4)]. However, as with any rare disease, it is difficult to know exactly how many people are actually affected. Extrapolating from the assumed incidence figures, it is estimated that the current worldwide prevalence may be 5,000-10,000 people—of both genders and of varying ages and ethnicities[(4)].The infantile form usually is fatal, with most deaths occurring within 1 year of birth. Males and females are affected with equal frequency because of autosomal recessive inheritance [(3)].

Pathophysiology

GAA is a gene which is located in chromosome 17 and is responsible for producing acid alpha glucosidase. It is responsible for the breakdown of glycogen to glucose in the lysosomes. In pompe disease GAA gene will undergo mutation which may result in the inhibition of the breakdown of glycogen to glucose. This causes the accumulation of glycogen especially in primary cells [(4)].Glycogen accumulation within the muscle, peripheral nerves, and the anterior horn cells results in significant weakness. In the infantile form, accumulation may also occur in the liver, which results in hepatomegaly and elevation of hepatic enzymes[(3)]. As the glycogenolysis is inhibited for a long time it causes continuous accumulation of glycogen in the lysosomes. This lead to swelling and rupture which results in cellular damage. The accumulation will result in degeneration of skeletal muscles, cardiac muscles etc. eventually results in loss of function.

Diagnosis

The diagnosis of pompe disease is a very complicated process and requires variety of tests. The first step is to rule out the most common disorders similar to pompe disease such as musculoskeletal disorders. In order to avoid the misdiagnosis

or under diagnosis of pompe disease due to phenotypic similarities caution should be taken. In case of infants symptoms will arise from the first month. The muscle biopsy can be done to confirm pompe disease. But biopsy is not sufficient and it always don't give a clear picture. So GAA enzyme levels in the blood should be done as the confirmatory test. It can be performed by blood assay method by using whole blood or dried blood spot. The normal level of GAA enzyme in the blood is greater than 0.5 nmol/mL/h. The affected individuals will have GAA enzyme level less than 0.5 nmol/mL/h. However the late onset can show higher level of enzyme activity. Patients with low levels of GAA enzyme should undergo molecular genetic analysis to determine the disease status. The specimen for the test should not be exposed above 25 degree Celsius so that the negative results won't be obtained[5]. Creatine kinase (CK) levels are usually elevated (ranging from 1.5 to 15 times the upper limit of normal in adults) in late onset Pompe disease patients. In some cases, however, CK levels are normal. In asymptomatic or mildly symptomatic individuals, persistent elevations of CK have led to further investigation and the subsequent diagnosis of Pompe disease [6].

Electromyographic (EMG) findings is also use in the diagnosis of pompe disease. EMG in limb muscles will be normal. But (EMG) findings often indicate myopathy with increased muscle membrane irritability in the form of fibrillation potentials, positive sharp waves, complex repetitive discharges or myotonic discharges in the absence of clinical myotonia. In patients with late onset Pompe disease, nerve conduction studies are normal. Respiratory evaluation is extremely important in patients who may have Pompe disease. Spirometric measurement of forced vital capacity (FVC) in both the seated and supine positions should be made whenever possible. A greater than 10% drop in FVC from the seated to the supine testing position is suggestive of diaphragm weakness and should raise the possibility of Pompe disease.

Clinical Presentation

The various symptoms include muscle and movement problems such as head lag, poor muscle tone, weakened mouth, difficulty in swallowing, difficulty in sitting up, crawling, loss of abilities etc. In infants pompe disease also includes heart problems such as enlarged heart due to excess glycogen building up, irregular rhythm of heart, and even cardiac failure[4]. The clinical spectrum ranges from the classical form with early onset and severe phenotype to not-classical form with later onset and milder phenotype [6]. Breathing and respiratory problems is also common which includes breathing difficulties, chance of getting respiratory infections and sometimes respiratory failure. So ventilation is very important for infants with pompe disease [4]. Respiratory failure in patients with Pompe disease can range from insidious to acute onset and respiratory muscle involvement is the most common cause of early death in these patients. The respiratory muscles involved are the upper airways, inspiratory muscles of the chest, and the diaphragm [6.] Respiratory failure in patients with Pompe disease can range from insidious to acute onset and respiratory muscle involvement is the most common cause of early death in these patients[6]. Digestive difficulties is also common due to enlarged and protruding tongue. So for underweight patients tube feeding is essential for maintaining the health. Enlarged liver is also common in pompe disease.

Treatment

It is unfortunate to say that there is no cure for pompe disease. But recently patient's got benefited from enzyme replacement therapy even though it remains as an expensive treatment. Historically, treatment of Pompe disease has focused on managing symptoms and offering supportive care, and these continue to be critical components of the overall treatment approach. ERT provides an exogenous source of GAA. Although the underlying basis of Pompe disease is progressive muscular degeneration, the disease can affect different organs and systems. Therefore patient care and management of this multisystemic disorder is best handled by a multidisciplinary team of healthcare providers. The management should be a team approach which comprises of specialists. Neuromuscular specialist, Neurologist, Cardiologist, Pulmonologist, Intensivist, Orthopedist, Rehabilitation therapist (eg, respiratory, physical, occupational, speech), Metabolic dietician ,Genetic counselor and pediatrician in case of children.

Management of clinical manifestations is expected to improve the life expectancy and quality of life. Respiratory support is given for the management which includes mechanical ventilation, secretion clearance and infection management. Mechanical ventilation helps to prolong the survival of patients with acute respiratory failure. Because of weakened respiratory muscles the patients will be having weak cough which causes the pulmonary secretions to get retained in the lungs which can lead to pneumonia and various other infection[6].

Physical rehabilitation should be designed exclusively for each patients based on his/her conditions. Wide range of physical therapies are available including Physical therapy, Occupational therapy, Speech therapy, Adaptive and assistive devices, Orthopedic intervention and/or surgery[6]. Infants are at risk for cardiomyopathy, cardiomegaly, congestive heart failure, arrhythmias, and cardiac arrest during surgery [7]. Psychological support should be given to patients and their family members about the disease. The counseling should be given on the risk off the disease and family planning [6]. Adequate nutrition should be given to patient which consist of 20-25% of proteins [7]. If patients are having problem in sucking and chewing then tube feeding should be recommended. Since the patients are having respiratory impairment the chance of having infection is high. Strict precautions such as immunization, hand washing etc. should be maintained [6]. As a part of the electrolyte replacement therapy Myozyme and lumizyme are the drugs which are used in the treatment of pompe disease. Both are taken by injections. Myozyme is recommended for babies and children. These drugs replace the missing protein and help the body to process the sugar correctly [8]. It should be administered at 1 mg/kg//hr IV initially and it can be increased to 2 mg/kg/hr and it should not exceed 7 mg/kg/hr.

In more than 10% of the patients various adverse effects are found such as Pyrexia, Rash, Diarrhea, Vomiting, Cough etc. After the administration of the drugs careful monitoring is required as life threatening anaphylactic reactions and severe hypersensitivity reactions are reported after IV infusions. The supporting staff should be always prepared to manage the anaphylactic reactions. After the administration the carbohydrate group on GAA molecule binds to mannose-6-phosphate receptors, then GAA is transported into cell where it undergo proteolytic cleavage resulting in enzymatic glycogen

cleavage. The half life of the drugs is considered to be 2-3 hours [9].

CONCLUSION

Pompe disease is a very rare inherited neuromuscular disorder. It is affected to all age groups and is characterised by muscle weakness. It is often due to the deficiency of GAA enzyme. The treatment is done mainly by electrolyte replacement therapy. The treatment is very expensive.

References

1. Reference, G. (2017). *Pompe disease*. [online] Genetics Home Reference. Available at: https://ghr.nlm.nih.gov/condition/pompe-disease#definition [Accessed 6 Apr. 2017].
2. Anon,(2017).[online]Availableat:https://www.pompe.com/en/patients/signs-symptoms.aspx [Accessed 6 Apr. 2017].
3. Emedicine. medscape.com. (2017). Type II Glycogen Storage Disease (Pompe Disease): Practice Essentials, Background, Pathophysiology. [online] Available at: http://emedicine.medscape.com/article/119506 [Accessed 6 Apr. 2017].
4. Anon,(2017).[online]Availableat:https://www.pompe.com/en/healthcare-professionals/ [Accessed 6 Apr. 2017].
5. Mayomedicallaboratories.com. (2017). *GAABS* - Clinical: Acid Alpha-Glucosidase, BloodSpot. [online]. Available.at:http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/89210 [Accessed 6 Apr. 2017].
6. FIORE MANGANELLI, L. (2017). Clinical features of Pompe disease. [online] PubMed Central (PMC)..Available.at:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3866902/ [Accessed 6 Apr. 2017].
7. Kishnani, P., Steiner, R., Bali, D., Berger, K., Byrne, B., Case, L., Crowley, J., Downs, S., Howell, R., Kravitz, R., Mackey, J., Marsden, D., Martins, A., Millington, D., Nicolino, M., O'grady, G., Patterson, M., Rapoport, D., Slonim, A., Spencer, C., Tifft, C. and Watson, M. (2017). Pompe disease diagnosis and management guideline.
8. Guides, A. (2017). Pompe Disease: Learn the Details About This Rare Disorder. [online] WebMD..Available.at:http://www.webmd.com/a-to-z-guides/pompe-disease#2 [Accessed 6 Apr. 2017].
9. Reference .medscape.com. (2017). Lumizyme, Myozyme (alglucosidase alfa) dosing, indications, interactions, adverse effects, and more. [online] Available at: http://reference.medscape.com/drug/lumizyme-myozyme-alglucosidase-alfa-342864 [Accessed 6 Apr. 2017].

****