British Journal of Pharmaceutical and Medical Research Vol.02, Issue 01, Pg.364-366, January-February 2017

Available Online at http://www.bjpmr.org

BRITISH JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

DOI: In-Process Volume 02, Issue 01, January-February 2017

Review Article

Clinical Outline on Progeria

Kirti Rani

Amity Institute of Biotechnology, Amity University Uttar Pradesh, Noida, Sec-125, Noida-201313 (UP), India.

ARTICLE INFO

Article History:
Received on 22th November, 2016
Peer Reviewed on 23th December 2016
Revised on 19th January, 2017
Published on 02nd February, 2017

Keywords:
Progeria; LMNA gene; Farnesyltransferase

ABSTRACT

Hutchinson Gilford Progeria Syndrome' commonly known as Progeria which is a fatal disease with no proper cure. Progeria patients are suffered from fast aging process with very fast pace. Usually, children born with this disease can live only upto their mid-teens and suffer from various aging symptoms e.g. growth failure, skin ageing, abnormal jaw size, pinched nose, alopecia, heart diseases. Various clinical researchers were discovered that this disease is caused by a mutation in the gene called LMNA ("lamin-a") that produce the lamin A protein which is the structural scaffolding that holds the nucleus of a cell together. The abnormal lamin A protein is called Progerin that caused Progeria. These is not still definite or proper treatment of Progeria and only use of Farnesyltransferase inhibitors can be effective in reducing its symptoms.

INTRODUCTION:

In Progeria, the growth of patients is less gradual, scalp hair falls off slowly and survival is observed mostly till adulthood only which follows autosomal recessive pattern of inheritance. The research executed in field of Progeria has gained much more importance in last two decades to understand the cellular and molecular biology behind progeroid syndromes various in-vitro and in-vivo models were studied by using several implemented clinical/diagnostic/statistical trials[1]. Probability of occurrence of Progeria was studied worldwide regardless of gender, race, geographical or ethnic predisposition and hence it is sporadic. The ratio of occurrence of this disease was observed 1:4 million new-borns with equal risk of both the boys and girls to suffer from this disease[2].In 2003, NHGRI (National Human Genome Research Institute) has been successfully discovered that Hutchinson Gilford Progeria Syndrome is occurred due to a tiny point mutation in a single gene known as Lamin A and Lamins C (LMNA)[3]. It was reported that cytosine is replaced with thymine at position 1824 of LMNA gene (Lamin A OR Lamin C gene) called LMNA. This mutation was resulted in abnormally short mature mRNA transcript which on translation yields an abnormal variant of Prelamin A whose farnesyl group cannot be removed that called 'progerin' which remains permanently attached to the nuclear rim and does not become a part of the nuclear lamina[4,5,6].

Previously, physician had to rely completely on physical symptoms for diagnosis in affected child e.g. abrupt skin changes, growth failure, failure weight gain when the child was 1-2 years old. But, these days, with advancement in clinical science and medical awareness, physicians/ researchers have been succeeded in finding out a effective genetic test for Hutchinson Gilford Progeria syndrome for diagnosing this disease timely[6,7].Researchers at NHGRI (National Human Genome Research Institute) and their other collaborators in the Progeria Research Consortium are involved to explore the steps in understanding the cause of this disease and the possible ways of developing new effective treatments by using drugs e.g. Pravastatin, Farnesyltransferase inhibitors or a combination of pravastatin and zoledronate which either block thre formation of farnesyl group or reduce the production of the abnormally synthesized lamin A protein in children with Progeria[7].

A recent trial has been reported that was started in April 2016 in which 2-drug trial was to decide the maximum tolerated dose (MTD) of the drug Everolimus with Lonafarnib that may block the progerin development and Everolimus (a kind of Rapamycin) which reported to allow the cells to clear out the toxic progerin more rapidly. As well as *Rapamycin, is well known* FDA-approved drug that has earlier been shown to extend the lives of non-Progeria mouse models in many clinical trials in labs and researchers of the National Institutes of Health were demonstrated that Rapamycin decreased the amount of the progerin by 50% that improves the abnormal shape of nucleus and acted as anti-ageing properties in mice[7,8].

CONCLUSION

So, this brief and instant review might be helpful to depict the clinical approaches to manage the Progeria disease and as well as, can be helpful to aware the common people about the ill-effects of disease at early stages and able to seek effective treatments at time.

ACKNOWLEDGMENT: I would like to express my cordially appreciation to Amity University Uttar Pradesh, Noida (INDIA).

REFERENCES

(1) Eriksson M, Brown WT, Gordon LB, Glynn MW, Singer J, Scott L. Recurrent de novo point mutations in lamin A cause Hutchinson-Gilford progeria syndrome. *Nature*. 2003;423:293–8.

(2) Glynn MW, Glover TW. Incomplete processing of mutant lamin A in Hutchinson-Gilford progeria leads to nuclear abnormalities, which are reversed by farnesyltransferase inhibition. *Hum Mol Genet*. 2005;14:2959–69.

(3) Gordon LB, McCarten KM, Giobbie-Hurder A, Machan JT, Campbell SE, Berns SD, et al. Disease progression in Hutchinson-Gilford progeria syndrome: impact on growth and development. *Pediatrics*. 2007;120:824–33.

(4) Gordon LB, Harling-Berg CJ, Rothman FG. Highlights of the 2007 Progeria Research Foundation scientific workshop: progress in translational science. *J Gerontol A Biol Sci Med Sci*. 2008;63:777–87.

(5) Sinha, J. K; Ghosh, S; Raghunath, M. "Progeria: a rare genetic premature ageing disorder".*Indian J Med Res*. 2014;139(5):667-674.

(6) McClintock D, Ratner D, Lokuge M; et al. (2007). Lewin, Alfred, ed."The Mutant Form of Lamin A that Causes Hutchinson-Gilford Progeria Is a Biomarker of Cellular Aging in Human Skin". *Plos One.* 2007; 2(12):e1269.

(7) Capell BC1, Erdos MR, Madigan JP, Fiordalisi JJ, Varga R, Conneely KN, Gordon LB, Der CJ, Cox AD, Collins FS. Inhibiting farnesylation of progerin prevents the characteristic nuclear blebbing of Hutchinson-Gilford progeria syndrome. *Proc Natl Acad Sci U S A.* 2005;102(36):12879-84.

(8) Gordon LB1, Kleinman ME, Miller DT, Neuberg DS, Giobbie-Hurder A, Gerhard-Herman M, Smoot LB, Gordon CM, Cleveland R, Snyder BD, Fligor B, Bishop WR, Statkevich P, Regen A, Sonis A, Riley S, Ploski C, Correia A, Quinn N, Ullrich NJ, Nazarian A, Liang MG, Huh SY, Schwartzman A, Kieran MW. Clinical trial of a farnesyltransferase inhibitor in children with Hutchinson-Gilford progeria syndrome. *Proc Natl Acad Sci U S A*. 2012;109(41):16666-71.