



Effects of Genetic Variations in the Cereblon Gene on How Well Thalidomide Treats Erythema Nodosum Leprosum (ENL)

Demelash Zemene*

Department of Pharmacology, University of Gondar, Gondar, Ethiopia

DESCRIPTION

Thalidomide is a glutamic acid derivative that was first created in the 1950s as an anticonvulsant before being used in early pregnancy as a sedative and antiemetic. However, when reports of birth deformities in children whose mothers had used thalidomide during pregnancy first reported in 1961, its teratogenic effect quickly came to know. As a result, it was taken off from the market. However, after a report on the effectiveness of the medicine in treating Erythema Nodosum Leprosum (ENL), its significance was later rediscovery. ENL is a potentially incapacitating condition that is difficult to treat as a result of leprosy. It is an inflammatory response that is characterized by painful cutaneous nodules that may become ulcerated, systemic involvement with fever and general malaise, and effects on multiple organs. Patients with Lepromatous Leprosy (LL) and Borderline Lepromatous Leprosy (BL), which are linked to greater bacillary loads, are affected by the reaction.

When used to treat ENL, thalidomide works quickly to relieve symptoms like fever and night sweats and to improve skin lesions. Thalidomide's efficacy in treating Multiple Myeloma (MM) and thereafter for other illnesses was established by the year 1999. Thalidomide's anti-inflammatory effect in ENL may be mediated by additional mechanisms in addition to its initial effect on TNF- α . A recent study identified the Cereblon protein as the main site of thalidomide teratogenicity. This molecule, which is a component of the E3-ubiquitin ligase complex CRL4CRBN, functions as a substrate receptor for ubiquitination, identifying particular substrates for subsequent destruction by the ubiquitin-proteasome system. The effectiveness of thalidomide and its analogues lenalidomide and pomalidomide (referred to as immunomodulatory medicines, or IMiDs) in the treatment of multiple myeloma has recently been demonstrated to depend on CRBN. The interaction between thalidomide and CRBN has been studied in relation to the teratogenic, immunomodulatory, and therapeutic effects of the

drug. There are no researches on the interaction of thalidomide and CRBN, on ENL.

Because the CRBN gene, which has 11 exons and is highly conserved, generates a protein of 442 amino acids, polymorphisms in its coding regions are uncommon. As a result, some studies have examined non-coding gene areas that may be involved in the regulation of gene expression. The thalidomide-binding region of CRBN is encoded by three exons, and bioinformatics techniques have identified three variations as potential modulators of splicing sites that may influence the expression or activity of the protein. As a component of the E3 ubiquitin ligase complex (CRL4CRBN), CRBN performs the function of a substrate receptor and regulates the expression of target proteins through their ubiquitination and destruction. Thalidomide's teratogenic effect depends on CRBN. Additionally, thalidomide and other IMiDs' ability to inhibit cell proliferation in MM depend on this protein. Theoretically, thalidomide changes the function of CRBN when it binds to it, inducing teratogenic consequences by inhibiting the degradation of proteins and/or by producing neosubstrates for ubiquitination and proteasomal destruction, both of which are essential for embryonic development. The neosubstrates Ikaros (IKZF1) and Aiolos (IKZF3) are attracted to the ubiquitin-ligase complex by thalidomide binding to CRBN in the case of MM, leading to an increase in the ubiquitination and degradation of these transcription factors in T cells and MM cells. A possible function for CRBN as a predictive biomarker for treatment response has also been suggested by studies that link low CRBN mRNA expression with poorer clinical response to IMiDs. It has been known since the 1990s that one of the main effects of thalidomide is to shorten the half-life of TNF mRNA, which accounts for part of its therapeutic effects. It has been demonstrated by the use of CRBN knockdown that the inhibitory effect of IMiDs on TNF- α production was impaired in the silencing of CRBN.

Correspondence to: Demelash Zemene, Department of Pharmacology, University of Gondar, Gondar, Ethiopia, E-mail: Zemene@gmail.com

Received: 03-Aug-2022, Manuscript No. CPECR-22-17987; **Editor assigned:** 08-Aug-2022, Pre QC No. CPECR-22-17987 (PQ); **Reviewed:** 22-Aug-2022, QC No CPECR-22-17987; **Revised:** 29-Aug-2022, Manuscript No. CPECR-22-17987 (R); **Published:** 05-Sep-2022, DOI: 10.35248/2161-1459.22.12.327.

Citation: Zemene D (2022) Effects of Genetic Variations in the Cereblon Gene on How Well Thalidomide Treats Erythema Nodosum Leprosum (ENL). J Clin Exp Pharmacol. 12:327.

Copyright: © 2022 Zemene D. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.