ANGIOGENESIS-RELATED POLYMORPHISMS IN THALIDOMIDE SURVIVORS.


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It's estimated that until the early 60s, about 10.000 babies were born with limb reduction defects and severe congenital abnormalities due to the Thalidomide use by pregnant women. Thalidomide was synthesized in 1954 in West Germany, it was removed from the market in 1962, and come back to treat a leprosy complication and later other conditions. Due to its identification as an immunomodulator and its antiangiogenic properties, it has been used in the treatment of conditions such as erythema nodosum leprosum and Multiple Myeloma. Despite the established knowledge of its therapeutic properties, teratogenic molecular mechanisms of Thalidomide remain not fully understood. The objective of the study is to evaluate the role of polymorphisms in NOS2, PTGS2 and VEGFA genes in humans with Thalidomide Embryopathy (TE) and compare with a control group without congenital abnormalities. Saliva samples were collected from 38 Brazilian people with TE and compared with 168 samples from controls matched by age and place of birth. The NOS2 SNPs rs2779249 and rs2297518; PTGS2 SNPs rs689465, rs689466 and rs20417; VEGFA SNPs rs699947, rs1570360, rs2010963 and rs3025039 were genotyped by PCR real-time or Sanger sequencing. The microsatellite (CCTTT)n NOS2 was assessed by fragment analysis. All polymorphisms were in Hardy-Weinberg's equilibrium. No statistically significant difference between the allele and genotype frequencies in both groups was identified. There was no statistical difference comparing the haplotype frequencies of all genes evaluated in both groups. A full understanding of the molecular mechanisms of TE, remains a challenge. It's known that the genetically susceptibility contributes to teratogenesis and must be more explored in future studies with other genes and polymorphisms. An understanding of the molecular targets of Thalidomide can, not only increase knowledge about the angiogenesis pathway and teratogenesis mechanisms, but also contribute to research a safer and non-teratogenic drug.

Key Words: Thalidomide – Polymorphisms - Angiogenesis
Acknowledgements: CNPq/INAGEMP, CAPES