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Cystic fibrosis transmembrane conductance regulator gene amplifiers in children and adolescents with different Cystic Fibrosis genotypes: the next generation gene therapy

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Abstract

Cystic fibrosis (CF) is an inherited autosomal recessive disorder caused by genetic mutations in CFTR protein. The FDA approved various CF gene modulators, the most recent was the next- generation gene therapy in 2019. This paper aimed at the efficacy of the first triple gene therapy in children and adolescents suffering from cystic fibrosis. A systematic review and metanalysis was conducted following PRISMA guidelines through PubMed/Medline, Clinical trials.gov, Google Scholar, Scopus, Embase, and Europe PMC using the keywords: "Ivacaftor," "Elexacaftor," "Tezacaftor," VX_661", VX_770", "VX_445", "cystic fibrosis" and "gene therapy." A total of ten randomized clinical trials were included for analysis. Significant absolute change was demonstrated from baseline through 4 weeks favors toward the triple CF gene potentiators in predictive FEV1 [MD=11.80,95%CI=8.47_15.12, p value=<0.00001]; as well as CF_QR score [MD=16.90,95%CI=12.73_21.06, p value=<0.00001] , and BMI kg/m² change [MD=1.04,95%CI=0.84_1.24, p value=<0.00001]. On the same hand, non-significant change was noticed for chloride ion channels activity in treatment group when compared to placebo or VX_770/VX_661 [MD= -12.57,95%CI=-94.46_69.32, p value=0.76]. For Ivacaftor therapy,only a significant reduction in sweat chloride test value toward the treatment group was observed by Ramsey et al., Davies et al., and Moss et al. through 24 weeks [MD=-35.89,95%CI=-59.31_-12.47, p value=0.003]. Tez/Iva group showed no difference between treatment and placebo in term of p FEV1 [MD=1.72,95%CI=-0.95_4.39, p value=0.21]; sweat chloride test [MD=-4.33,95%CI=- 10.43_1.78, p value=0.16]; respiratory domain score [MD=1.82,95%CI=0.92_4.56, p value=0.19]; and a non-notifiable BMI change from baseline [MD=0.03,95%CI=-0.09_0.14, p value=0.66]. In children aged ≥ 6 y old and adolescents with F508del_CFTR mutation, Elexacaftor–Tezacaftor–Ivacaftor tend to be more effective than first-generation therapy, which showed promising results by improving the lung function, body weight, and respiratory-related quality of life.

Biography

Alla Hamdan has done MBBS from Omdurman Islamic university, Sudan. She is a Registrar of pediatrics at Sudan medical specialization board (S.M.S.B). She is also a Research collaborator at Larkin community hospital division of clinical and transitional research, south Miami, Florida, USA