CORRELATION BETWEEN CALCIUM SENSING RECEPTOR WITH CALCIUM HOMEOSTASIS IN MAJOR β-THALASSEMAIA PATIENTS

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ABSTRACT: The extracellular calcium ion (Ca\(^{2+}\))-sensing receptor (CaSR) enables key tissues that maintain Ca\(^{2+}\) homeostasis to sense changes in the Ca\(^{2+}\) concentration. These tissues respond to changes in Ca\(^{2+}\) with functional alterations that will help restore Ca\(^{2+}\) to normal. This study was conducted to evaluate the calcium sensing receptor as predictive Biomarkers for detection the bone turnover in major β-thalassemia patients. (95) sample individuals were collected, (65) of them were β-thalassemia patients (31 males and 34 female), which attended to thalassemia center at Azadi Teaching Hospital in Kirkuk city and the remaining (30) individuals (15 males and 15 female) were apparently healthy subjects with age ranged from (18-45) years. Total individuals had hormonal assay calcium sensing receptor (CaSR) and biochemical assay (calcium, ionized calcium, corrected calcium and Albumin ). CaSR levels increased with no significant difference (P>0.05) but Calcium, corrected calcium, ionized Calcium and Albumin levels decreased with no significant difference (P>0.05) in β-thalassemia patients when compared with control group. It was concluded that bone health compromised in major β-thalassemia and bone related hormones and biochemical abnormalities, these results due to iron over load or due to nutrition deficiency.

Key words: β-thalassemia, calcium sensing receptor, calcium, corrected calcium and ionized calcium.


INTRODUCTION

Thalassemia is categorized by abnormal production or reduction in rate of formation of normal alpha (α) globin or beta (β) globin subunits of hemoglobin (Hb) A. Hemoglobin A comprises of two alpha and two beta globin subunits (α2; β2). Genes responsible for making β globin are positioned on chromosome 11, while α globin genes are found on chromosome 16 (Adly et al., 2015). Hemoglobin is protein that is present in red blood cells (RBCs), which is accountable for carry the oxygen from alveolus to tissues. There are three types of hemoglobin that are present in preprints normal adult such as HbA, HbA2 and HbF that consist of α2; β2, α2; δ2 and α2; γ2 (Thein, 2018). Thalassemia is categorized as β, α, δγ, δβ as well as γδβ, depending upon which globin chain is affected. While, α and β thalassemia are two major categories of thalassemia and occurrence depends upon two genes for β globin and four genes for alpha thalassemia. It is produced by more than numerous hundred modifications in the consistent DNA segment. The unpaired globin chains are not stable. They precipitous in cells, which lead to immature destruction of precursors of RBCs and shortening of life-span of mature RBCs in blood. Hemoglobin breaks down in iron and heme that catalyze chemical reactions and produce the reactive oxygen species (ROS), which cause the impairment of hepatocytes as well as functions of islets of Langerhans (Stauder et al., 2018).

The intracellular signaling by CaSR is expected to occur in different stages. The first stage after receptor activation is the coupling of CaSR to Gi/o and Gq/11 families of heterotrimeric G proteins that consequently activate signaling pathways. The phospholipases are also activated, which in turn activate inositol triphosphate (IP3) and diacylglycerol (DAG) pathways. Gi/o along and adenylate cyclase (AC) inhibits cyclic adenosine monophosphate (cAMP) production. The inositol phosphate pathway oversees the control of the intracellular calcium levels, especially in the endoplasmic reticulum (ER). The second stage is when the activated
reabsorption; each response helps promote normalization of Ca^{2+} levels. Further work is needed to determine whether the CaSR regulates other parameters of renal function (e.g., 1, 25-dihydroxyvitamin D 3 synthesis, intestinal absorption of mineral ions, and/or bone turnover) (Wongdee et al., 2019).

In this study, calcium, corrected calcium and ionized calcium were decreased in β-thalassemia patients and there was no significant differences (p > 0.05), when compared with control group. There were positive correlation between CaSR and calcium, corrected calcium and ionized calcium in β-thalassemia patients.

These result was agree with Waheeb et al. (2019), Thiagarajani et al. (2019), Majumder and Basu (2020), Sfh et al. (2019), Tangngam et al. (2018), El-Sayed et al. (2015).

The imbalanced bone remodeling process, hypocalcemia possibly due to a decrease in calcium absorption has been reported in thalassemic patients. The alterations of the intestinal calcium-transport mechanisms in thalassemia direct evidence of thalassemia-induced changes in calcium transporters and/or the related proteins involved in intestinal calcium absorption calcium-binding proteins, which take part in the cytoplasmic calcium translocation, also play an important role in intestinal calcium transport. In addition to decrease in the intestinal expression of calbindin-D9k in thalassemia, there was early life iron deficiency anemia that induced a decrease in calcium-binding protein in hippocampus (Waheeb et al. (2019). Eventhough the decreased in iron deficiency anemia came from a different organ system, it suggested a possibility of anemia-induced downregulation of calcium-binding protein expression in thalassemia. Taken together, the reduced levels of calcium transporters and related proteins could account for the impaired intestinal calcium transport as can be seen in thalassemic patients. Thalassemia-induced calcitropic endocrinopathies (Thiagarajani et al., 2019).

**CONCLUSION**

High calcium sensing receptor levels may serve as a marker of increased osteocyte activity in β-thalassemia patients. Increase levels of calcium sensing receptor in β-thalassemia patients rather than control. Decrease levels of calcium, corrected calcium and ionized calcium, in β-thalassemia patients rather than control.

**REFERENCES**


