RESEARCH
www.commprac.com
ISSN 1462 2815

SICKLE CELL ANEMIA DISEASE TREATMENT ONGENETICS MOLECULAR LEVEL IN BASTER, CHHATTISGARH, A REVIEW

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DOI: 10.5281/zenodo.8385187

Abstract

SCA is a hereditary blood disorder considered by irregular haemoglobin causing in the production of sickle shaped red blood cell. Baster in Chhattisgarh a state in central Indian faces a significant problems of sickle cell anemia with a high prevalence among tribal population. This abstract highlight the genetic molecular level treatment methods in baster, Chhattisgarh to take SCA. The advent of molecular biology and genetic research has covered the way for innovatives therapeutics strategies for SCA. Which involve nucleotide substitution in beta globin gene. The genetics molecular level treatment is hematotropoietics stem cell transplantation also known as bone marrow transplantation in baster, Chhattisgarh. Effort are proceeding to expand the availability and accessibility of (HSCT) for a sickle cell anemia patients with an emphasis on increasing the number of suitable donor through awareness campaign. Conclusion genetics molecular level treatment approaches for a SCA in baster, Chhattisgarh are gaining momentum and hold great promises foe the management and potentials cure of this unbearable disease the addition of hematopoietics, stem cell transplantation gene therapy, along with continual research effort. Contributed for individual with SCA in baster, chhattisgarh and beyond.

Keyword: Haemoglobinopathies, β-thalassemia, hemoglobin, altering the Patient's Genetic constitution, Allogeneic Bone Marrow Transplantation, Gene editing, HemoglobinS Polymerization.

INTRODUCTION

A collection of heritable conditions of haemoglobin are nominated as Haemoglobinopathies. They affect4.5 of the world populace(Indian Pediatr 2000; 37391- 6). The frequency of β- thalassemia particularity and sickle cell in India differs among 3- 17 and 1- 44 singly for the reason that of blood association and estate and zone endogamy. Each time, 10,000 of children with β- thalassemia main born in India,[1]. Hereditary haemoglobin conditions are an significanteffect of disease and death. The restorative treatment like bone gist transplantation is precious and so prevention is the cost effective strategy, which includes population netting, heritable comforting and prenatal diagnosis.Sickle- cell anaemia(also known as sickle- cell

complaint or sickle- cell complaint) is a heritable blood complaint, wherever the RBC haveirregular haemoglobin(Hb S) called sickle haemoglobin cell[2]. As a result RBC which are generally discoid in shape, come sickle shaped when they are carries to low oxygen situations. Sickle cell illness(SCD) includes a group of conditions considered by the presence of the sickle haemoglobin(HbS). It's classified as SCA, haemoglobinopathy SC, sbeta thalassemia(HbS-beta) and other relatives of mutant hemoglobin with HbS. SCA complaint is the maximum mutual heredities complaint overal worldwide with varying clinical strictness and presumably severe complications.[2]the gestation in sickle cell anemia complaint is a veritably high threat. numerous reports have proved a largematernalrisk of disease and death and high perinatal adverse consequence.TheFemaleshave with SCD have an enlarged threat ofpre-eclampsia and motherly death, deliveries, preterm carriages, and small- for-gravid- age babies. The frequence of SCA is veritably mutual in the ethnical region of Centraland Southern corridor of India which contains ethnical in the countries of Madhya Pradesh,Gujarat, Maharashtra, Orissa, Tamil Nadu and Kerala, Chhattisgarh.[2,3]

Demographıcs of Dıstrıct Bastar

According to the 2011 tale baster quarter have a population of is equivalent to the nation of swazirland and US national of Hawaii. this give the data it a position of 348th in india (out of the aggregate of 640). the region has a people rate of 140 inhibitant per forecourt kilometer(360/ sqm). Baster have a coitus chance of 1024 womanish for every 1000 males, and the knowledge rate of baster is54.94. giving to tale of india 2001 introductory data of quarter baster, the total caste lineage population is 866,488 and 66to total population[4,5] Baster the land of line and natural coffer, is the largest ethenical quarter of the lately made india state-run of Chhattisgarh. About 70 of the wholepeople of baster quarter include of ethenical people living, which is26.76 of the total ethenical people of Chhattisgarh[5]. the major ethnical of the baste quarter are the halbaaAbhui, Maria,gond ,bhatra, dhruva. the gong of baster are one of the most notorious ethnical in india,[5,6] The tribial people of Baster quarter be deposited well-known for their single and characteristic racial art, music, and literature and heritage in all over the world. Each racial group in Baster have their own different traditional and loves their own single traditional living styles. Each lineage have a settled its own languages and differs from each other in their vesture, eating habits, customs, traditions and indeed worship different form of god and goddess[7,8]

Etiology and Pathophysiology of Sickle Cell Anemia Disease

The straight cause of SCA complaint is corpus- to- T change in the codon for amino acid location 6 in the β- haemoglobin genetic factor(HBB). Since of this alteration is a valine is filtrate changes the regular glutamic acid filtrate(glu6val) and HbS β- globin chains are replaced for normal HbA β- globin chains Studies of the haplotypes of the β- globin – suchlike gene cluster recommended that the HbS mutations had five isolated origins in tropical of Africa and, maybe, the Central East and India[9]. Sickle cell complaint is cause by an irregular HbS(α2β S 2) in which glutamic acid at site 6 of the β- globin chain of haemoglobin is different to valine. Goldstein etal.(1963) presented that this amino acid relief get up from a only base alteration(A> T) at codon 6(rs334).[10] These conduct spark a affected ofpro-inflammatory exertion situation off colorful pathology causes that also contain neutrophils platelets, neutrophils and vascular endothelium(Sunddetal., 2019). The common release of cell-free Hb from

haemolysis reduces , the significance of which is the compact the bioavailability of nitric oxide(NO), and vascular endothelial disfunction that causes the habitual organ damage in SCD case.[10] The sickle RBC do not just relate with the vascular endothelium but also it induce activation of neutrophiles, monocytes and platelets in sickle cell anemia cases. cases with SCD have over normal values of a monocytes, neutrophils and platelets which more growth through acute events(Villagraetal, 2007). Neutrophilia have been regularly linked with SCD carefulness(Ohene- Frempongetal, 1998; Milleretal, 2000); neutrophils play a essential part in vaso- occlusion through their relations with both RBCs and endothelium upregulating look of a cytoadhesion molecules similar as P- andE-selectins, current remedial targets[11,12]

Figure: 1

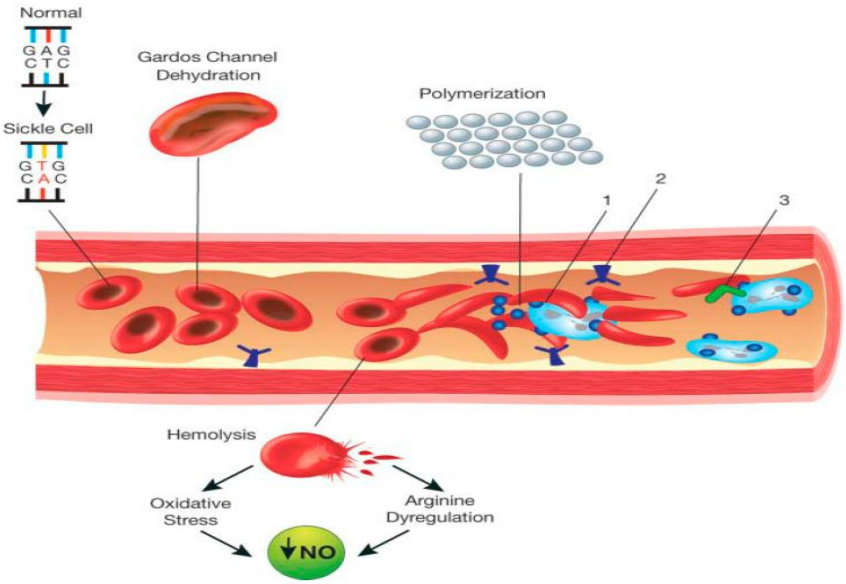
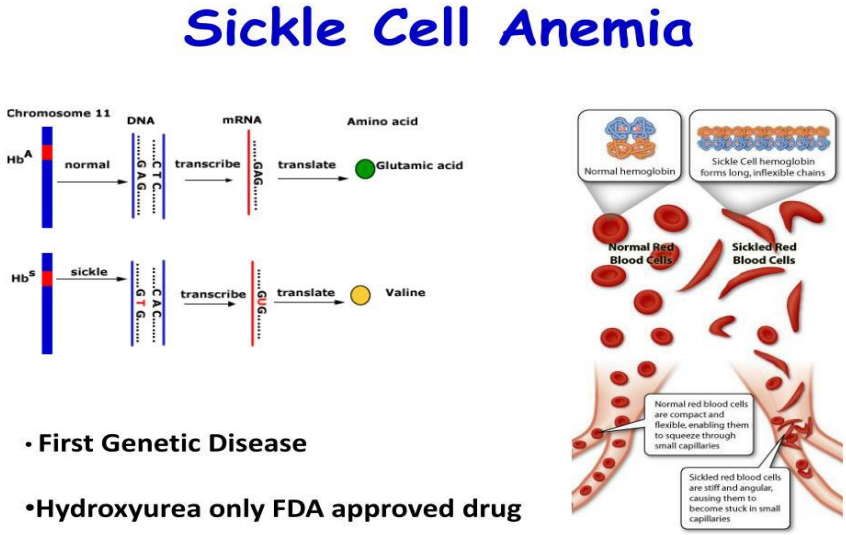
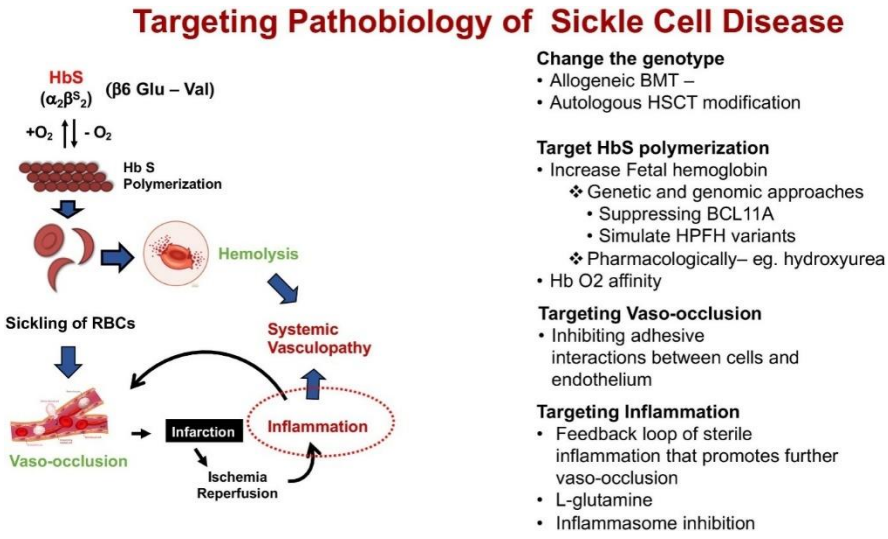


Figure: 2





Symptoms:

- WEAKNESS
- PALE SKIN
- COLD HAND AND FEET
- SWELLING AND PAIN
- DIZZINESS
- REDUCING IMMUNITY
- SHORTNESS OF BREATH
- AUNDICE

Medically Test For SCA:

1) BLOOD TEST
2) Hb ELECTROPHOROSIS TEST
3) HEMATOCRIT TEST
4) SERUM HEMOGLOBIN TEST

Governmentnhm Polıcy for Precuatıon and Control of SCD in Baster:

As of my knowledge cutoff in September 2021, the national health mission in india has been implementing various policie and programme to prevent and damage SCA. which is a genetics blood disorder prevelant in certain region of the country. however, its significant to note that police and programs may have been updated or changed since then, and its advisable to refer to the latest information from the NHM or the ministry of heathand family welfare for the most accurate and up to date details.

At the national level, the NHM has been working in collaboration with state government to address SCA through the following strategies.

Screening and diagnosis: NHM support thr screening of highrisk population, particularly in the region with a higher prevelance of SCA, this includes neonatalshowing programs and screening of pregnant women to identify carries and individuals pretentious by the disease.

Genetics counselling and education: the NHM promote genetics counselling sevices to provide information and support to individual and families at risk of sickl cell anemia. this help in raising awareness, understading the inheritance pattern, and making informed reproductive choice.

Health service and management: NHM support the provision of comprehensive healthcare service to individual affected by sickle cell anemia. Thisincludespecialized treatment centers, access to essential medicine, and regular follow up care

Capacity building l the NHM focuses on capacity building activities for health cere professional, including training programs, workshop, and conference, to enhance knowledge and skill in handling sickle cell anemia.

Awareness and advocacy: the NHM conduct awareness campaigns and advocacy activities to promotes undertaking of SCA reduced stigma. And encouraged early detection and treatment.

Its important to note that specific police and programs may vary from state-run to state in india, the implementation of health care service is primary the responsibility of individual state governments. [13,14]

Surveycaste Wıse Suspected Cases Identıfıcatıon

According to the medical report of maharani medical college ofjagdalpur, the totally sickle cell anemia patient.the highly percentage of SC population (31.85%) who were affected from sickle cell anemia.its observe that 29.82% of OBC population in the study was suspected and 27.82%in ST ,11.28 %IN GENERAL category were suffering from SCA. its clear that from the study that were there is marriage found in close relationship in were the genetic disorder aas like SCA is distributed in baster.

Table -1

CASTE	NUMBER	PERCENTAGE
SC	42	31,58
ST	37	27.82
OBC	15	11.28
GENERAL	133	100.00

Treatment On Genetıc Molecular Level

Altering the Patient's Genetic constitution

SCA is a genetics condition caused by a alteration in the haemoglobin genetic factor .resulting in the production of abnormal haemoglobin molecule .modifying the patients genotype to treat sickle cell anemia would involve correcting or altering the underlying genetics mutation responsible for the disease .there are several approaches being explored to modifying the patient genotype and potentially provide thetreatment for sickle cell anemia.some of these approaches include :gene therapy[15] :gene treatmentobjects to introduce a functional copy the hemoglobin gene into the patients cell to produce normal haemoglobin .this can be achieved by using viral vectors or other therapy system to insert the corrected gene into the patients bone marrow cell or stem cell . the modifying cell are the transplanted back into the patients potentially leading to the production off healthy red blood cell.CRISPR-Cas9:the gene editing techonolgy has shown promise in treating genetics disease .in the case of SCA CRISPR-Cas9 can be used to edit the mutated hemoglobin gene in the patients cell , correcting the genetics defect . this approach is the still under investigation,and clinical

trial are ongoing to asses its safety and effectiveness.fetal hemoglobin induction: another strategy involves increasing the making of fetal hemoglobin (HbF)in the patients with SCA ,fetal hemoglobin is a type of Hb that is normally produced during the fetal development and has a higher affinity foe oxygen ,thus the reducing the SCA red bloob cell.Research are exploring various metod to induce the making of fetal hemoglobin in adult patients . such a pharmaceutical agent or gene -based therapy. [16]

The Treatment Allogeneic Bone Marrow Transplantation:

Allogenic bone marrow transplant (BMT)also knowm as allogenic (HSCT),is a potential treatment option for the individual with SCA. BMT involves replacing the patients disease bone marrow,which produces abnormal red blood cell,with healthy bone marrow from a compatable donor.the procedure can potentially cure SCA by providing a new source of healthy bolood cell.

Here is an overview of the involved in allogenic bone marrow transplant for SCA

Doner selection: the first step is to identify a suitale bone marrow donor.ideally, the donor is a close genetic match,such as a sibling who share the same tissue type. however,if a sibling is not available or does not match,other potentially donor can be considered, including unrelated donor identified through national or international registries.

Conditioning regimin: before the bone marrow transplant.the receipient undergoes a conditionalaims to destroyed the recipient existing bone marrow cell and suppress the immune system to prevent refusal of the donor cell.[17]

The Autologous Haemopoietic Stem Cell Transplant Modification:

Autologous (HSCT) is a potentially option of SCA ,a genetics blood disorder characterised by the making of abnormal hemoglobin molecule . in the autologous a genetics (HSCT) , the potient s own stem cell are collected , process ,and the reintroduced into the patients body after undergoing intensive chemotherapy or radiation to destroyed the existing bone marrow .

Here is an overview of the autologous HSCT for SCA :

Stem cell collection: before the transplantation procedure, the patients own hematopoietics stem cell , which have to potentially to developed into deffernt type of blood cell) are composed from either the bone marrow or peripheral blood . peripheral blood group is the method as it is less invasive and simpler .

Stem cell transplantation : after the conditioning therapy . the collected stem cell are infused back into the patienta blood stream , similar to a blood transfusion . the stem cell transplantation then involved portable to the bone marrow and start producing healthy blood cells .[18]

Gene editing:

SCA is a genetics blood disorder characteried by abnormal ,the protein responsible foe carrying oxygen in RBC . gene editing technology , such as a crispr -cas9 have shown promises in potentially providing a cure for genetic disease like sickle cell anemia , while there has been progress in using gene editing to treat the condition , its important to note that as of my knowledge cutoff in September 2021 , gene editing therapy foe SCA were still in the experiment stage and not widely available .

The goal of gene editing for the SCA is to correct the genetic mutation responsible for the disease. The mutation affect the a specific gene called HBB. Which provide the instruction for the producing the beta -globin protein. in the sickle cell anemia this mutation cause the production of irregularHb molecule that results in the characteristics sickle cell anemia – shaped RBC and the associated health problem.[18]

With gene editing technique like crispr -cas9, scientist aim to the patients owm sten cell,

Which have the potentially to developed into the different type of blood cell. the idea Is to correct the HBB gene mutation in these stem cell so the produced normal, healthy hemoglobin.

In recent year, these have been some encouraging development in the of gene editing for the sickle cell anemia. in 2009, for example, researchers reported successful results from the clinical trial in which the used cripr-cas9 to edit the hbb gene in the stem cell of patients with the SCA disease. the edit stem cell were the transplanted back into the patients.[19]

Targeting the HemoglobinS Polymerization

SCA isageneticsdisorder characterised by the occurrence of the irregular hemoglobin fragment, which can cause the RBC to become sickle shaped and lead to several health complication. while there is no cure foe sickle cell anemia, there have been significant advancement in the treatment of the disease. one of the approaches to target hemoglobin polymerization, which is the key reasonin the pathogenesis of SCA , is complete the use of disease – modifying therpie , here the few treatment option that aim to addres hemoglobin polymerization **.**

Hydroxyurea: this medication have been widely used in the treatment of SCA. it works by increasing the production of fetalhemoglobin(HbF), which inhibit the polymerization of the sickle cell hemoglobin (Hbs). Hydroxyurea have been shown to reduced the frequency of pain full crises, severe chest syndrome, and the requirement for blood transfusion in some individuals.

l- glutamine: recently, l-glutamine oral powder has been approved for the treatment of SCA, it helps increase the availability of the antioxidant molecule glutahionine, which reduced oxidative stress and decrease the polymerization of HbS,CRISPR-Cas9 gene editing : this emerging technology offer the potentially to directly modifying the genetics sequence of a patients cell .including hematopoietic stem cell,

to correct the mutation causing SCA , early research has shown capable results in preclinical and early – stage clinical trials ,[20]

Targeting Vasocclusion

SCA is a genomic bold disorder characterised by abnormal, cresent – shaped red blood. one of the maximum significantcomplicationof sickle cell anemia disease is vaso – occlusive criss, which the occur when the sickle cell anemia shaped red blood vessel important to tissue injury and severe pain.

While there is no treatment for SCA – several treatment approaches aim to manage symptoms and complication, including targeting vaso – occlusion. here are some strategies that have been explored or are currently being investigated.

Pain management: pain during vaso -occlusion cries is a mark of SCA. pain relivers such as nonsteroidal anti-inflammatory drug (NSAIDS) and opioidal are normally used to achieve acute pain episodes.

Hydration : maintaining adequate hydration is crucial for patient role with SCA to prevent the dehydration that can exacerbate vaso -occlusion . drinking plenty of fluid and , in some case receiving intravenous fluid , help keep the blood flowing smoothly.

Blood transfusion: regular blood transfusion can help decrease the number of SCA in circulation and improve oxygen delivery to tissue . transfusion are typically used for severe complication or as a prevent measure in children with a high risk of stroke .

Hydroxyurea: hydroxyurea is a medication that arouse the creation of fetal hemoglobn, which inhibit the sickling of red blood cell . it have been exposed to decrease the incidence of vaso – occlusion crises and the need for blood transfusion in some patients.[21,22]

Targeting Inflammation: SCA is a genetics disorder characterised by the occurrence of the abnormal Hb in red blood cell, which leads to the cell taking on a sickle cell shaped. this abnormal shaped caused the RBC to become stiff and sticky, leading to bolokages in blood vessel and reduced oxygen delivery to tissue.[23]

While the primary cause of SCA is a genetics mutation, the disease can results in various complication, including chronic inflammation play to a important role in the pathophysiology of sickl cell anemia, contributing to the progress of vaso -occlusion cries, organ damage,and overall disease progression , therefore , targeting inflammation has become an significant therapeutics approach in managing sickl cell anemia ,anti-inflammatory medication [24]

CONCLUSION

In conclusion the treatment of sickle cell anemia on a molecular level holds great promise for addressing the underlying genetics cause of the disease by targeting the specific genetic mutation responsible for the production of abnormal hemoglobin researches have been able to develop innovative therapies that aim to correct or mitigate the effect of sickle cell anemia.

One of the most promising approaches is gene therapy, which involve introducing healthy copies of the affected gene into the patient s cell, this can be achieved through the use of viral or gene editing technologies such as CRISPR-Cas9. By correcting the genetic defect gene therapy offers the potential to produces functional healthy red blood cell, therapy allevatinig the symptoms of sickle cell anemia. Another avenue of research focuses on small molecule drugs aim to molecule drug that specifically target the mechanism underlying sickle cell disease. These drug aim to modulate the expression or function of gene involved in hemoglobin production, ultimately promoting the production of normal, no sickling red blood cell. Recent advancement in drug development have shown promising results with several candidate drug currently in clinical trials.

Further the advancement in our understanding of the molecule pathway involved in sickle cell anemia have passed the way for the development of novel therapeutics strategies targeting the process that lead to red blood cell sickling such the inflammation ,oxidation stress and adhesion ,can potentially reduce the severity of the disease and improve patient outcome.

In conclusion, the advancement in genetics and molecular research have opened up exciting possibilities for the treatment of sickle cell anemia .by targeting the underlying genetic mutation and molecular pathway involved in the disease research are working toward developing innovative therapies that have the potential to transformation the lives of individual living with SCA.

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