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Effect of hydroxyurea on quality of life with a moderating role of healthcare professionals' performance: A view from the beta-thalassemia patients.

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Abstract

Background: Transfusion-dependent (TDT) β –Thalassemia patients have lower HRQoL than healthy individuals. The impact of Hydroxyurea is always measured with the clinical investigations in terms of laboratory diagnosis. This study aimed to seek out the impact of the drug Hydroxyurea on improving physical health problems of Quality of Life (QoL) of β – Thalassemia patients with the moderating role of healthcare professionals.

Methodology: In this research, a deductive approach was adopted whereby hypotheses were originated first, followed by organizing a well-structured questionnaire as a tool for measuring the data. The nature of the research was explanatory and based on primary quantitative data. The data was collected from 290 patients visited in the outpatient and daycare departments of the National Institute of Blood Diseases and Bone Marrow Transplantation Hospital.

Results: This study revealed that the impact of Hydroxyurea therapy on improving the physical health problems of Beta Thalassemia is not evident as per the analysis (r=0.079; p=0.178). Similarly, a weak positive non-significant correlation exists between Hydroxyurea therapy and the performance of healthcare professionals in the hospital (r=0.016; p=0.782). Moreover, no significant improvement was observed in physical health problems and health domain of QoL of BT patients by moderating the role of healthcare professional performance (p=0.4471 and 0.4102, respectively).

Conclusion: It is concluded that moderating the role of healthcare professionals' performance does not improve the impact of Hydroxyurea on physical health problems and domains of QoL of β – Thalassemia patients.

Keywords

Quality of Life, Physical Health, Beta-Thalassemia, Hydroxyurea, Healthcare Professional Performance.

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Introduction

Thalassemia is a genetic disorder of hemoglobin (Hb) synthesis[1]. Its diagnosis is hypochromic microcytic anemia, either due to reduction or absence in the synthesis of the globin chain in hemoglobin, characterized as alpha or beta Thalassemia[2]. According to the WHO report 150, 000, 00 individuals around the globe are identified with carrier traits of this genetic disorder[3]. The complexity of its physical composition is caused by the imbalance ratio of β-globin, classified into blood transfusion-dependent (TDT) and non – transfusion-dependent (NTDT) BT patients. Modern treatment approaches are considered for TDT patients for monthly transfusions to maintain hemoglobin (Hb) levels ranging between 9-10 g/dL. The lifelong transfusion has caused an accumulation of iron, resulting in iron overload, which leads to organ damage. NTDT patients must maintain Hb level to 7 g/dL. In the liver, due to chronic anemia, they also develop iron[4]. The inherited trait may be Homozygous, resulting in β-Thalassemia major, while heterozygous results in β-Thalassemia trait[5].

BT in Pakistan is diagnosed in every community regardless of ethnicity they have. The carrier rate is approximately 5-8%. Annually 5000-6000 births with this autosomal disorder, and registered cases are approximately 100,000. The probability of birth of a child with β- Thalassemia major is 25%, carrier trait 50%, and normal 25% at every pregnancy when two carrier traits or thalassemia minor individuals tie a wedding knot[6]. BTM patients presented with common symptoms of progressive pallor and failure to thrive and need regular blood transfusions for their survival, splenomegaly (abdominal enlargement), growth retardation, and delayed puberty[7]. In 2017, evaluation surveys calculated births with serious hemoglobin disorders as approximately 300,000-400,000 annually with 23,000 cases of BTM. An economic burden of 90% of the population is towards low- or middle-income developing countries[8].

The conventional treatment approach of BTM has regular transfusion therapy, which causes complications associated with iron overload, endocrinological and cardiological issues, organ damage like liver fibrosis, and cirrhosis[9]. The current approaches not only for the management of BT but also work on the improvement of Health-related Quality of Life (HRQoL) of patients with regular transfusions, iron – chelation, allogeneic hematopoietic stem cell transplantation (AHSCT) are lifelong conventional therapies which increase the economic burden to the families of Thalassemic patients. Fetal Hb augmenting agents Hydroxyurea (HU) used in-vitro and in vivo increases fetal hemoglobin to fulfill the decreased level of adult hemoglobin. The success rate of HU has upsurged in past years, and responders showed transfusion independence to improve the life expectancy of patients[6].

The concept of QoL has significantly regulated health care delivery for Thalassemic patients. Traditionally it was assumed that physicians only deliver quality treatment by using safe and effective therapies to manage the disease complications. Today, we focus on improving QoL with managing other complications of the diseases[10]. The factors affecting the QoL are physical health, psychological, social- functioning, and school- functioning of Thalassemic patients. Assists healthcare practitioners in developing awareness programs and counseling sessions to improve QoL in TDT patients[11]. In BT, patients' physical health and growth-related issues are necessary to deal with as it enhances their way of living and the meaning of health. Physical growth in Thalassemic children results in growth retardation compared to healthy individuals; these patients fail to achieve normal height in their adolescence. In early childhood, growth retardation is a complication that varies in Thalassemic children with age, nutritional deficiencies, chronic hypoxia, and iron toxicity. It is estimated that stunt growth in children is observed globally in 25-66%, while nationally, 20-57%. In the later stage, these factors affect the bone mineralization has compromised the physical growth in Thalassemic individuals[12].
Now in studies, disease-specific tools can be used to be more precise about collecting the disease-specific questions that have been asked to

authenticate the analysis. Transfusion-dependent QoL questionnaire (TranQoL) was developed to exactly determine QoL in TDT patients[13]. This research highlights the impact of HU on the physical health domain of QoL, patient satisfaction with the use of medication, and the role of healthcare professionals in bridging the gap between the right use of medicine and the management of Thalassemia disease. It also focuses on the performance of healthcare professionals that acts as a moderator in creating an impact of Hydroxyurea on QoL of BTM patients, which should be the goal of healthcare professionals.

Methodology

For this study, primary data were collected using a quantitative research design and analyzed to evaluate the impact of Hydroxyurea (HU) on BT patients' physical health. The respondents for this investigation were recruited from TDT on Hydroxyurea therapy enrolled in the outpatient department (OPD) of NIBD & BMT hospital, Karachi. A deductive approach was adopted in this study. First, a theoretical prototype was developed, which further led to the formulation of a hypothesis along with a structured electronic and online questionnaire to collect data from the calculated sample size of targeted individuals.

Patients with β-Thalassemia were eligible for the homozygous and heterozygous β-Thalassemia trait. They had been on transfusion therapy using Hydroxyurea either in the category of Complete, Partial, and Non – Responder status of therapy. They were willing to participate in the study by signing an informed consent form in English /Urdu version under a designated clinical research associate's supervision. Patients unwillingness to participate or with other hemoglobinopathies, or patient undergoing transplant was excluded from the study.

WHO sample size calculator was used for the estimated number of true study representatives. Two hundred and ninety individuals from the Outpatient Department and Daycare departments of NIBD & BMT hospital participated in this study after completing an online questionnaire in English to evaluate the physical health domains of QoL of BT patients, Treatment Satisfaction of HU, and moderating role of healthcare professionals in improving the living standards of patients.

In this study, the QoL of BT patients was measured using the TranQoL questionnaire. The physical health domain comprises six questions[13]. The TSQM-09 – [Treatment Satisfaction Questionnaire for Medication] was used to measure and compare the impact of Hydroxyurea on a patient's life. The questionnaire comprises 06 questions that deal with the effectiveness, convenience, and global satisfaction of Hydroxyurea[14]. Healthcare professionals' performance was measured using Healthcare Satisfaction Generic Module-3.0, consisting of 24 questions that were used to evaluate six domains: Information, Inclusion of Family, Communication, Technical skills, Emotional Needs, and Overall satisfaction from the viewpoint of patients[15].

The questionnaire was administered over three months, and respondents duly signed the consent form. Out of 290 respondents, questionnaires were further subdivided according to their HU response into Complete Responder, Partial Responder, and Non–Responder before further analysis. The data were analyzed using SPSS version 23.0. The statistical analysis of the data includes descriptive analysis, reliability analysis, correlation, and Regression analysis, and moderation is done using Process Hayes model 3.5.2.

Results

Out of 290 respondents, 169(58.3%) were males, and 121(41.7%) were females. Of the respondents, 52.1% were studying, while 47.6% were not studying. After taking Hydroxyurea, responders were classified into three categories: complete responders (15.9%) who were independent of blood transfusion dependency; partial responders (27.6%) who were remained on transfusion but with increased interval, and non-responders (56.6%) who were remained on the same frequency of blood transfusion, after six months of treatment. In context with the transfusion status (84.1%) of

respondents still visit the hospital for blood transfusion, while (15.9%) had shifted to a stable transfusion – Free State.

The data was collected in the electronic and online questionnaire using the Likert scale, with 1-5 and 1-7. The constructs' reliability (internal consistency) was measured through Cronbach's alpha (α). Table 1 showed that all the variables had α greater than the recommended value of 0.50[16]. Hypothesis Testing compares an alternative hypothesis (Ha) with a null hypothesis (Ho). The rejection hypothesis is based on the p-value obtained through the coefficient test of regression analysis on SPSS version 23.0. The level of significance (α) is 0.05. When p – value > 0.05, we fail to reject the null hypothesis. Table 1 shows the correlation of the independent variable (hydroxyurea therapy) with the dependent variable physical health problems and the introduction of moderating variable healthcare professional performance. A weak positive relationship between Hydroxyurea and the physical health of BT patients has been seen, and a weak positive association exists between Hydroxyurea and the performance of healthcare professionals in the hospital.

Table 1: Correlation of healthcare professional's performance with hydroxyurea therapy and physical health problem.

Variables	r(p-value)	Alpha Value
Hydroxyurea Therapy	1	0.872
Physical Health problem	0.079(0.178)	0.895
Performance of Healthcare Professionals	0.016(0.782)	0.898

Table 2 predicts the improvement in physical health problems from Hydroxyurea therapy, and the p > 0.178 shows that Hydroxyurea therapy has insignificant impact on improving physical health problems of BT patients.

Table 2: Regression Analysis predicting the improvement in physical health problems from Hydroxyurea therapy.

Variable	Unstandardized Coefficients		Standardized Coefficients	p-value
	B	Std. Error	Beta	
Hydroxyurea Therapy	0.095	0.070	0.079	0.178

Dependent Variable: Physical Health problem

Table 3 showed the R and R2 value of model 1 by process procedure for SPSS Version 3.5.2 by Hayes. The R-value has shown the correlation and is 0.0961 indicating that the Hydroxyurea correlation with physical health problems of BT patients in addition to the performance of healthcare professionals. The R2 value indicates the total variation in the DV -physical health problems of BT patients with the interaction of the performance of healthcare professionals' is 0.92% is explained by the Hydroxyurea therapy. The impact of Hydroxyurea is not improving the physical health problems of BT patients in the presence of healthcare professionals' performance. The Model Table shows a p-value of 0.4102 that moderation does not have an impact on Hydroxyurea in improving the physical health domain of quality of life of BT patients.

Table 3: Moderation Analysis.

Model Summary							
Model	**R**	**R2**	**MSE**	**F**	**df1**	**df2**	**P**
1	0.0961	0.0092	2.7364	0.8892	3	286	0.4471
Model							
	Coeff	**SE**	**t**	**p-value**	**LLCI**	**ULCI**	

Hydroxyurea Therapy	0.1806	0.2933	0.6157	0.5386	-0.3967	0.758
HEPH	0.0742	0.0805	0.9225	0.357	-0.0842	0.2326
Interaction	-0.0097	0.0118	-0.8248	0.4102	-0.0329	0.0134

Coeff.-Coefficient, SE-Standard error, LLCI-Lower level confidence interval, ULCI-Upper-level confidence interval, HEPH-Hydroxyurea Effect on Physical Health

Discussion

As investigated after the detailed analysis of the results, there is no impact of Hydroxyurea on the physical health problems of the BT patients. The study reported that Transfusion dependent BT patients, especially children in the given study, have considerably poor physical QoL compared to different worldwide studies[13]. Previous studies have revealed that as children move towards adolescence, they have slow growth and hormonal balance. The TDT patients receiving monthly transfusions with supportive treatment with iron-chelating agents experience darkening of skin, growth retardation, and delayed or no onset of pubertal cycle[12]. Patients addressed that the disease therapy and its complications have affected their daily routine and sleeping patterns. Although Hydroxyurea has improved certain factors associated with the physical health of TDT patients still, it is debatable[17]. These complications hurt the physical and psychological health of Thalassemia children. They have low self-esteem, are emotionally stressed, and are conscious of their physical appearance[18]. Thalassemic children have more depressive symptoms and poor QoL than healthy children[19].

The analyzed data has revealed no evidence of the significant role of healthcare professionals' in moderating the impact of Hydroxyurea on the physical health domain of QoL. There is no association of performance of healthcare providers through counseling and awareness about the disease to play a pivotal role in improving QoL of BT patients[20]. The respondents religiously follow whatever healthcare providers prescribe them. The literature has revealed that Kaplan and Bush used HRQoL as the generic measurement of disease burden in terms of quality-adjusted life-years (QALYs)[21]. The traditional practices of healthcare physicians have improved in the last five years; apart from empirical treatment of BT patients, they work on increasing the life expectancy of these patients estimated by QALYs[22]. Hydroxyurea therapy still has no association with the moderating role of healthcare providers. The hospital tried to fill this gap with a panel discussion with an endocrinologist about the anthropometric measurement of TDT children after age 10 to minimize the complications associated with adolescence age. Growth–retardation is the first burden that changes the definition of health. It affects physical health and slowly and gradually damages the psychological and spiritual well-being of individuals[23].

Since limited time was one of the main constraints for the conduction of this study so (290 responses) were unable to follow for intervals to validate the impact of Hydroxyurea on the QoL of Beta Thalassemia patients. Secondly, the research was single-center, so the impact of Hydroxyurea on the QoL of Beta Thalassemia patients with moderating role of healthcare professionals' performance was analyzed in single-center, and it may have contrasted result when a study conducted in multicenter. Thirdly, it only evaluates the impact of Hydroxyurea on the QoL of Beta Thalassemia patients' results were more reliable when compared with other hemoglobinopathies. The current study is important in healthcare organizations, especially tertiary care hospitals. Healthcare professionals were recommended to make progress in the QALYs of Beta Thalassemia patients through awareness sessions, proper counseling, and teamwork with multidisciplinary professionals, which include hematologists, endocrinologists, gynecologists, psychologists, and other paramedical staff for improving determinants of QoL by effecting on their physical, psychological and social health increase their life expectancy and prepare them more inclined towards their well - being.

Conclusion

It has been concluded that the physical health problems in beta thalassemia patients after analysis are not dependent on Hydroxyurea therapy to have a better QoL. While with the introduction of healthcare professionals' performance as a moderator does not improve the link between Hydroxyurea and physical domain of QoL.

Conflicts of Interest

The authors have declared that no competing interests exist.

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