

Study of the Types of Refractive Disturbances Observed during Hyperglycemia in Humans

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Abstract

Introduction: Refractive disturbances have been observed during hyperglycemia. However, there remains controversy as to the types of disturbances that it induces. **Objective:** To determine the types of refractive disturbances observed during hyperglycemia in humans. **Population and Methods:** This was an observational and cross-sectional study with an analytical purpose conducted from July to November 2021. Emmetropia, hypermetropia, and myopia as well as blood glucose levels were compared between day 0 (D0) and day 30 (D30) after initiation of hypoglycemic therapy in 222 people (444 eyes) with recently discovered hyperglycemia (Chi-2; $p < 0.05$). **Results:** At D0, the mean of blood glucose was $18.1 \text{ mmol/L} \pm 8.2$ vs $6.9 \text{ mmol/L} \pm 3.0$ at D30 ($p = 0.001$). At day 0, 80% ($n = 355$) of eyes were hypermetropic compared to 73.9% ($n = 328$) at D30 ($p = 0.02$). At D0, 14.2% of eyes ($n = 63$) were myopic compared to 11.3% ($n = 50$) at D30 ($p = 0.02$). Refraction improved from 0.75 to 1.5D for 34.5% ($n = 18$) of hypermetropic eyes and 10.2% ($n = 2$) of myopic eyes. **Conclusion:** Our results show that hypermetropia is the most common ametropia during hyperglycemia. Moreover, these data suggest that the normalization of blood glucose improves refraction.

Keywords

Hyperglycemia, Hypermetropia, Myopia, Hypoglycemic, Treatment, Libreville

1. Introduction

Refraction is the set of deviations that a light ray undergoes during its passage

through the transparent environment of the eye before reaching the retina [1]. Refractive disorders or ametropia are frequent reasons for ophthalmological consultation [2]. During hyperglycemia, transient visual disturbances may occur, often caused by refractive changes [3] [4].

These changes have been described during acute hyperglycemia caused experimentally in humans but also during hyperglycemia in diabetic subjects [5]-[14]. However, the mechanisms explaining these refractive disorders remain to be demonstrated. Morphologically, some authors report changes in thickness, refractive index and radius of curvature at the corneal and crystalline levels [15] [16] [17] [18] [19]. Its changes could result from the elevation of glucose concentration in the aqueous humor described by Kastelan *et al.* It would result in an increase in the level of hydration of the lens and probably the cornea causing the visual decrease [20].

However, other disturbances such as accommodative disorders are described [9].

Furthermore, there is controversy about the type of refractive disturbance that hyperglycemia induces, but also about the evolution of it after improvement of glycemia. Some authors agree that it causes myopia, while others think that it is rather responsible for hyperopia [21] [22] [23]. We believe that hyperglycemia induces hypermetropia. We also think that the evolution after improvement of glycemia would be done either by maintaining this initial hypermetropia with however a change in dioptric power, or towards myopia or emmetropia.

This work aimed to verify this hypothesis by determining the type of ametropia observed during a recently discovered hyperglycemia.

2. Population and Methods

2.1. Population

This was an observational, cross-sectional and descriptive study with an analytical aim, during the period from June to November 2021. The recruitment of the population was done in the endocrinology department of the University Hospital of Libreville (CHUL). The target population consisted of subjects with recently discovered hyperglycemia. This work was carried out according to the recommendations of the Helsinki Declaration of Ethics on the use of living beings [24]. Indeed, informed consent and assent for minors were obtained from the participants. Likewise, the authorizations of the Medical Director of the University Hospital of Libreville and the head of the endocrinology department had been obtained. Furthermore, all subjects of the study were guaranteed respect for the confidentiality of the data collected during the study.

2.2. Inclusion Criteria

Any person consenting to participate in the study, aged 15 years old and over and presenting with hyperglycemia discovered at the time of the study, was included.

2.3. Non-Inclusion and Exclusion Criteria

It was not included, known diabetic people, as well as those with eye pathologies resounding on refraction. In addition, patients with cylindrical ametropia and strong hyperopia and myopia, *i.e.* greater than 6 diopters, had not been selected.

It was removed from the study, subjects who have not benefited from glycem-ic control and refractometry at day 30, but also those who voluntarily stopped their hypoglycemic treatment during the investigation period.

3. Methods

3.1. Population Recruitment Method

The recruitment of participants was voluntary and consecutive in the endocri-nology department of the CHUL. The study population is composed of people coming to consult in the endocrinology department for suspected hyperglyce-mia.

After confirmation of the state of hyperglycemia (venous blood glucose assay by Humalyzer Primus™, Human®; urine strip by Multitix™, Siemens®), subjects presenting the selection criteria were referred to an ophthalmologist. He carried out an ophthalmological examination using a biomicroscope (Haag Streit®). This examination consisted of examining the anterior and posterior segments of the eye after pupillary dilation. In practice, its purpose was to determine the ex-istence of eye lesions having an impact on refraction. As a result, at the end of this ophthalmological evaluation, people who had not been included in the study and who had ocular pathologies were offered treatment in an ophthalmology department.

Conversely, those with a state of hyperglycemia but having no abnormality on the ophthalmological examination were taken care of by an endocrinologist. Thus, during the study period, 312 people with recent hyperglycemia and pre-senting the eligibility criteria had been selected. At the end of the investigation, the population definitively selected was 222 participants (444 eyes) (Figure 1).

3.2. Refraction Measurement Method

So as to determine the types of refractive disturbances, an ophthalmologist per-formed a subjective refraction using an automatic refractometer (GILRAS GRK-7000®) in all participants. Five successive measurements were taken automati-cally on each eye and their mean was the retained value [3].

3.3. Method for Determining the State of Hyperglycemia

So as to confirm the state of hyperglycemia, all participants with the eligibility criteria received a clinical examination by the endocrinologist. During this eval-uation, peripheral venous blood samples were taken in a consultation room al-located for this purpose.

Thus, for each participant, five milliliters of venous blood were collected in a fluoride tube and then sent to the analysis laboratory (Biochemistry laboratory

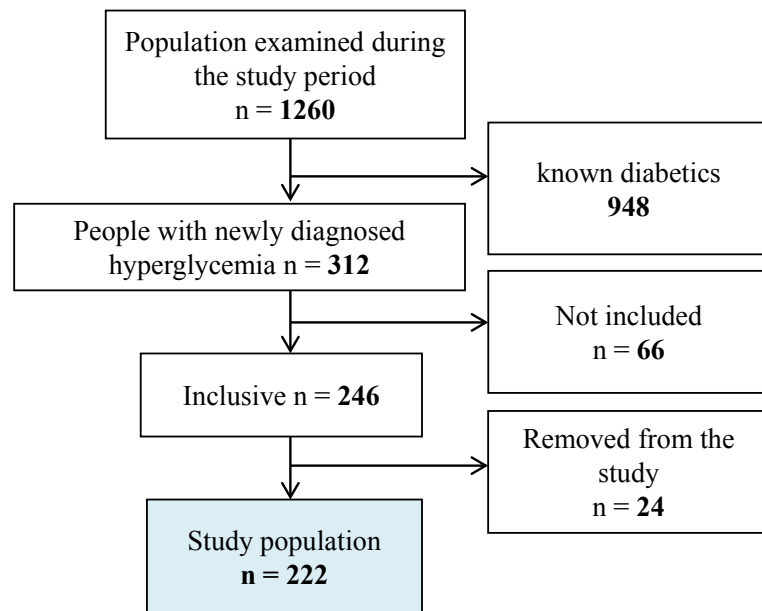


Figure 1. Flowchart describing the selection of the study population.

of the FMSS). Plasma glucose assay was performed by spectrophotometry (Humalyzer Primus™, Human®, Germany). The procedure performed was that described in the protocol proposed by the manufacturer (Biolab®, BioSystems™). Fasting blood glucose above 7.00 mmol/L is defined as hyperglycemia [25].

3.4. Hypoglycemic Treatment

As soon as the participant was included, a therapeutic protocol for hypoglycemic purposes was systematically proposed. The prescription of the latter was left to the responsibility of the endocrinologist. The therapeutics used were hygienic-dietary measures and oral antidiabetics.

Patients were considered observant when the number of tablets missing from the medicine box corresponded to the dosage prescribed for a period of 30 days.

3.5. Control of Blood Glucose and Refractometry at Day 30

The measurements of refraction, as well as blood glucose were carried out under the same conditions, 30 days (D30) after the start of hypoglycemic treatment.

Conversely, ocular morphological examination was carried out only on day 0 (D0) to look for the ophthalmological criteria of non-inclusion in the study.

3.6. Definition of Variables

Refraction expressed in dioptic power was our dependent variable and divided into three categories: a zero dioptic power (0) reflecting emmetropy, a negative dioptic power (–) and positive (+) reflecting myopia and hypermetropia respectively.

The change in refraction was calculated in absolute value according to the following formula: Δ refraction = Refraction D30 – Refraction D0. Fasting blood

glucose above 7.00 mmol/l defined hyperglycemia [25]. The blood glucose level (mmol/l) was expressed as a mean and its variation between D0 and D30 calculated according to the following formula: Δ blood glucose = glycemia D30 – blood glucose D0.

3.7. Statistical Analyses

The data was collected on a standardized card and then entered on an Excel table from Microsoft Office[®]. Refractive and blood glucose values were expressed as mean and standard deviation. The statistical analysis was done using state software 12.0, College station, Texas 77845 USA[®]. The chi-2 test was used for the comparison of means. The difference was statistically significant when the p was less than 0.05 ($p < 0.05$).

4. Results

4.1. Socio-Demographic Characteristics of the Population

The mean age of the study population was 45.1 ± 13.3 years. Males accounted for 49.5% ($n = 110/222$) of the population, a male/female ratio of 1.

4.2. Comparison of Mean Glycemia Values between D0 and D30

Mean of glycemia was $18.1 (\pm 8.2)$ mmol/l in the study population at day 0 compared to $6.9 (\pm 3.0)$ mmol/l at day 30 after the start of hypoglycemic therapy ($p = 0.001$).

4.3. Comparison of Refractive Types between D0 and D30

Table 1 summarizes the types of refraction measured at day 0 and day 30.

At day 0, 80% ($n = 355$) of eyes were hypermetropic compared to 73.9% ($n = 328$) at day 30. At day 0, 14.2% of eyes ($n = 63$) were myopic compared to 11.3% ($n = 50$) at day 30 ($p = 0.02$).

4.4. Refractive Changes between D0 and D30

Table 2 summarizes the refractive changes between D0 and D30. At day 0, 80% ($n = 355$) of eyes were hypermetropic, of which 65.1% ($n = 289$) remained hypermetropic, 4.1% ($n = 18$) became myopic and 10.8% ($n = 16$) emmetropic 30 days after initiation of hypoglycemic treatment. At day 0, 14.2% ($n = 63$) of eyes were myopic, among them, 4.3% ($n = 19$) had remained myopic and 5.9% ($n = 26$) had become hypermetropia.

At the time of diabetes diagnosis, 14.2% ($n=63$) of eyes were nearsighted. After initiation of antidiabetic therapy, 4.3% ($n = 19$) remained nearsighted, 5.9% ($n = 26$) became farsighted and 4.1% ($n = 18$) emmetropic.

4.5. Dioptric Power Change of Hypermetropic Eyes between D0 and D30

For eyes that were hypermetropic at day 0 and remained so at day 30, refraction

Table 1. Types of refractive disturbances between day 0 and day 30.

Type of ametropia	D0	D30	p
Emmetropia	26 (5.9)	66 (14.9)	
Hypermetropia	355 (80.0)	328 (73.9)	0.020
Myopia	63 (14.2)	50 (11.3)	
Total	444 (100.0)	444 (100.0)	

Table 2. Changes in type of refractive disturbances between D0 and D30 after hypoglycemic treatment.

Refraction	D30				
	Emmetropia	Hypermetropia	Myopia	Total	
	n (%)	n (%)	n (%)	n (%)	
D0	Emmetropia	0 (0.0)	13 (2.9)	13 (2.9)	26 (5.9)
	Hypermetropia	48 (10.8)	289 (65.1)	18 (4.1)	355 (80.0)
	Myopia	18 (4.1)	26 (5.9)	19 (4.3)	63 (14.2)
	Total	66 (14.9)	328 (73.9)	50 (11.3)	444 (100.0)

improved by less than 0.75D for 63.8% of them and by 0.75 to 1.5D for 34.5% (n = 18) (Table 3).

4.6. Dioptric Power Change of Myopic Eyes between D0 and D30

For eyes that were myopic at day 0 and remained so at day 30, refraction had improved by less than 0.75D for 89.5% of this population and by 0.75 to 1.5D for 10.5% of them. No nearsighted eye had degraded its refraction (Table 4).

5. Discussion

5.1. Hypermetropia

Hyperopia is the most common ametropia during glycemic disturbances in our study. This result confirms our hypothesis and corroborates the results of previous studies [5] [6] [7] [8]. Indeed, Shristi *et al.* had studied refractive disturbances in 170 (340 eyes) diabetic patients.

For this, subjective and then objective refraction had been evaluated. More than half of the population had been identified with predominantly hypermetropic refractive disorders [5]. In the same sense, Rakesh *et al.* had studied refractive disorders during induced hyperglycemia on 26 non-diabetic and emmetropic subjects (52 eyes) [6]. The purpose of this study was not only to look for a relationship between ocular refraction and blood glucose but also to assess the time to return to initial refraction. It was found that more than half of the participants had hyperopia after glucose administration. This hypermetropia was transient with improvement 30 days after the start of antidiabetic treatment [6].

Song *et al.* had studied the prevalence of refractive disturbances in previously

Table 3. Changes in dioptric power of hypermetropic eyes between D0 and D30.

Dioptric power	Improvement		Degradation	
	n	%	n	%
<0.75	146	63.8	32	53.3
0.75 - 1.5	79	34.5	18	30.0
>1.5	4	1.7	10	16.7
Total	229	100.0	60	100.0

Table 4. Change in dioptric power of myopic eyes between D0 and D30.

Dioptric power	n	%
<0.75	17	89.5
0.75 - 1.5	2	10.5
Total	19	100.0

diagnosed type 2 diabetic subjects. Subjective refraction was measured using an automatic refractometer. At the end of their study, a high prevalence of hypermetropia subjects had been identified [7]. This evolution towards hypermetropia would have a pathophysiological explanation. Indeed, Charman *et al.* had demonstrated that there are two refractive indices at the level of the lens, in particular central and surface. For them, hypermetropia changes would be the most likely to be observed during hyperglycemia due to the decrease in the central crystalline index. Such a process would be initiated by changes in osmotic pressure induced by the increase in glucose in the aqueous humor [8].

5.2. Myopia

It was also found in the present study some cases of refractive change in the direction of myopia. Indeed, some previous studies had corroborated this result [9] [10] [11]. Abokyi *et al.* had studied the impact of hyperglycemia on ocular refraction in type 1 diabetic subjects. These subjects were evaluated before insulin therapy and then three months after. They had found a refractive change in the direction of myopia and a tendency to emmetropization after insulin therapy [9]. So to as, Mwale *et al.* studied refractive errors in 96 balanced and unbalanced type 2 diabetic subjects and then sought to establish the relationship between initial refractive status and blood glucose. At the end of their study, they had found that unbalanced diabetic subjects had nearsighted refractive changes unlike balanced diabetic subjects who were emmetropic [10].

In the same sense, Furushima *et al.* had studied refractive changes after induction of hyperglycemia in subjects free of diabetes and ametropia. They had measured ocular refraction in these subjects before glucose ingestion and three days after. It emerged from this study, a predominance of myopic subjects three days after ingestion of glucose [11].

On the pathophysiological level, Umezurike *et al.* and kastelan *et al.* had car-

ried out studies to understand the involvement of hyperglycemia observed during diabetes on ocular refraction [12] [20]. According to them, this hyperglycemia would result in excessive absorption of glucose in the lens and would causally cause the formation of covalent bonds. The sorbitol pathway would thus be activated with intracellular accumulation of it, fluid influx into the aqueous humor and then lenticular swelling. This would cause an increase in crystalline curvature inducing index myopia, while normalization of blood sugar would lead to index hypermetropia. However, this myopia induced by this sudden fluctuation in the refractive power of the lens would be reversed shortly after prolonged treatment and glycemic control. This allowed them to conclude that the refractive defects induced by hyperglycemia were transient [12] [20].

5.3. Emmetropia

In the present study, the proportion of myopia and hypermetropia subjects at the time of discovery of diabetes decreases after initiation of treatment in favor of emmetropia. In the literature, some authors had found results along the same lines, including Ragni *et al.* who had studied the prevalence of refractive disturbances in a population of 437 unbalanced type 2 diabetic subjects. At the end of the study, a high prevalence of emmetropic subjects had been found, compared to those with hyperopia and myopia [23]. The fact that some patients are emmetropic at the time of diagnosis of diabetes and subsequently tend towards hypermetropia or myopia 30 days after initiation of antidiabetic treatment could inform us about the initial refraction of these subjects. The change in refraction in this sense reflects the fact that these patients are initially ametropic.

6. Limitations of the Study

There is controversy about the type of refractive disturbances that hyperglycemia induces, but also about the evolution of it after improvement in blood glucose level. In this work, our research hypothesis was that hyperglycemia induces hypermetropia and that the evolution of this after improvement of glycemia would be done either by maintaining this initial hyperopia with however a change in dioptric power, or towards myopia or emmetropia. This work aimed to verify this hypothesis by determining the type of ametropia observed during a recently discovered hyperglycemia. To confirm this hypothesis, we measured refraction and blood glucose at the time of diagnosis of hyperglycemia and then compared these parameters 30 days after initiation of hypoglycemic therapy.

In total, the analysis involved 222 people (444 eyes) with recently discovered hyperglycemia. This study had some limitations because of its monocentric character and the relatively short follow-up interval that did not allow to assess refraction after glycemic disturbances.

Our results show that hypermetropia is the most common ametropia during hyperglycemia. In addition, they suggest that the normalization of glycemia improves refraction.

7. Conclusion

The purpose of this work was to determine the type of ametropia observed during a recently discovered hyperglycemia in humans. From this study, it emerges that hypermetropia is the most common ametropia during hyperglycemia. Moreover, these data suggest that the normalization of blood glucose improves refraction. However, it would be appropriate to deepen this study by evaluating the refraction after equilibrium of glycated hemoglobin which is the reflection of glycemic balance.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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