Article

Hypothetical Reason for the Restoration of HbA1c Level for Pre-Diabetic Patients through the Recovery of Arterial Blood Flow Access to Rhomboid Fossa

Alexandre A. Vetcher 1,2,*, Kirill V. Zhukov 1, Bagrat A. Gasparyan 1 and Alexander Y. Shishonin 1

1 Complementary and Integrative Health Clinic of Dr. Shishonin, 5 Yassogorskaya Str, 117588 Moscow, Russia
2 6 Miklukho-Maklaya St, Peoples’ Friendship University of Russia (RUDN), 117198 Moscow, Russia
* Correspondence: avetcher@gmail.com

Abstract: We demonstrate that the recovery of cervical vertebral arterial blood flow access to the rhomboid fossa causes the restoration of HbA1c level for the patients with pre-diabetic (pre-DM) condition. This observation is in good agreement with the consideration of the human body as a dissipative structure. Such consideration is the focus of the recently announced centralized aerobic-anaerobic energy balance compensation (CAAEBC) theory. According to the theory, observed connections between high blood pressure (HBP) and the lifted level of HbA1c can be hypothetically linked through the restrictions of blood flow access to rhomboid fossa, causing the delivery of incorrect information of blood oxygen availability. Below we provide detailed information of how in this case CAAEBC theory explains the very initiation of multiple chronic diseases, starting with type 2 Diabetes Mellitus (DM).

Keywords: HbA1c; arterial hypertension; osteochondrosis; rhomboid fossa

1. Introduction

From the beginning, observations of DM were connected to the higher level of glucose in urine. This observation was performed such a long time ago that we were unable to attribute the theory to a certain physician; however ancient Indian physicians named it madhumeha (Sanskrit (Ayurveda), ‘honey urine’) because it attracts ants [1]. The adjective Mellitus (Latin, ‘sweet like honey’) was introduced in 1798 by the British Surgeon-General, John Rollo, to separate this type of diabetes from other types of diabetes (insipidus). Since diabetes at this time was mostly associated with the sugar content in urine, it was considered that people without diabetes possessed tasteless urine. Dr. Rollo was the first to document the higher level of blood sugar (BGL) [1] for DM patients. Since then, BGL gradually became the main laboratory index for the diagnosis of DM [2]. However, for the diagnosis of DM, it is possible to use a stable compound of glucose with hemoglobin-glycated hemoglobin (also known as glycosylated hemoglobin, HbA1c, and hemoglobin A1c (A1C) [3]). HbA1c has been approved by WHO since 2006 [4]. According to the recommendations of the American Diabetes Association (ADA) in 2015, the HbA1c level ≥6.5% (48 mol/mol) was chosen as the diagnostic criterion for DM. In pre-DM, HbA1c corresponds to the interval 5.7–6.4% [5].

HbA1c is an indicator of the average blood glucose level over the last 3 months (corresponding to the lifetime of red blood cells), i.e., this indicator demonstrates trends and is not affected by the random factors (food, stress, physical activity, etc.) that can change significantly, e.g., fasting blood sugar level or even meal glycemic load. Figure 1 shows the schematic of HbA1c. The formation of glycated hemoglobin is a normal part of the physiologic function cycle. However, as the average plasma glucose increases, so does the amount of glycated hemoglobin in the plasma. HbA1c is an important indicator of glucose.
Long-term glycemic control means the ability to reflect the cumulative glycemic history of the preceding two to three months; in other words, it is an average glucose level. HbA1c not only provides a reliable measure of chronic hyperglycemia but also correlates well with the risk of long-term diabetes complications. In addition, HbA1c is the most abundant (>90%) glycated hemoglobin. HbA1c consists of two α- and two β-chains as non-glycated hemoglobin HbA0. HbA1c level is calculated according to Equation (1):

$$%HbA1c = \frac{HbA1c}{HbA1c + HbA0} \times 100\%$$

Figure 1. The schematical representation of HbA1c. Glucose residues (G) are attached to N-terminal Val of β-chains. In HbA1c, α-chains are non-glycated.

It is of great interest to clarify the reasons of reported correlation between the excessive levels of HbA1c and HBP [6–9]. In our recent report, we demonstrated how CAAEBC theory connects cervical cartilage’s damage with blood pressure (BP) elevation [10]. The analysis of accumulated data also statistically connect cervical disc degeneration with some chronic diseases, including DM [11]. We already investigated the credible hypothesis that arterial hypertension (AHT) appears as a reaction of oxygen detectors in the rhomboid fossa to the reduction in the oxygen availability in the blood flow, as a result of the jam caused by the cervical cartilage damage. This jam initiates a successive cascade of the processes [10,12]. The CAAEBC theory considers HBP as a result of the attempt to maintain a constant level of energy metabolism (E\text{CONST}). The brainstem tries to keep this constant level through energy balance compensation between aerobic (AE) and anaerobic (AN) ways of glycolysis. CAAEBC theory postulates that, for this reason, rhomboid fossa controls the balance between microcirculatory and cellular levels of the AE (oxygen—E\text{AE}) and AN (glucose, lipoproteins, etc.—E\text{AN}) molecular components of the metabolism [10,12]. The goal of rhomboid fossa is to achieve:

$$E\text{CONST} = E\text{AE} + E\text{AN}$$

Since the reactions of AN compensation, being less energy-efficient than AE [13], then turn on AN compensation reactions, and will lead to an increase in the AN metabolism of sugars, phospholipids, and other energetically rich biochemical compounds. The purpose of this reaction is to maintain the balance of E\text{CONST}, which can be done at a reduced E\text{AE} by increasing E\text{AN}. In all cases of a narrowing or jamming of the lumen of the cervical vertebral arteries, the manifestations of the action of the “slow” adaptation with a shift in the AE ≡ AN balance, namely pre-DM [12,14], should be observed. Then, if we intend to recover the access of blood flow to the located rhomboid fossa oxygen detector, we will need to open the lumen to normalize arterial linear blood flow velocity ($V_A$) through cervical vertebral arteries.

The current study is focused on the preliminary evaluation of the consistency of the abovementioned hypothesis. In other words, we tried to find the dependence between...
the restoration of $V_A$ and the recovery of HbA1c level. This recovery takes place after normalization of BP, which was reported earlier and corresponds to the anticipations of CAAEBC theory [12].

2. Materials and Methods

2.1. Study Design

The data from medical records of 4287 adult patients (from 40 to 80 y.o.) treated in Complementary and Integrative Health Clinic of Dr. Shishonin (further clinic) for AHT from January to December 2021 were analyzed. This group consists of 2494 female (F) ($64.5 \pm 9.2$ y/o) and 1793 male (M) ($66.1 \pm 9.7$ y/o) patients. The BP data were collected with CS-106 mechanical tonometer (CS Medica Corp., Moscow, Russian Federation). On the first and last visits, these measurements were followed by triplex sonography to determine linear velocity of arterial blood flow ($V_A$) on Mindray DC-40 (Mindray Medical Ltd., Shenzhen, China) [10,15,16], according to the manufacturer’s recommendations, as well as rules and regulations in Russian Federation, accepted in the clinic. All patients signed their informed consents before starting therapy, according to the ethical regulations of both the Swiss and Russian federations [17,18]. From this group, the sample was selected according to the following rules.

2.2. Sample Selection

From the above mentioned group, we chose the area of obtaining HbA1c measurements in medical records. From this area, we chose the patients with pre-DM criteria (HbA1c (5.7–6.4%) from the medical records as the sample, which consists of 19 M ($63.1 \pm 11.7$ y/o) and 29 F (F) ($65.5 \pm 12.2$ y/o) patients. For them, HbA1c data were obtained by independent lab INVITRO, Ltd. (Moscow, Russia) approximately 3 months after the first measurements. The flow process of the sample selection is shown in Figure 2. The size of the sample is detailed in Section 4.

![Figure 2. The flow process of the sample selection.](image-url)
2.3. Therapy

Therapy consists of two parts—one-time manual correction and subsequent strengthening. The correction of the cervical intervertebral discs is performed manually to recover the cervical vertebral arteries’ blood flow. It starts from the location of the area of hypertonicity of the collar zone and neck muscles. The hypertonicity is removed by applying pressure on the sagittal plane’s muscles. It is performed by pushing the thumb on the occipital–vertebral muscles, located between the transverse processes of C1–C7. The pressure is applied on the cervical spine zone’s muscles in the same way. The patient is laid down during these manipulations. The detailed description of successive steps had been recently reported [10,12,15,16].

Abovementioned procedure allowed the cervical vertebral arteries’ blood flow to be restored. The correction is followed by strengthening exercises, which provide an opportunity to create a muscular corset to fix the unjammed lumen geometry after recovery [12]. The correction is usually followed by a cycle of 12 visits, devoted to the corrective exercises. The goal of them is to strengthen the neck’s muscular corset. These visits lasted from 14 to 40 days. We already reported that these procedures provide BP normalization for the vast majority of the patients [12]. We need to underline that these corrective exercises were focused mostly on cervical area. So far, we were unable to detect measurable outcomes, depending on the chosen certified manual practitioner in the clinic. As in recovery of \( V_A \), the systolic peak (PS) data were employed as a criterion [12].

2.4. Statistical Analysis

The data are presented as AVG ± SD. The Wilcoxon (rank paired) test was applied to find the statistical significance of changes after treatment in the clinic in BP, PS, HbA1c. The significance was set as \( \alpha < 0.005 \). Changes are considered positive if they are towards commonly acceptable normal value, irrespective of the arithmetical sign of these changes.

3. Results

We are still in search of the best parameters to demonstrate the recovery of \( V_A \) [16]. To simplify the current report, in Table 1 we choose the PS data to demonstrate the changes in arterial blood flow as the most traditional method of recovery representation [19].

<table>
<thead>
<tr>
<th>Parameter</th>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>19</td>
<td>29</td>
</tr>
<tr>
<td>Age, years</td>
<td>63.1±11.7</td>
<td>65.5±12.2</td>
</tr>
<tr>
<td>BP before treatment ( P_{AB} ), torr</td>
<td>159.5±18.3</td>
<td>163.5±17.9</td>
</tr>
<tr>
<td>BP after treatment ( P_{AA} ), torr</td>
<td>132.3±19.2</td>
<td>131.7±16.6</td>
</tr>
<tr>
<td>Changes in BP, torr</td>
<td>-27.2±10.1</td>
<td>-31.7±11.3</td>
</tr>
<tr>
<td>Positive changes in BP</td>
<td>19</td>
<td>29</td>
</tr>
<tr>
<td>Critical values for ( \alpha = 0.005 )</td>
<td>32</td>
<td>100</td>
</tr>
<tr>
<td>PS before treatment ( P_{AB} ), cm/s</td>
<td>22.5±8.1</td>
<td>21.9±9.3</td>
</tr>
<tr>
<td>PS after treatment ( P_{AA} ), cm/s</td>
<td>41.7±6.7</td>
<td>43.2±7.4</td>
</tr>
<tr>
<td>Changes in PS, cm/s</td>
<td>19.2±7.7</td>
<td>21.3±7.1</td>
</tr>
<tr>
<td>Positive changes in PS</td>
<td>19</td>
<td>29</td>
</tr>
<tr>
<td>Critical values for ( \alpha = 0.005 )</td>
<td>32</td>
<td>100</td>
</tr>
<tr>
<td>HbA1c before treatment, %</td>
<td>6.03±0.34</td>
<td>6.11±0.45</td>
</tr>
<tr>
<td>HbA1c after treatment, %</td>
<td>5.7±0.63</td>
<td>5.73±0.51</td>
</tr>
<tr>
<td>Changes in HbA1c, %</td>
<td>-0.33±0.58</td>
<td>-0.38±0.42</td>
</tr>
<tr>
<td>Positive changes in HbA1c</td>
<td>17</td>
<td>24</td>
</tr>
<tr>
<td>Negative changes in HbA1c (rank)</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Actual sample size</td>
<td>17</td>
<td>25</td>
</tr>
<tr>
<td>Critical values for ( \alpha = 0.005 )</td>
<td>23</td>
<td>68</td>
</tr>
</tbody>
</table>

In this Table, BP means “Systolic BP”, and PS—“Systolic Peak”.
According to the CAAEBC theory, as soon as cervical vertebral arteries are unlocked and access of the blood flow to the rhomboid fossa is restored, the pressure and heart rate should return to normal [20,21]. Therefore, if we can heal the patients from AHT through the restoration of lumen geometry and confirm that the HbA1c level is developing toward restoration, then our hypothesis should be considered proven. The normalization of AHT through the restoration of the cervical vertebral arterial blood flow is relatively easy to register by measurement of BP and PS (Table 1).

Table 1 demonstrates the absence of significant gender differences. However, the application of Wilcoxon signed-rank paired data test to PS, \(P_{AX}\), and HbA1c before and after treatment confirms the statistical significance of changes in PS, \(P_{AX}\), and HbA1c. We need to underline that changes are still statistically significant even if we separate the sample for M and F patients and analyze the significance in each part.

The collected data suggest that if we can return the access oxygen to the rhomboid fossa, then the brain stem reorganizes the regulation of biochemical processes from the position of “lack of oxygen” to “normal”. In addition, we observe the continuous recovery as a reduction in HbA1c for the patients with pre-DM conditions.

4. Discussion
Both WHO and ADA underline the advantages of the use of HbA1c for DM screening: ease of sampling (not necessarily on an empty stomach; sample stability), marker reflecting a long period, variability is lower than that of glucose determination, the same test for diagnosis and monitoring, the evaluation method is more standardized than BGL. Refs. [3,4] Pre-DM often precedes DM and is often confused with metabolic syndrome (also known as syndrome X or insulin resistance syndrome). As we already mentioned above, the contemporary studies revealed some correlations between the excessive levels of HbA1c and HBP [6–9]. The diagnosis of pre-DM is established in the presence of any three signs of the following:

- Abdominal obesity;
- Elevated blood triglyceride levels;
- Low blood high-density lipoprotein (HDL) cholesterol;
- HBP;
- Fasting BGL of 5.6 mmol/L or higher [3,4].

It appears during the sample selection that it is hard to find patients with AHT who are aware of their pre-DM conditions for obvious reasons. Their primary care physicians (PCP) connect all patients’ complaints with AHT and, for this reason, rarely ask patients to check HbA1c levels until they start to exhibit DM symptoms (e.g., often urination). We chose the patients with pre-DM, since they haven’t started DM-related pills consumption yet; therefore, their reaction to PS restoration is the cleanest. The size of the sample that we were able to collect is useful to the preliminary confirmation of the hypothesis, but it is too narrow to study, e.g., the role of practitioner’ skills or preferences. We need to underline that all practitioners were from our clinic and conduct manual correction according to our clinic standards.

Another set of considerations are associated due to the demonstrated link between DM and metabolic acidosis [22–24]. According to the CAAEBC, DM could be developed this way in the form of impaired insulin metabolism and disruption to the normal functioning of the pancreas or so on [10,12]. Therefore, recovery from even pre-DM should lead to normalization of the blood pH. From this angle, it is important to obtain a set of measurements, confirming the fact of recovery from metabolic acidosis in each case. We plan to clarify it in further works.

5. Conclusions
We demonstrated that the recovery of access of the arterial blood flow to the rhomboid fossa leads to the restoration of arterial BP in the first 40 days and HbA1c in 90 days in AHT and pre-DM patients. This observation confirms the central role of the rhomboid
fossa in homeostasis regulation according to CAAEBC theory. In our forthcoming studies, we plan to study the behavior of some other biochemical parameters, e.g., pH, [Fe], etc., in association with the access of the arterial blood flow to the rhomboid fossa.

**Author Contributions:** Conceptualization, A.Y.S. and A.A.V.; methodology, A.Y.S.; software, B.A.G.; validation, B.A.G. and K.V.Z.; formal analysis, A.Y.S. and A.A.V.; investigation, A.Y.S. and K.V.Z.; resources, A.Y.S.; data curation, B.A.G.; writing—original draft preparation, A.Y.S. and A.A.V.; writing—review and editing, A.Y.S. and A.A.V.; visualization, A.A.V.; supervision, A.Y.S. and A.A.V.; project administration K.V.Z.; funding acquisition, A.Y.S. All authors have read and agreed to the published version of the manuscript.

**Funding:** This paper has been supported by the RUDN University Strategic Academic Leadership Program (recipient A.A.V.)

**Institutional Review Board Statement:** Since we employed a retrospective analysis as a method, and, therefore, analyzed already collected data, then, there is no any necessity to obtain any Review Board Statement, according to both Swiss and Russian regulations [10].

**Informed Consent Statement:** Written informed consent has been obtained from the patient(s) to publish collected data.

**Data Availability Statement:** As a method, we employed a retrospective analysis and we are able to provide the employed data with the exception of the part, that is covered by the The Russian Federal Law on Personal Data (No. 152-FZ).

**Acknowledgments:** The authors wish to thank BS V.D. Bystrykh for her assistance with the editing of the submission’s final version. Alexandre Vetcher expresses acknowledgments to the RUDN University Strategic Academic Leadership Program for the obtained support.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**

14. Levit, S.; Giveon, S.; Philippov, Y.I.; Panchev Domuschiev, I.; Zivony, A. Type 2 diabetes therapeutic strategies: Why don’t we see the ELEPHANT in the room? *Diabetes Mellit.* 2016, 19, 341–349. [CrossRef]


