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METABOLIC CONNECTIONS IN DM PATIENTS ON HEMODIALYSIS

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✓ ***Resume***

Background. About 80% of kidneys insufficiency/ develops due to Diabetes Mellitus (DM). Patients with end stage of renal disease (ESRD) presents wide range of biochemical abnormalities and requires hemodialysis. Glycemic level is critical for hemodialysis outcome. We proposed that glucose fluctuation on hemodialysis linked to blood biochemical abnormalities.

Material and methods. Total in 45 patients, 15 with DM1 and 21 with DM2, admitted to hemodialysis unit at the Republican Specialized Scientific Practical Medical Center of Endocrinology were observed. Patient blood pressure, body weight, MDRD, blood glucose, blood biochemistry had been assessed.

Results. 46 patients with ESRD on hemodialysis differs by average age (35.9 vs 64.6 years old), body weight (70.32 kg vs 87.82kg), average DM duration were comparable (19.6 vs 20.79). There were not found any differences in systolic and diastolic pressure, blood serum enzymes ALT, AST levels, serum creatinine and MDRD between DM1 and DM2 groups. About 40% of DM1 and 64% of DM2 patients with ESRD on hemodialysis have total Hb level below 90 mg%. However, when patients distributed according to total hemoglobin level Hb<90 and Hb>90 there were significant difference in blood serum albumin (in DM1 Hb>90 group 42.69±0.88 g/L vs DM2 Hb>90 group 39.5±1.29 g/L, p<0.05), blood serum sodium level (in DM1 Hb<90 group 128±2.4 mmol/L vs DM2 Hb<90 group 134.9±2.11 mmol/L), phosphates (DM1 Hb>90 group 2.03±0.07 mmol/L vs DM2 Hb>90 group 1.66±0.07 mmol/L) levels. Comparing glycemia before and after hemodialysis were not showed any significant differences between DM1 and DM2 groups. However, distribution the groups according to Hb level showed lower glycemia in Hb<90 DM2 group before (in 1.4 times, p>0.05) and after (in 1.4 times, p<0.05) hemodialysis, which were not seen in DM1 group. We concluded that DM2 group especially those with Hb<90 should be aware hypoglycemia during hemodialysis. Since we found relationship of some parameters with Hb level correlational analysis were performed with all studied parameters. Interestingly, that total Hb showed well correlation link with glycemia before and after hemodialysis in both DM1 and DM2 groups, whereas in DM1 patients Hb correlation were shown with DAD, AST, Potassium and sodium level, whereas in DM2 group correlation Hb were shown with body weight and MDRD.

Conclusion. To determine risk of hypoglycemia and outcome in DM patients checking blood total hemoglobin level is recommended, if it is lower than 90 mg% be aware hypoglycemia in DM2 patients.

Key words: Diabetes Mellitus, hemodialysis.

МЕТАБОЛИЧЕСКИЕ ВЗАИМОЗАВИСИМОСТИ У ПАЦИЕНТОВ САХРНЫМ ДИАБЕТОМ НАХОДИВШИХСЯ НА ГЕМОДИАЛИЗЕ

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✓ ***Резюме***

Пациенты с терминальной стадией диабетической нефропатией (ХПН) имеют широкий спектр биохимических нарушений. Уровень гликемии является важным в успешном проведении гемодиализа. Мы предполагаем, что колебания гликемии взаимосвязаны с биохимическими нарушениями. 45 пациентов с сахарным диабетом (СД) с ХПН, 15 с СД1 и 21 с СД2, находившиеся на стационарном лечении в отделении гемодиализа Республиканский Специализированный Научно Практический Медицинский Центр Эндокринологии были обследованы. У пациентов определяли артериальное давление, вес тела, MDRD, уровень гликемии, биохимические показатели крови. Результаты показали, что пациенты СД1 и СД2 различались по возрасту (35.9 лет при СД1 и 64.6 лет при СД2), весу тела (70.32 кг при СД1 и 87.82кг при СД2), продолжительность заболевания СД была сопоставима (19.6 лет при СД1 и 20.79 лет при СД2). Около 40% пациентов с СД1 и 64% с СД2 находившихся на гемодиализе имели уровень общего Hb крови ниже 90 mg%. У пациентов уровень альбумина плазмы крови (p<0.05), уровень натрия (p<0.05), фосфатов (p<0.05) различался в зависимости от уровня Hb крови. Сравнение гликемии до и после гемодиализа показало низкую гликемию только в группе с СД2 с низким уровнем Hb крови как до (в 1.4 раза, p>0.05), так и и после (в 1.4 раза, p<0.05) гемодиализа. Мы пришли к выводу, что пациенты с СД2 на гемодиализе особенно те, у которых уровень Hb крови <90 мг% должны быть насторожены по поводу гипогликемии. В то же время, корреляционный анализ показал зависимость между общим Hb крови и гликемией, как до, так и после гемодиализа при СД1 и 2 типа. Пациенты с СД1 имели сильную корреляционную зависимость Hb крови с уровнем ДАД, уровнем АсТ, калия, натрия, тогда как в группе с СД2 корреляция была показана между уровнем Hb крови и весом тела, MDRD.

Ключевые слова: сахарный диабет, гемодиализ.

ГЕМОДИАЛИЗ БИЛАН ДАВОЛАНАЕТГАН ҚАНДЛИ ДИАБЕТ БЕМОРЛАРДА МЕТАБОЛИК БОҒЛИҚЛИКЛАР

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✓ ***Резюме***

Терминал даражадаги диабет нефропатияси (ХПН) бўлган беморлар кенг кўламдаги биокимёвий ўзгаришлар билан намоён бўладилар. Гликемия гемодиализ самарали бўлиши учун муҳим аҳамиятга эгадир. Гемодиализ вақтидаги гликемиянинг ўзгарувчанлиги биокимёвий ўзгаришлар билан боғлиқ деб таҳминладик. Қандли диабети (ҚД) ва ХПН бўлган 45 беморда, улардан 15 тасида ҚД 1 ва 21 тасида ҚД2 билан Республика Ихтисослашган Илмий Амалий Эндокринология Тиббиёт Маркази гемодиализ бўлимида назоратда бўлдилар. Беморларда артериал қон босими, тана вазни, MDRD, қондаги глюкоза миқдори, биокимёвий кўрсаткичлар аниқланди. Натижалар ҚД1 ва ҚД2 беморлар гуруҳи орасидаги фарқланиш беморлар ёши (35.9 ва 64.6 ёш), тана вазни (70.32 кг ва 87.82 кг) да кўрилиб, касаллик давомийлиги деярли тенг бўлди (19.6 ва 20.79 йиллар). ҚД1 гуруҳда 40% ва ҚД2 гуруҳда 64% беморда умумий қондаги Hb миқдори 90 мг% дан камлиги кўрсатилди. Беморларда қон зардобидаги альбумин миқдори (p <0.05), натрий (p <0.05), фосфатлар (p <0.05) миқдори Hb миқдорига қараб фарқланди. Гликемия миқдорини солиштириш гликемиянинг пастлаб кетишини фақат ҚД2 да Hb миқдори кам бўлган гуруҳда гемодиализдан аввал (1.4 марта, p>0.05) ва кейин (in 1.4 times, p<0.05) кузатилди. ҚД2 беморларда айниқса Hb <90 мг% дан кам бўлганларда гемодиализ даврида гипогликемия хавфидан огоҳ бўлишлари зарур деб хулоса қилинди. Шу билан бирга корреляцион таҳлил қондаги умумий Hb миқдори билан гемодиализдан аввал ва кейинги гликемия миқдори орасида кўрилди. ҚД1 гуруҳдаги беморларда умумий Hb миқдори ДАД, қондаги АсТ, натрий, калий миқдорлари билан, ҚД2 гуруҳда эса тана вазни ва MDRD билан корреляцион боғлиқлик кўрсатилди.

Калит сўзлар: қандли диабет, гемодиализ.

Introduction]

Diabetes Mellitus is a worldwide pandemic [1] due to chronic complications shortens life expectancy, worsens peoples' life quality, causes blindness, amputations, renal failure, increases pain and suffer of peoples, dramatically raises health care expenditure. One of the serious chronic complications of DM is nephropathy causes renal failure, which requires hemodialysis [10]. About 80% of kidneys insufficiency develops due to Diabetes Mellitus (DM).

Glycaemia is a critical factor for the development and progression of diabetes and its complications. Maintaining its normal level is important for preventing of diabetes complications and defines a clinical future. Diabetic nephropathy (DN) is a one of the severe complications of DM, develops about 40% patients with DM1 and in 5-10% patients with DM2 whose have genetic predisposition and poor glycemic control (5,6). Clinically DN presents in 5 stages begins with mild microalbuminuria progress to overt proteinuria towards kidney failure where people need in hemodialysis (6,7,13). During the hemodialysis glycaemia level may change even cause emergency situations like hypoglycemia, hypoxia, provoke heart failure or stroke (3,4). Patients during hemodialysis often have shown problems such as myocardial infarction or stroke due to vessel and blood coagulation [3,4,7]. Another main problem is hypoglycemia and tissue hypoxia due to glucose fluctuation [5,6]. People with renal failure addicted to hypoglycemia due to alteration of insulin degradation by kidney in one side and metabolic acidosis and uremia in another side [2,8].

We proposed that blood glycaemia level has fluctuations during hemodialysis, which would be not the same in patients with DM1 and DM2. Moreover, this fluctuation depends from blood biochemical markers. Glycemic level is critical for hemodialysis outcome. We proposed that glucose fluctuation on hemodialysis linked to blood biochemical abnormalities.

Based on proposal on the above, the aim of our study is to analyze the glycemic levels in patients with DN who undergo hemodialysis. With this goal we analyzed the way hemodialysis procedure changing glucose levels in patients with DM1 and DM2 by analyze the patients with end-stage renal diseases' data by common blood test and biochemistry marker in blood during a year.

Material and methods.

Totally 45 patients were observed (Table 1). All patients are suffered diabetic mellitus with end-stage of diabetic nephropathy and received hemodialysis treatment at the Republican Specialised Scientific Practical Medical Center of Endocrinology after the name of academician Turakulov Y.Kh., the Health Ministry of Uzbekistan. The patients is divided into 2 main groups which is DM1 and DM2 to compare each other for finding out any differences between types of DM and in case, there is which one is the main differences and cause and also divided into subgroup which is blood total hemoglobin level (Hb) and its derivatives red cell distribution width (RDW-CV).

Patients body weight weighed before hemodialysis in the mechanical scale manually. Blood pressure measured using automated BP meter "Omron 3" (Omron Health Care, USA). Blood glucose level checked before and after hemodialysis by glucometer Accu-Chek Instant Kit. Total blood count, urine analysis, blood biochemistry i.e. creatinine, ALT, AST, Sodium, Calcium, Potassium, Phosphates, Iron, HbA1c level were performed at the central laboratory unit of the hospital by standard methods approved by the Health Ministry of Uzbekistan. Lab data were taken from patient's card in laboratory test results part. Kidneys function estimated by Modification in Diet Renal Disease (MDRD) equation (6,7).

All data were calculated by Microsoft Excel application and expressed as M±m and considered as significant when $p<0.05$ by Student (14). To show relationship between parameters correlation analysis performed between the groups and subgroups. Correlation were considered as significant when $r>0.3$ (14).

Table 1.

Patients characteristics by groups

Groups	DM1	DM 2	P (DM1 to DM2)
Total	15	30	-
Man	5	21	-
Woman	10	9	-
Average age	35.93±2.03	64.59±1.40	P<0.05
DM duration	19.60±1.47	21.24±1.33	P>0.05
Body weight	70.32±3.51	87.86±2.48	P<0.05
MDRD	6.48±0.53	8.05±0.77	P>0.05

Results

As were shown in Table 1 DM1 and DM2 group patients with ESRD on hemodialysis differs by average age (35.93±2.03 vs 64.59±1.40 years old, P<0.05), body weight (70.32 3.52 kg vs 87.82±2.48 kg, P<0.05) and related with etiology and pathogenesis of these two diseases. Interestingly, the average DM duration were almost the same and were 19.60±1.47 and 21.24±1.33 years (P>0.05) in DM1 and DM2 groups subsequently.

Moreover, MDRD were comparable between two groups and suggested about renal insufficiency (table 1).

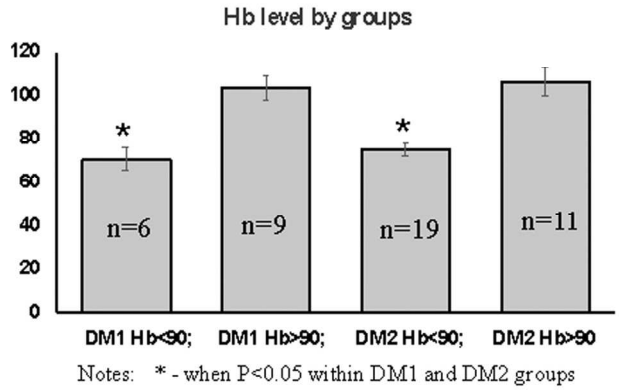

Fig.1 Blood hemoglobin level Hb<90mg% and Hb>90 mg% in DM1 and DM2 patients on hemodialysis.

In addition, there were no any differences in systolic and diastolic blood pressure, or blood serum enzymes ALT, AST, and creatinine level between DM1 and DM2 groups and suggested about comparable metabolic abnormalities due to ESRD.

Although patients on hemodialysis were taken erythropoietin regularly, about 40% of DM1 and 64% of DM2 patients had total blood hemoglobin (Hb) level below 90 mg% (Fig.1). Moreover, RDW-CV were higher in DM2 group by 10%, p<0.05 than in DM2 and together with lower hemoglobin data suggested about severe impact on tissue oxygenation in DM2 patients.

Blood serum albumin content were lower in patients on hemodialysis and shown relationship with blood total Hb level in type 1 DM, but not in type 2 DM (in DM1 with Hb>90mg% group 42.69±0.88 g/L vs DM2 Hb>90mg% group 39.5±1.29 g/L, p<0.05). These results suggested about better regeneration processes in type 1 DM, probably related to pathogenesis of disease and younger age.

Blood serum sodium level is important for muscle contractility, nerve conduction, heart rate, fluid retention and body vitality. Interestingly, blood serum sodium level (Fig.2) were higher in Hb>90mg% group in DM1 patients, but not in DM2, which probably related to better capacity to renew and younger age in DM1.

However, blood serum phosphorus level (Fig.2) were differs in Hb>90 DM1 group. High blood phosphorus level in patients on hemodialysis related with insufficient kidneys function. Interestingly, in DM2 blood hyper-

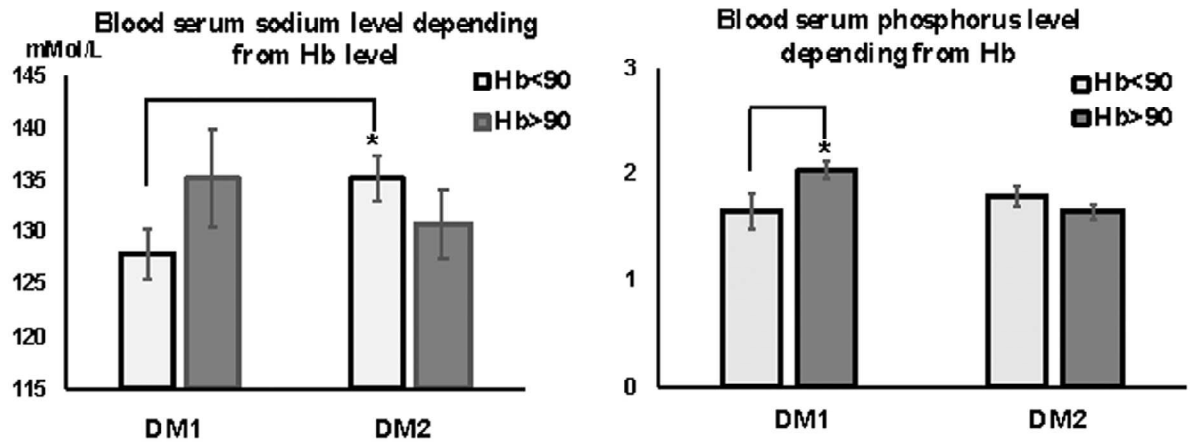

Fig.2. Blood serum sodium and phosphorus level depending from Hb level in patients on hemodialysis. Notes: * - when P<0.05 between groups

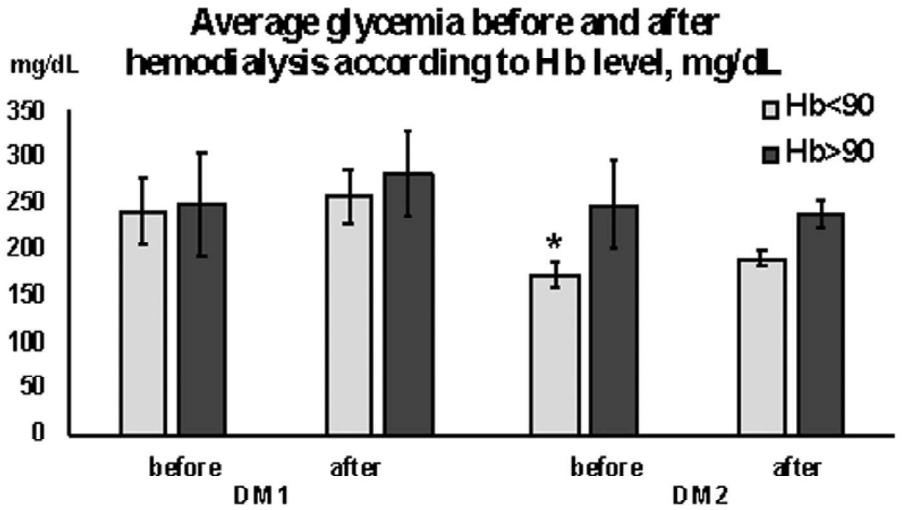

Fig.3. Glycemia level before and after hemodialysis in groups according to Hb level. Notes: * - when P<0.05 between Hb<90 and Hb>90 groups

phosphatemia state shown tendency to lower in Hb>90 mg% and supposed about relationship between blood Hb level and kidneys function.

We compared kidney function between the groups. Blood serum creatinine and MDRD were not differs between the groups and indicated decline of kidneys function in all patients on hemodialysis.

Blood glucose level before and after hemodialysis showed that no changes in DM1 group, whereas final glycemia in DM2 group were significantly lower than in DM1 (Fig.3). Normally, body should maintain glucose level by gluconeogenesis and glycogenolysis. That mechanisms are too weak in people with DM, especially in those with ESRD. During hemodialysis dextrose solution usually prevents hypoglycemia in patients with DM. Our results showed that during hemodialysis DM2 patients should be in tight control to prevent wide glucose fluctuations and hypoglycemia episodes. Moreover, lower blood Hb level promotes lower glycemia in DM2 patients. That means red blood cells hemoglobin level should been corrected in DM2 patients on hemodialysis. This may be related erythrocytes functions such as insulin binding and insulin delivery as were proposed in patients with DM in other studies (12).

In the next step we did correlational analysis between total Hb and other parameters (Fig.4). It was surprising that total blood Hb level had mild correlation link with hematocrit in DM1 (r=0.4) and were in strong correlation in DM2 (r=0.9). These results may be explained by red blood cell distribution width RDW-CD data which was significantly differ between the groups (13.37 0.3 in DM1 vs 14.64 0.47 in DM2) and was in agreement with data about erythrocytes functional activity in DM (15,16).

Blood total hemoglobin level were found in correlation with ACT (r=0.4), blood sodium (r=0.35), calcium (r=0.43), phosphates (r=0.38) in DM1 group and with body weight (r=0.57) and blood iron (r=0.38) in DM2 group. In patients with ESRD due to kidneys damage filtration and concentration functions were altered.

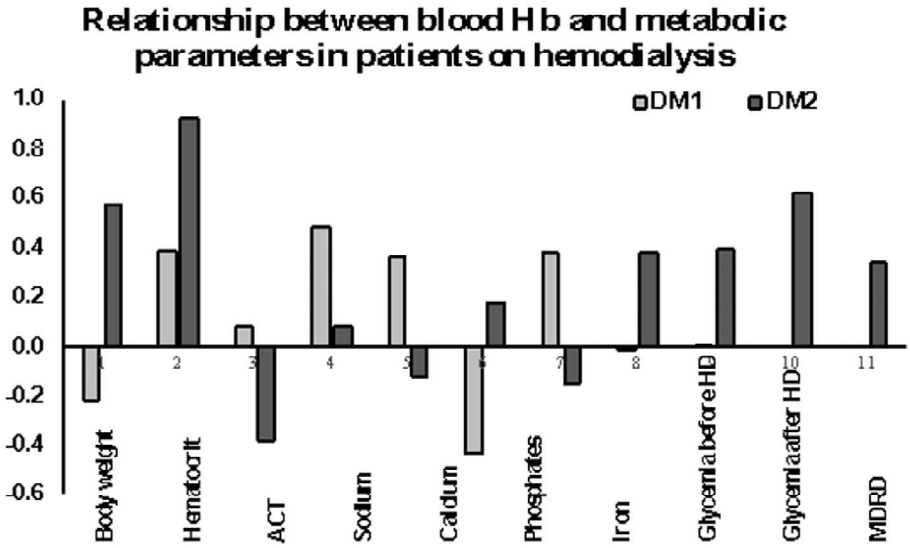

Fig.4. Relationship between blood Hb and metabolic parameters in patients on hemodialysis (HD).

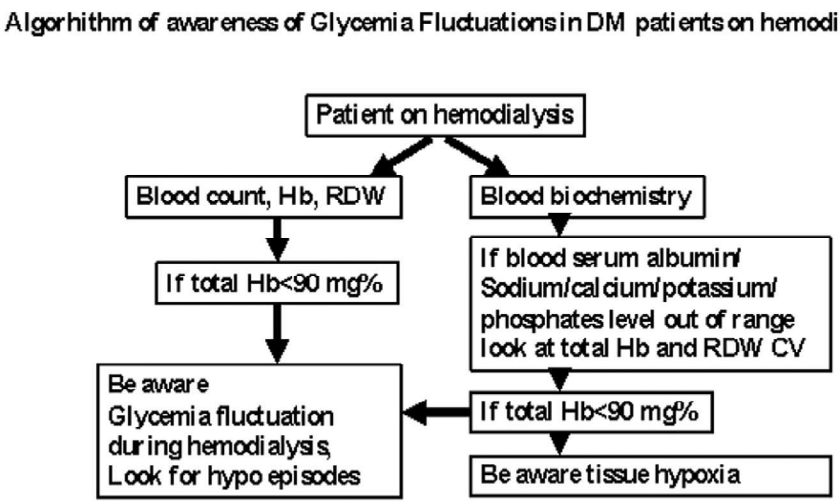

Fig.5. Algorhithm of awareness of glycemia fluctuations in DM patients on hemodialysis.

Interesting data were shown in DM2 group by correlation between total blood Hb with glycemia level both before (r=0.49) and after (r=0.7) hemodialysis, whereas no any correlation shown in DM1 group. These results were in agreement with RDW-CD data and suggested about importance of blood hemoglobin level in glycemia fluctuations in DM2 patients on hemodialysis.

Based on obtained data we composed an algorhithm of awareness of glycemia fluctuations in DM patients on hemodialysis (Fig. 5).

According that algorhithm doctors can easily check blood count and blood biochemistry data. If Hb is <90mg% or if blood serum albumin, sodium, calcium, phosphates level will out of normal ranges glycemia fluctuations should be checked to avoid hypoglycemia episodes.

Conclusion

To determine risk of hypoglycemia and outcome in DM patients checking blood total hemoglobin level and insulin treatment regime are recommended, if it is lower than 90 mg% be aware hypoglycemia in type 2 DM patients. In DM patients on hemodialysis in those with total hemoglobin lower than 90 mg% frequently check sodium and phosphates in blood biochemistry is recommended.

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