Volume 2, Issue 5, May 2024 ISSN (E): 2938-3765

MODERN ASPECTS OF CORRECTION OF BLOOD SUGAR LEVELS IN PATIENTS WITH ACUTE HEART FAILURE WITH TYPE 2 DIABETES MELLITUS

Boltayev E. B.1, 2
Bukhara State Medical Institute, Bukhara, Uzbekistan1
Republican Scientific Center for Emergency Medical Care, Bukhara, Uzbekistan2

Abstract
Despite the studies verified by the World Health Organization on regulating the blood level in patients with acute sedentary insufficiency with type 2 diabetes mellitus, the optimal method for regulating the blood level in these patients has not been worked out. The state of research and optimization of elevated blood sugar levels in diabetic patients with acute heart failure and adequate results.

Keywords: Diabetes mellitus, acute heart failure, hyperglycemia.

Introduction

The risk of cardiovascular diseases (CVD) and mortality from them in diabetes is 2-5 times higher than in the population [2,15,16,57]. Among patients with acute myocardial infarction complicated by heart failure (AHF), the proportion of patients with type 2 diabetes, according to the most conservative estimates, is 20-25% [40], and the number of patients with unimpaired carbohydrate metabolism is less than half [40]. These data from the European Heart Survey were fully confirmed by a similar study conducted in China, which found only 35.8% of patients with normal glucose metabolism [1]. Hyperglycemia is the most characteristic manifestation of diabetes, the importance of which as a risk factor for CVD has been shown in many studies [3,13,64,60]. The role of this potentially controllable factor in the acute period of myocardial infarction complicated by AHF naturally attracts the closest attention.

Bolk et al. [4,7], based on 336 patients, established a relationship between blood glucose levels on admission and mortality from AHF, regardless of the presence of previously diagnosed diabetes. Patients were divided into 4 groups according to blood glucose levels I: <5.6 mmol/l, I: 5;6 - 8.3 mmol/l, III: 8.4 - 11.0 mmol/l, IV: 11 .1 mmol/l. The average age of patients was 68±11 years, 34% of patients were diagnosed with anterior AMI. The follow-up period was 14.2 months. The 1-year mortality rate was 19.3% for patients with blood glucose levels less than 5.6 mmol/L and 44% for patients with blood glucose levels >11 mmol/L. Thus, mortality within a year was higher in patients with higher glycemic levels ($p < 0.05$).

In 2000, Capes et al. [25] showed the relationship between blood glucose levels on admission, mortality and the development of AHF in patients with MI, both with and without diabetes. The average age of patients included in the study was 50 - 68 years. Researchers have proven a positive correlation between hyperglycemia in the acute period of myocardial infarction complicated by

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

AHF and mortality as a result of AHF. In patients without concomitant type 2 diabetes with a glucose level > 6.1 mmol/l, the relative risk of mortality was significantly increased (relative risk 3.9; 2.9-5.4) than in patients without diabetes and hyperglycemia. In patients with proven diabetes and glucose levels >10 mmol/l, the risk of death was higher (1.7; 1.2-2.4) c. compared with patients with diabetes but without hyperglycemia on admission. Patients with type 2 diabetes had an increased risk of developing heart failure and cardiogenic shock.

The REGICOR cohort study conducted in Spain [5,23] examined 28-day mortality in 662 consecutive patients with AHF admitted to the Gerona Hospital. Of these, 195 (29.7%) had previously established diabetes, but hyperglycemia above 6.67 mmol/l upon admission was noted only in 69% of patients. This level of glycemia was associated with an increased risk of 28-day mortality after a complicated MI, which was statistically significant for individuals with newly diagnosed diabetes. At the same time, previously diagnosed diabetes was an independent risk factor for 28-day mortality.

A prospective study of 2127 patients with acute coronary syndrome [6,39] also showed that the risk of early development of left ventricular failure and death from cardiovascular causes during hospitalization depended on blood glucose levels on admission. Thus, in patients with a glycemic level of less than 5.8 mmol/l, the risk of left ventricular failure is 6.4%, for patients with a blood sugar level > 10 mmol/l - 25.2%; the risk of death from cardiovascular causes is 0.7 and 6.1%, respectively, with a high degree of statistical significance in both cases.

In Wahab NN., et al. [8,46] analyzed the medical records of 1664 consecutively hospitalized patients from the MI registry. Patients were stratified by history of diabetes (yes, no) and hyperglycemia >11 mmol/L (yes, no). According to the results of the study, it was established that earlier development of AHF was significantly more often observed with hyperglycemia of 11 mmol/l, both among patients with a history of diabetes and without it. A significant increase in mortality was found at higher glycemic levels, however, only among patients who did not have a history of diabetes. The fact that for patients with previously unknown diabetes, hyperglycemia is a more significant predictor of poor short-term prognosis than for patients with previously known diabetes was confirmed in a more recent study [9,38].

Naturally, the data obtained cannot be interpreted in such a way that patients with diabetes with a long course have a better prognosis. A special study showed that the survival rate of patients with long-term diabetes and various forms of coronary artery disease is lower than that of patients; in whom hyperglycemia was first detected during the acute period of myocardial infarction [10,53]. The worse prognosis for patients with MI in combination with both newly diagnosed and previously diagnosed diabetes was confirmed in the large VALIANT study [48]. Thus, the point is that hyperglycemia itself is a predictor of poor prognosis in patients in the acute period of myocardial infarction, which is especially obvious with a short duration of diabetes, when other cardiac risk factors (nephropathy, etc.) have not yet formed.

In 2003, the PAMI (Primary Angioplasty in Myocardial Infarction) study was conducted, which involved 3362 patients. Patients with MI underwent primary angioplasty. Factors influencing the results of the procedure were assessed. It turned out that hyperglycemia on admission was the most influential risk factor in deteriorating blood flow and delaying the recovery of left ventricular myocardial contractility, even despite successful angioplasty [11,31].

In a study from Japan, Kosuge et al demonstrated the effect of different glucose levels on left ventricular function in patients with anterior myocardial infarction and thrombolysis. The study

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

included 210 patients. 142 patients had blood glucose levels greater than 8.9 mmol/L on admission, of which 49% of patients still had high blood glucose levels above 8.9 mmol/L at 48 hours. A multivariate analysis showed that it is precisely in patients with long-term hyperglycemia that more pronounced disturbances in the functioning of the LV myocardium develop, which is expressed by a lower ejection fraction before discharge, p = 0.001 [13].

In a study from the Netherlands, patients undergoing acute MI underwent percutaneous balloon coronary angioplasty. The effect of hyperglycemia on the occurrence of study endpoints, which were considered death, recurrent myocardial infarction, and AHF with LV ejection fraction less than 30%, was studied. A similar outcome occurred in 89 (21%) of 417 patients, and death occurred in 4% of patients. It turned out that the occurrence of study end points was observed significantly more often in patients with an average glucose level on admission of 10.1 ± 3.7 mmol/l than in patients with a glycemic level of 9.1 ± 2.7 ($p < 0.0001$) . It has been proven that with a mean 48-hour glycemia level of 9 ± 2.8 mmol/L, study endpoints occur more often than with glycemia of 8.1 ± 2 mmol/L ($p < 0.001$), [12,14].

The pathogenetic role of acute hyperglycemia is explained in many clinical and experimental studies. The negative impact of acute hyperglycemia on the cardiovascular system is manifested in a violation of ischemic preconditioning, which is a protective mechanism during ischemic damage. In the case of myocardial infarction, this leads to an increase in its size [36]. In severe hyperglycemia, a reduction in collateral coronary blood flow has been demonstrated [17,41]. Acute hyperglycemia can cause the induction of cardiomyocyte apoptosis [26,37], or the death of cardiomyocytes as a result of excessive damage caused by ischemia and reperfusion [28,59].

The effects of acute hyperglycemia may include changes in blood pressure, increased catecholamine levels, coagulation disorders, and electrophysiological changes. Thus, in a study conducted in Italy, Marfella et al. [32,55] revealed the hemodynamic effects of acute hyperglycemia in patients with type 2 diabetes. The study included 20 patients with newly diagnosed type 2 diabetes, without complications. It was proven that acute hyperglycemia, maintained for 2 hours at a level of 18 mmol/l, caused a significant increase in systolic blood pressure in patients from 115.5 ± 9.1 to 120.3 ± 8.2 mmHg, ($p < 0.01$) and diastolic blood pressure from 70.3 ± 7.8 to 79.7 ± 5.3 mmHg, ($p < 0.01$), an increase in heart rate from 75.2 ± 7.8 to 80.8 ± 5.4 beats/min, ($p < 0.01$) and an increase in plasma catecholamine levels ($p < 0.05$).

The same researchers proved that acute hyperglycemia causes QT segment prolongation, which in turn increases the risk of coronary heart disease and sudden death. They induced acute hyperglycemia - 15 mmol/l and maintained it for 2 hours in 20 healthy men (10 people) and women (10 people), which caused a significant increase in systolic and diastolic blood pressure, an increase in heart rate, prolongation of the QT segment, prolongation of the PR interval and increase in catecholamine levels ($p<0.05$) [27,34]. Other studies have shown a relationship between acute hyperglycemia and increased blood viscosity, increased blood pressure [47,50] and increased levels of atrial natriuretic peptide [11,52].

Glycemic control in the acute period of myocardial infarction

Accumulated data from epidemiological, experimental and clinical studies have clearly shown the association of high hyperglycemia on admission and an unfavorable prognosis for myocardial infarction, and have put the problem of glycemic control in the acute period of this disease on the agenda. The birth of a metabolic approach to the treatment of IHD is traditionally associated with

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

a glucose-insulin-potassium mixture (GIC). Sodi-Pallares, in 1962, for the first time, in a small non-randomized study, showed that GIK has a positive effect on ECG dynamics in the acute period of myocardial infarction complicated by AHF, and improves early survival [24,58].

Subsequent studies have had conflicting results, many with poor designs. In particular, in a number of studies, GIK therapy began 48 hours after the onset of an anginal attack. [49,54].

However, Rackley et al. showed in a randomized trial that administration of GIK within an average of 2.5 days after the onset of MI resulted in a reduction in mortality [51]. A 30% glucose solution containing 50 units of insulin and 80 Meq of potassium chloride per liter was used. According to a meta-analysis of 9 studies (n=1932), in which GIK was used in the first 48 hours after the onset of AHF, in-hospital mortality was reduced by 28% (p=0.004%) [38,56].

Of interest are the data from a small study conducted exclusively using continuous insulin infusion, with the exception of glucose infusions. Patients (33 people) with acute MI and type 2 diabetes were divided into two groups: in one, patients received only tablets, in the other, a continuous infusion of insulin to maintain the target level of 4-7 mmol/l. researchers proved a reduction in mortality in the intensive care group in the first year by 42%, in the second - by 17%, $p < 0.05$ [60].

Currently, studies are of interest where GIK was used against the background of thrombolytic therapy (TLT) or primary balloon angioplasty [40,56]. Convincing evidence of the positive effect of GIK during reperfusion therapy was obtained based on the results of a large prospective randomized trial, ECLA (Estudios Cardiologicos Latinoamerica) [13]. The reduction in hospital mortality in the group receiving GIK was 66% (p=0.008).

It is noteworthy that in patients who did not receive reperfusion therapy, the therapy did not affect the mortality rate.

One of the most famous studies using intensive glycemic control using insulin in patients with AHF was Diabetes Insulin-Glucose in Acute Myocardial Infarction - DIGAMI [18]. It was carried out by the cardiology departments of nineteen hospitals in Sweden from 1990 to 1995. The study included 620 patients with MI that developed in the previous 24 hours and with a blood glucose level >11 mmol/l. Patients were randomized into two groups. In the first, patients (n=306) received intravenous infusions of insulin and 5% glucose for at least 24 hours, followed by subcutaneous insulin injections 4 times a day for 3 months. In the second, control (n=314), patients received traditional treatment accepted in this hospital. In addition to glucose-lowering therapy, both groups received the same treatment for MI in accordance with accepted standards. Basal blood glucose levels in both groups did not differ and were 15.4±4.1 mmol/l in the intensive insulin therapy group, and 15.7±4.2 mmol/l in the comparison group. Blood glucose levels decreased in the first 24 hours in the intensive insulin therapy group to 9.6 ± 3.3 mmol/l in the traditional therapy group 11.7 ± 4.1 mmol/l ($p <0.001$).

The results of DIGAMI were impressive: the proportion of deaths by the end of the 1st year after MI in the group of patients receiving insulin infusion was 18.6%, and in the control group - 26.1%, thus a 29% reduction in mortality was recorded in group of intensive insulin therapy ($p = 0.027$). A particularly significant reduction in patient mortality was found in the group of low-risk patients who did not receive insulin before the onset of MI. In these patients, hospital mortality rates decreased by 58% ($p<0.05$), and the number of deaths during the year decreased by 52% ($p<0.02$) compared with the control group, which included similar patients [45] .

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Further follow-up (average 3.4 years) showed that these differences persisted [29]. When interpreting these promising results, it was unclear which component of insulin therapy provided them: insulin infusion in the acute period of MI or insulin therapy subsequently, after discharge from the hospital.

These issues were addressed in the even larger and international study DIGAMI 2 [35]. It was conducted in 44 centers in the Scandinavian countries and the UK and included 1253 patients with type 2 diabetes and glucose levels >11.0 mmol/l hospitalized for MI. Three strategies were compared in the treatment of patients suffering from type 2 diabetes in the acute period of myocardial infarction. The first group (n=474) received infusions of insulin and glucose and, over the next 3 months, subcutaneous injections of insulin. The second group (n = 473) also received a 24-hour continuous infusion of a glucose-insulin mixture; further control tactics were determined by the attending physician. The third group (n = 306) received traditional treatment accepted in this institution. The average follow-up time for patients was 2.1 years (1.03-3.00).

The results of DIGAMI 2 did not confirm the data obtained in the first DIGAMI: hospital mortality and survival within a year after MI did not differ in all three groups of patients. Mortality in the first and second groups was 23.4% versus 22.6% (p = 0.8), there were no differences in deaths between the second and third groups - 22.6% versus 19.3 (p = 0. 2), there were no differences in the occurrence of recurrent MI and strokes.

The results of DIGAMI 2 destroyed certain ideas about the effectiveness of insulin itself and the glucose-insulin mixture in improving the prognosis after MI in patients with diabetes. In many ways, these hopes were associated with the renaissance of the glucose-insulin-potassium mixture (GIK) in the treatment of MI and reperfusion syndrome [22,30]. GIK is attributed to the role of a metabolic protector of cardiomyocytes, primarily by suppressing the increased concentration of free fatty acids caused by hypercatecholaminemia and increased myocardial oxygen demand.

Clinical studies on the use of GIK in patients with myocardial infarction, including patients with type 2 diabetes, have given ambiguous results [44], which is also observed for DIGAMI 1 and DIGAMI 2. However, the understanding that a glucose-insulin mixture or GIK is not a panacea, gives no reason to doubt the epidemiological data on the connection between glucose levels and the prognosis of patients with AMI and diabetes, transferring the question to the plane of how to achieve such control [46].

These findings were confirmed in the Australian study - The Hyperglycemia: Intensive Insulin Infusion In Infarction - HI-5 study [29]. It started in 2001 and ended 3.5 years later. The study involved 240 patients, 116 patients suffered from type 2 diabetes. The purpose of this study was to examine the effect of improved glycemic control achieved by varying insulin infusion rates on survival in patients with hyperglycemia during the acute phase of myocardial infarction. Patients in the acute period of myocardial infarction were divided into 2 groups: receiving insulin for at least 24 hours until glucose levels reached <10 mmol/l or conventional therapy. It was found that insulin infusion did not affect mortality (4.8 and 3.5%, p = 0.75), as well as mortality after three (7.1 and 4.4%, p = 0.42) and six months (7.9 vs 6.1%, p = 0.62) However, in the intensive insulin therapy group there was a lower incidence of AHF (12.7 vs 22.8%, p = 0.04) and cases of recurrent AMI over the next 3 months (2.4 and 6.1%, p = 0.05). When analyzing glucose levels achieved within 24 hours, it was found that mortality in patients with glucose levels < 8 mmol/L compared with the group > 8 mmol/L (2 vs 11% after 6 months, p = 0.02) was smaller.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

In summary, three large studies aimed at strict glycemic control in patients with diabetes in the initial period of AMI, and using infusions of an insulin-glucose mixture, gave conflicting results regarding the reduction in the proportion of deaths during the first year of follow-up. Naturally, these results caused a lively discussion. First of all, attention is drawn to the differences in study design [31,44,53]. In particular, DIGAMI 2 did not include patients with type 1 diabetes and, unlike the first DIGAMI, there was no restriction on the level of glycemia on admission > 11 mmol/l, which is why the initial glucose levels in patients included in the studies differed -15.5 ± 4.5 mmol/l in DIGAMI 1 and 12.8 ± 4.5 mmol/l in DIGAMI 2 [55]. In the HI-5 study, insulin infusion was started later than in DIGAMI, after other therapeutic measures had been completed. According to the CREATE-ECLA study [24], it is known that infusion of GIK before reperfusion has a significantly greater effect, since it reduces reperfusion damage [20]. Therefore, one of the ways to increase the effectiveness of metabolic therapy is to administer it as early as possible.

Due to the success of DIGAMI, the protocol used in this study, as well as in the DIGAMI 2 study [19], intended for use by coronary intensive care nurses, has become widely known. The infusion protocol and protocol tracking scale are presented below.

Protocol for infusion of insulin - glucose mixture for use by nurses in intensive care units for coronary patients:

- 80 units of short-acting insulin dissolved in 500 ml - 5% glucose and (1 unit of insulin in 6 ml of solution)

- Start infusion at a rate of 30 ml/hour. Check glucose levels after 1 hour. Set the infusion rate according to the tracking scale. The target glycemic level is 7-10 mmol/l. Determine blood glucose levels one hour after changing the infusion rate or after 2 hours if there is no change. If the initial decrease in blood glucose level exceeds 30%, the infusion rate does not change, provided that the glycemic level exceeds 11 mmol/L. Reduce rate to 6 ml/hour if glycemic levels are close to target levels

-If glucose levels are stable and <10.9 mmol/L, after 22 hours, reduce the infusion rate by 50%.

Infusion protocol tracking scale

Table 1

Level glycemia	Algorithm of actions
>15 mmol/l	Administer 8 units of short-acting insulin intravenously and increase the insulin delivery rate by 6 ml/hour
11-14,9 mmol/l	Increase infusion rate by 3 ml/hour
7-10,9 mmol/l	Leave the infusion rate unchanged
4-6,9 mmol/l	Reduce the injection rate by 6 ml/h
<4 mmol/l	Stop the infusion for 15 minutes, if hypoglycemia is symptomatic, administer 20 ml -30% glucose, then restore the infusion at a rate reduced by 6 ml/h

An important advantage of this protocol is the relatively small amount of fluid infused, since the dangers of using large amounts of glucose have already been noted in other studies using GIK [43].

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

However, this algorithm is not ideal. First, the selected target blood glucose level is 7-10 mmol/L, higher than the target levels that follow from the epidemiological studies cited above. But even these glycemic levels were not achieved in all patients. In the DIGAMI study, the average blood glucose level was 9.6 mmol/l; in the DIGAMI 2 study it was lower and amounted to 9.1 mmol/l.
Secondly, cases of hypoglycemia were noted in the studies. In the DIGAMI study, patients in the continuous insulin infusion group experienced hypoglycemic conditions in 15% of cases. In the DIGAMI 2 study, blood glucose levels less than 3 mmol/l, both with and without symptoms, were observed in the first group in 12.7% of cases, in the second group in 9.6% of patients, in the third group only in 1% patients experienced hypoglycemia.
In this regard, this treatment protocol cannot be considered safe, this is confirmed by a study conducted in Sweden, which included patients with diabetes and AHF, and proved that hypoglycemia during hospitalization, as well as hyperglycemia upon admission, are an independent risk factor for mortality within 2 years [21].
Thus, this algorithm for the treatment of patients with type 2 diabetes in the acute period of MI complicated by AHF cannot be considered ideal. And although the protocol we reviewed is not the only one [33], there is no reason to believe that successful methods and protocols have been found for the treatment of patients with AHF suffering from type 2 diabetes.

Summary

Numerous epidemiological studies indicate the widespread prevalence of the combination of type 2 diabetes and AHF. Uncontrolled hyperglycemia in the acute period of MI, even when detected for the first time, is a significant predictor of the development of AHF and death after AMI.
Although recent advances in cardiology have significantly improved survival in patients with AHF, patients with diabetes remain at increased risk of mortality. In this regard, patients with type 2 diabetes require more intensive therapy and metabolic control.
Despite the studies conducted, optimal algorithms for metabolic therapy in patients with acute heart failure have not been found. The question remains about the possibility of insulin therapy to improve the prognosis in patients with AHF and diabetes. The effect of strict control of blood glucose levels on the contractility of the left ventricular myocardium has not been studied, which dictates the need for additional studies aimed at studying the effect of glycemic control on the course and prognosis of AHF and will help optimize the treatment of patients in this category.

References

1. Дедов И.И. Шестакова М. В.Сахарный диабет М.:«Универсум Паблишинг». 2003; - 282с
2. Johnstone M.T., Nesto R..Kahn R.C. et al. Joslin's Diabetes Mellitus, Lippincott Williams & Wilkins. 2004; P. 976 - 977.
3. Clement S, Braithwate S et al. Management of diabetes and hyperglycemia in hospitals. Diabetes Care. 2004; 27:553 - 597.
4. Bartnik M.et al. Newly detected abnormal glucose tolerance: an important predictor of long-term outcome after myocardial infarction. Eur. Heart J. 2004; 21: 1880 - 1890.
5. Da-Yi Hu, Chang-Yu Pan, Jin-Ming Yu for the China Heart Survey Groop. The relationship between coronary artery disease and abnormal glucose regulation in China: the China Heart Survey. Eur Heart J. 2006; 27: 2573 - 2579.
6. Bloomgarden, Z.: Cardiovascular Disease. Diabetes Care. 2006; 29: 1160 – 1166.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

7. Bolk J, van der Ploeg T, Cornel JH, Arnold AE, Sepers J, Umans VA: Impaired glucose metabolism predicts mortality after a myocardial infarction. Int J Cardiol. 2001; 79: 207 – 214.
8. Sala J, Masia R, Gonzalez de Molina F-J, Fernandez-Real JM, Gil M, Bosh D, Ricart W, Senti M and Marrugat for the REGICOR Investigators: Short-term mortality of myocardial infarction patients with diabetes or hyperglycemia during admission. Journal of Epidemiology and Community Health. 2002; 56: 707 – 712.
9. Foo K, Cooper J, Deaner A, Knight C, Suliman A, Ranjadayalan K, Timmis A.D.: A single srrum glucose measurement predicts adverse outcomes across the whole range of acute coronary syndromes. Heart (London) 2005; 5: 12 – 516.
10. Wahab NN., Cowden EA, Pearce NJ et al., on behalf of the CONS Investigators. Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? J Am Coll Cardiol. 2002; 40: 1748 –1754.
11. Kosiborod M, Rathore SS, Inzucchi SE, Masoudi FA, Wang Y, Havranek EP, Krumholz HM: Admission glucose and mortality in elderly patient patients hospitalized with acute myocardial infarction: implications for patients with and without recognized diabetes. Circulation. 2005; 111: 3078 – 3086.
12. Goyal A, Mahaffey KW, Garg J, Nicolau JC, Hochman JS, Weaver WD, Theroux P, Oliveira GB, Todaro TG, Mojcik CF, Armstrong PW, Granger CB. (2006) Prognostic significance of the change in glucose level in the first 24 h after acute myocardial infarction: results from the cardinal study. Eur Heart J. 27: 1289 – 1297.
13. Lenzen M, Ryden L, Ohrvik J, Bartnik M, Malmberg K, Scholte op Reimer W, Simoons Ml: Diabetes known or newly detected, but not impaired glucose regulation, has a negative influence on 1-year outcome in patient with coronary artery disease: a report from the Euro Heart Survey on diabetes and heart. Eur Heart J. 2006; 27: 2969 – 2974.
14. Aguilar D, Solomon S.D, Kober L, Roulean J-L, Skali H, McMurray J.J.V, Fransis G.S, Henis M, O'Connor C.M, Dias R, Belenkov Y.N, Varshavsky S, Leimberger J.D, Velazquez E.J, Califf R, Pfeffe M.A: Newly diagnosed and previously known diabetes mellitus and 1-year outcomes of acute myocardial infarction – the VALsartan In Acute myocardial infarction. Circulation. 2004; 21: 1572 – 1578.
15. Хайитов, Д. Х., & Болтаев, Э. Б. (2022). ПОСТРЕАНИМАЦИОН КАСАЛЛИК НАТИЖАСИДА КЕЛИБ ЧИКАДИГАН АСОРАТЛАРНИ БАРТАРАФ ЭТИШДА ЗАМОНАВИЙ ИНТЕНСИВ ТЕРАПИЯ. КЛИНИК АМАЛИЕТДА УЧРАГАН ХОЛАТ. Academic research in modern science, 1(9), 172-178.
16. Yarashev A.R., Boltaev E.B., Shabaev Y.K. A retrospective analysis of complications of percutaneous dilated tracheostomy // New day in medicine, 2020. 4 (32). P. 301-304.
17. Boltayev E.B.U., Sabirov J.M. Organization of oxygen therapy using a nasal mask and ventura mask in severe patients with Covid-19 corona virus infection. Eme. Jou. Edu. Dis.Lif. Lea. [Internet], 2021Aug. 24 [cited 2021 Oct.17]; 2(08):6-10.
18. Khayotovich, K.D., & Bekmurodugli, B.E. (2022). Case in clinical practice: Modern intensive care in the treatment of post-resuscitation complications caused by cardiac arrhythmias. ACADEMICIA: An International Multidisciplinary Research Journal.
19. Турдиев, У. М., Болтаев, Э. Б., & Кодиров, М. Д. (2020). ПОКАЗАТЕЛИ ЦИТОКИНОВ У БОЛЬНЫХ С ОСТРЫМ КОРОНАРНЫМ СИНДРОМОМ В ЗАВИСИМОМТИ ОТ ВИДА

АНТИТРОМБОТИЧЕСКИОЙ ТЕРАПИИ. In Высшая школа: научные исследования (pp. 93-97).

20. Qoyirov, A. Q., Kenjaev, S. R., & Xaitov, S. S. (2020). Egamova NT, Boltaev EB The role of delirium in patients with myocardial infarction of complicated acute heart failure. New Day in Medicine, 3(31), 68-71.

21. Эшонов, О. Ш., & Болтаев, Э. Б. (2020). СПОСОБ ЭКСТРЕННОГО ОПРЕДЕЛЕНИЯ СТЕПЕНИ ТЯЖЕСТИ ЭНДОТОКСИКОЗА ПРИ НЕОТЛОЖНИХ СОСТОЯНИЯХ. Новый день в медицине, (1), 462-464.

22. Boltayev E.B. Choice of respiratory therapy in severe patients with new coronavirus infection covid-19 // Achievements of science and education. Founders: Olympus. № 8. P. 70-74.

23. Koyirov A.K. et al. Non-invasive lung ventilation in acute respiratory failure caused by new coronavirus infection Covid-19 // New Day in Medicine, 2021. №. 1. P. 107-114.

24. Shodmonovov, J. B. (2023). Conduct respiratory therapy in patients with severe coronavirus infection. Eurasian Research Bulletin, 20, 12-17.

25. Qoyirov, A. Q., Azimov, A. A., & Boltayev, E. B. (2022). The Role of High-Flow Ventilation in the Treatment of Acute Respiratory Failure. Eurasian Research Bulletin, 15, 89-101.

26. Болтаев, Э. Б. (2022, October). ЎТКИР НАФАС ЕТИШМОВЧИЛИГИ БИЛАН АСОРАТЛАНГАН ЯНГИ КОРОНАВИРУС ИНФЕКЦИЯСИ COVID-19да НОИНВАЗИВ ЎПКА ВЕНТИЛЯЦИЯСИ. In PROBLEMS OF MODERN SURGERY, INTERNATIONAL SCIENTIFIC AND PRACTICAL CONFERENCE WITH THE PARTICIPATION OF FOREIGN SCIENTISTS MATERIALS. Андижанский государственный медицинский институт.

27. Shoyimkulovich, E. O. (2022). Lymphotropic Therapy in Patients with Acute Brain Injury in the Acute Period. INTERNATIONAL JOURNAL OF HEALTH SYSTEMS AND MEDICAL SCIENCES, 1(6), 368-373.

28. Boltayev Elmurod Bekmurod ugli. (2023). Choice of respiratory therapy in severe patients with new coronavirus infection COVID-19. Eurasian Research Bulletin, 20, 18–22. Retrieved from https://geniusjournals.org/index.php/erb/article/view/4107

29. Ураков Ш.Т., Эшонов О.Ш., Болтаев Э.Б. Послеоперационная когнитивная дисфункция. Новый день в медицине. 2019; 2 (26): 56–60. ID: 44647992.

30. Urakov, Sh. T., Eshonov, O. Sh., & Boltaev, E. B. (2019). Postoperative Cognitive Dysfunction. A new day in medicine, (2), 56-60.

31. Shoyimkulovich, E. O. (2023). Monitoring of Hematological Indices in Prediction of Outcomes in Critical Conditions in Neuroreresistance Patients. Eurasian Research Bulletin, 20, 88-97.

32. Boltayev E.B., & Umurov B.F. (2023). Liver Functional Status in Severe Forms of Covid-19 Disease. Eurasian Research Bulletin, 20, 163–173. Retrieved from https://www.geniusjournals.org/index.php/erb/article/view/4534

33. Kersten J, Schmeling T, Orth K, Pagel P, Warltier D: Acute hyperglycemia abolishes ischemic preconditioning in vivo. Am J Physiol. 1998; 275:721 – 725.

34. Kersten J, Toller W, Tessmer J, Pagel P, Warltier D: Hyperglycemia reduces coronary collarteral blood flow through a nitric oxide-mediated mechanism. Am J Physiol. 2001; 281: 2097 – 2104.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

35. Ceriello A, Quagliaro L, D'Amico M, Di Filippo C, Marfella R, Nappo F, Berrino L, Rossi F, Giugliano D: Acute hyperglycemia induces nitrotyrosine formation and apoptosis in perfused heart from rat. Diabetes 2002; 51:1076 – 1082.
36. Verma S, Maitland A, Weisel R, Li S, Fedak P, Pomroy N, Mickle D, Li R, Ko L, Rao V: Hyperglycemia exaggerates ischemia-reperfusion-induced cardiomyocyte injury: reversal with endothelin antagonism. /J Thorac Cardiovasc Surg. 2002; 123:1120–1124.
37. Marfella R, Nappo F, Angelis LD, Paolisso G, Tagliamonte M, Giugliano D: Hemodynamic effects of acute hyperglycemia in type 2 diabetic patients. Diabetes Care. 2000; 23: 658 – 663.
38. Marfella R, Nappo F, Angelis LD, Siniscalshi M, Rossi F, Giugliano D: The effect of acute hyperglycaemia on QTc duration in healthy man. Diabetologia. 2000; 43:571 – 57.
39. Cinar Y, Senyol A, Duman K: Blood viscosity and blood pressure: role of temperature and hyperglycemia. American J Hypertens. 2001; 14: 433–438.
40. McKenna K, Smith D, Tormey W, Thompson C: Acute hyperglycaemia causes elevation in plasma atrial natriuretic peptide concentrations in type 1 diabetes mellitus. Diabet Med. 2000;17: 512–517.
41. Malmberg K, Ryden L, Efendic S, Herlitz J, Nicol P, Waldenstrom A, Wedel H, Welin L: Randomised trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI Study): effects on mortality at 1 year. J Am Coll Cardiol. 1995; 26: 57 – 65.
42. Malmberg K, Ryden L et al: Effects of insulin treatment on cause- specific one-year mortality and morbidity in diabetic patients with acute myocardial infarction. European Heart J. 1996; 9:1337 - 1344.
43. Malmberg K: Prospective randomized study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. BMJ. 1997; 314: 1512 - 1520.
44. Malmberg K, Ryden L, Wedel H, Birkeland K, Bootsma A, Dickstein K, Efendic S, Fisher M, Hamsten A, Herlitz J, Hildebrandt P, Macleod K, Laakso M, Torp-Pedersen C, Waldenstrom A: Intense metabolic control by means of insulin in patients with diabetes mellitus and acute myocardial infarction (DIGAMI 2): effects on mortality and morbidity. Eur Heart J. 2005; 26:650 – 661.
45. Melikian N, Farzin Fath-Ordoubadi: The role of glucose-insulin-potassium therapy in the current management of acute myocardial infarction. The British Journal of Cardiology. 2003; 1:10.
46. Van der Horst ICC, Zijlstra F, van't Hof AWJ, Doggen CJM, de Boer MJ, Suryapranata H, Hoorntje JCA, Dambrink JHE, Gans ROB, Bilo HJG: Glucose-insulin-potassium infusion in patients treated with primary angioplasty for acute myocardial infarction. J Am Coll Cardiol. 2003; 42:784 – 791.
47. Apstein CS. The benefits of glucose-insulin-potassium for acute myocardial infarction (and some concerns). J Am Coll Cardiol. 2003; 42:792–795.
48. Hirsch I., Goldfarb B. Study confirms need for metabolic control in diabetes after heart attack. DIGAMI 2 fails to replicate key result of DIGAMI 1, but study design may by a factor. DOCNews 2004 Oct 1, Vol 1, 2: 1 http://docnews.diabetesjournals.org
49. N. Wah Cheung, PHD, Vincent W. Wong, PHD and Mark McLean, PHD The Hyperglycemia: Intensive Insulin Infusion In Infarction (HI-5) Study A randomized controlled trial of insulin infusion therapy for myocardial infarction. Diabetes Care. 2006; 29: 765 - 770.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

50. Hirsch I. Were we wrong about insulin and acute myocardial infarction? /DOCNews 2004, Vol 1, 2: 4.
51. Irl B. Hirsch, Richard M. Bergenstal, Christopher G. Parkin, Eugene Wright, Jr., and John B. Buse, A Real-World Approach to Insulin Therapy in Primary Care Practice. Clinical Diabetes. 2005; 23:78 – 86.
52. M. Kosuge , Kazuo Kimura, Toshiyuki Ishikawa, Tomoaki Shimizi, Kiyoshi Hibi, Noritaka Toda, Yoshio Tahara, Masakio Kanna, Kengo Tsukahara, Jyunn Okuda, Naoki Nozawa, Satoshi Umemura Persistent hyperglycemia is associated with left ventricular dysfunction in patients with acute myocardial infarction. Circulation Journal. 2005; Vol. 69, N 123 - P.23-28. т
53. Zarich S, Nesto R. Implications and Treatment of Acute Hyperglycemia in the Setting of Acute Myocardial Infarction. Circulation. 2007; 115: P436 - 439.
54. Strongin L.G., Beliaeva N.G. Aggressive glycemic control preserves cardiac function in patients with acute myocardial infarction and diabetes mellitus. Diabetologia. 2007; 50. Suppl. 1: 47.
55. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary: The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Eur. Heart J. 2007; 28(1): 88 - 136.
56. Beliaeva N.G., Strongin L.G., Shevcova N.U., Panova E.I. Effect of improved diabetic control in patient with acute myocardial infarction and diabetes mellitus. European Journal of Clinical investigation. 2007; 37. – Suppl. 1:70.
57. Svensson A, Darren K, Dellborg M: association between hyper- and hypoglycaemia and 2 year all-cause mortality risk in diabetic patients with acute coronary events. Eur Heart J. 2005; 26: 1255 – 1261.
58. Goldberg et al: Implementation of a safe and effective insulin infusion protocol in a medical intensive care unit. Diabetes care 2004; 27: 46.
59. Vogelzang M. and Zijlstra F. Glucose metabolism and acute myocardial infarction. Eur. Heart J. 2006; 27(11): 1264 - 1265.
60. Grainger A., Eiden K., Kemper J., and D. Reeds. A Pilot Study to Evaluate the Effectiveness of Glargine and Multiple Injections of Lispro in Patients With Type 2 Diabetes Receiving Tube Feedings in a Cardiovascular Intensive Care Unit Nutr Clin Pract. 2007; 22 (5): 545 – 552.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5