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Article

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Do acute ischemic stroke patients receive the right treatment in non-stroke units?

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Abstract: Background: Modern treatment of acute ischemic stroke includes thrombolysis and thrombectomy performed for eligible patients in specialized stroke centers. However, a number of patients are admitted in Neurosurgical or Intensive Care Departments of emergency hospitals, units where routine treatment strategies are applied. *Objective*: To evaluate the management of patients admitted in these departments that do not benefit from thrombolytic or endovascular treatment. *Methods*: A retrospective analysis was performed, including all patients admitted to the Neurosurgery Department and Intensive Care Unit (ICU) of the "St. Pantelimon" Clinical Emergency Hospital with the primary diagnosis of acute ischemic stroke in the year 2016. The following data was retrospectively collected: patient age and sex, comorbidities, risk factors for ischemic stroke, level of consciousness at admission, neurological deficits, stroke location, blood glucose levels, interval from stroke onset to admission, treatment and discharge status. *Results*: In 2016, 63 patients with primary diagnosis of acute ischemic stroke confirmed by head CT scan were admitted in our hospital. None presented indication for decompressive craniectomy. Over a half of them (57,14%) were comatose. The majority of patients admitted to the ICU (76,47%) received glucose 10% infusions in the first 24 hours from admission, despite increased blood glucose levels at admission. A number of 38 (60,32%) of these patients died. *Conclusions*: Patients with acute ischemic stroke should be treated in stroke units with proper equipment and specialists. National public health institutions should take the necessary measures in order to ensure that patients get to the best facility in order to receive the right therapy in the right amount of time.

Key words: ischemic stroke, hyperglycemia, glucose 10% infusion

Introduction

Stroke is the third cause of death and the first cause of neurological disability worldwide (1). In the European Union, 1 million people develop an ischemic stroke yearly and it is estimated that in 2020 the total prevalence will be 6,2% of the total population. Over 4,7 million strokes occur worldwide every year.

During their lifetime, approximately 1 in 6 individuals will develop a stroke (2).

The management of ischemic stroke has evolved from treatment of risk factors and management of complications, to i.v., i.a. thrombolysis or thrombectomy for eligible patients, which could be supplemented in the future with neuroprotective and stem cell treatment.

Current treatment options are performed in units specialized in endovascular treatment, considered "standard of care" for patients with ischemic disabilitating stroke. These new therapies are performed by neurologists and neurointerventional radiologists during the opportunity window of up to 6 hours from stroke onset or from time last seen well.

Not all patients with ischemic stroke are admitted to medical centers specialized in their treatment and only a part of them arrive during the therapeutic time window.

In our emergency hospital, patients with neurological deficits arrive by ambulance in the Emergency Department, where they are diagnosed and admitted to the Neurosurgical Department or Intensive Care Unit (ICU).

The aim of this study is to evaluate the management of patients admitted in these departments that do not benefit from thrombolytic or endovascular treatment.

Material and methods

This study encompasses all patients admitted to the Neurosurgery Department and ICU of the "St. Pantelimon" Clinical Emergency Hospital in the year 2016 with the primary diagnosis of acute ischemic stroke.

All patients were brought in by ambulance to the Emergency Department and were admitted with the diagnosis of acute ischemic stroke, based upon the neurological examination and emergency head CT scan. If the initial head CT scan was inconclusive, the investigation was repeated after 12-24 hours.

Conscious patients were hospitalized in the Neurosurgical Department while the ones that were comatose or presented decompensated comorbidities were admitted in the ICU.

All patients' medical records were reviewed and the following data was collected: patient age and sex, comorbidities, risk factors for ischemic stroke, level of consciousness at admission, neurological deficits, stroke location, blood glucose levels, interval from stroke onset to admission, treatment and discharge status.

In our hospital, thrombolytic or endovascular treatment is not available.

In the case of comatose patients, management goals were sustaining vital functions, stabilization of paraclinical parameters and treatment of risk factors and comorbidities. We have particularly evaluated the outcome of patients and the treatment they received during hospitalization.

Patients with a favorable neurological evolution, meaning alleviation or stabilization of motor deficits were transferred to a neurological recovery department or discharged at home.

Results

In the year 2016, 63 patients with a primary diagnosis of acute ischemic stroke confirmed

by head CT scan arrived in the emergency room and were admitted in our hospital.

The majority of patients were over 60 years old (58 cases, 92,06%), without a significant difference regarding gender distribution (Table 1).

Regarding comorbidities, most patients presented high blood pressure (55; 87,3%), atrial fibrillation (47; 74,6%) and diabetes mellitus (24; 38,1%).

At time of presentation 36 patients were comatose (57,14%) and the remaining 27 (42,86%) were conscious (GCS≥9).

On the basis of neurological deficits (hemiparesis, aphasia, seizures), 52 (82,54%) developed an ischemic stroke in the anterior circulation, while vertigo and balance disorders suggested the stroke's location in the posterior circulation in 16 cases (25,39%).

The presumptive diagnosis of ischemic stroke and its location were confirmed by cerebral CT scan that showed loss of grey-white matter differentiation, an area of hypodensity and/or hyperattenuation of a blood vessel.

TABEL I

Patient characteristics

	Number	Percentage
Total number	63	
Gender		
Male	29	46,03%
Female	34	53,97%
Age group		
30-39	1	1,59%
40-49	2	3,17%
50-59	2	3,17%
60-69	16	25,40%
70-79	22	34,92%
80-89	14	22,22%
90-99	6	9,52%
Comorbidities		
High blood pressure	55	87,30%
Atrial fibrillation	47	74,60%
Diabetes mellitus	24	38,10%
Congestive heart failure	22	34,92%
Hypercholesterolemia and obesity	13	20,63%
GCS at presentation		

3 - 8	36	57,14%
9 - 15	27	42,86%
Admission department		
Neurosugery	19	30,16%
Intensive Care Unit	44	69,84%
Neurological deficits		
Hemiparesis	35	55,56%
Aphasia	17	26,98%
Balance disorders	16	25,39%
Coma	36	57,14%
Seizures	3	4,76%
Stroke location		
Anterior circulation	52	82,54%
•Unilateral MCA	40	63,49%
•Bilateral MCA	7	11,11%
•Terminal ICA	2	3,17%
Posterior circulation	13	20,63%
Evolution		
Discharged at home	16	25,40%
Transfered to neurological recovery department	9	14,28%
Deceased	38	60,32%

In only 29 patients the time interval between the stroke onset to admission could be established. Out of these, only 7 were admitted in less than 6 hours from symptoms' onset.

Although only 24 patients were previously diagnosed with diabetes mellitus, initial blood sugar levels were above the normal range in 53 patients of which 15 were admitted in the Neurosurgery Department and 38 in the Intensive Care Unit.

The 38 cases in the ICU with increased blood glucose levels, in addition to support of vital functions, routinely received glucose 10% infusion in 26 cases in the first day of hospitalization (76,47%), 5 (14,71%) from the second day, 2 (5,88%) from the third day and 1 (2,94%) from the fourth.

Out of the 63 admitted patients, a number of 38 (60,32%) patients died (12 male and 26 female).

Out of the 44 patients admitted in the ICU, of which 36 were comatose (GCS 3=12, GCS 4=7, GCS 5=2, GCS 6 = 9, GCS 7 = 4, GCS 8 = 2) and 38 had increased blood sugar levels, 34 received treatment with glucose 10% and 38 died.

Only 6 patients from to the Intensive Care Unit group survived, that presented normal blood sugar levels on admission.

Among the 25 patients admitted in the Neurosurgery Department, only 5 received treatment with glucose initiated in the third and fourth day of hospitalization. All these patients presented a favorable evolution and were transferred to neurological recovery departments.

Patients that died in the ICU were in critical condition at admission (various degrees of coma). None of these cases presented indication for decompressive craniectomy.

Discussion

Stroke is defined as an acute disruption of cerebral function of a presumed vascular cause that produces a neurological deficit which lasts more than 24 hours or leads to death in the first 24 hours.

Ischemic stroke is caused by absence of blood flow in a part or the entire brain, that induces nerve cells' deprivation of glucose and oxygen. The most frequent cause of ischemic stroke is occlusion of a cerebral artery, but it can also be induced by deprivation of oxygen only (in the case of a cardio-respiratory arrest) or glucose deprivation only as, in the case of diabetic patients treated with insulin overdoses.

Patients with ischemic stroke present, on admission to hospital, in up to two thirds of cases, increased blood sugar levels. (3) Hyperglycemia is defined as a blood glucose concentration greater that 115 mg/dl (6,1 mmol/l).

Between 20% and 50% of acute stroke patients presented with hyperglycemia at admission in the studies of Gray and Toni (4, 5).

Hyperglycemia in these cases can be the result of:

•previously diagnosed diabetes mellitus patients, that represent 8-20% of stroke patients, with poor glycemic control

•patients with undiagnosed diabetes mellitus represent 5-28% (6, 7)

•as a result of early hormonal response to cerebral ischemia (stress response) (8, 9).

Hyperglycemia enhances acidosis and ischemic neuronal damage by facilitating free radical formation, activating pH-dependent endonucleases, enhancing glutamate release and excessive influx of calcium, with the end result of neuronal death (10).

Hyperglycemia accelerates the ischemic process in stroke.

In stroke patients, hyperglycemia is associated with larger infarct volumes, poor functional outcome, increased stroke mortality independent of age, stroke severity or stroke type. (11–13)

Our in-hospital mortality is very high (60.32%), by comparison with 7,8% reported by Ihara in a recent study performed in Japan (14). The majority of admitted stroke patients were outside the opportunity window for thrombolysis/thrombectomy and already in critical condition (comatose), which can explain the high rate of in-hospital mortality. In addition, most of them received a potentially harmful treatment, consisting of glucose 10% infusions administered in the first

24 hours from stroke onset, to patients that were already hyperglycemic.

In Stead et al's study, ischemic stroke patients with hyperglycemia were 2,3 times more likely to be dead within 90 days, by comparison with those with normal glucose levels (15).

In diabetic patients with ischemic stroke, the 30-day mortality rate is 2 fold higher. (11)

Hyperglycemia has been suggested as an independent risk factor for the hemorrhagic conversion of stroke after administration of thrombolytic therapy.

In the setting of stroke, euglycemia should be the clinical goal. Glucose levels should be tested repeatedly and if it is higher than 140-180 mg/dl, treatment with insulin is indicated (1).

Insulin is administered subcutaneously because intravenous administration increases the risk of hypoglycemia.

Scott et al (3) infused 500 ml of 10% dextrose with 16 U insulin and 20 mmol potassium chloride (GKI) in mild to moderate hyperglycemia following acute stroke and considered it a pragmatic intervention which effectively lowers plasmatic glucose levels within the normal range.

However there is limited evidence as to whether reduction of glucose levels in acute ischemic stroke improves patient outcome.

European Stroke Initiative (EUSI) guidelines consider that routine use of insulin infusion regimes in patients with moderate hyperglycemia and acute ischemic stroke cannot be recommended. (16) Blood glucose levels exceeding 180 mg/dl have to be reduced. Maintaining a blood glucose level of 140 mg/dl seems to be reasonable, as more aggressive targets may worsen outcome. (17)

The use of intravenous saline and avoidance of glucose solutions in the first 24 hours after stroke is common practice in stroke units. (18)

In our study, 36 patients were in a critical condition at presentation (GCS<8) and 38 presented hyperglycemia.

The administration of 10% glucose to ischemic stroke patients with hyperglycemia in the first 24 hours is harmful to nerve cells, hastens the expansion of the stroke's core in the penumbra, enlarges the infarction zone and increases the rate of mortality.

A decompressive craniectomy could have been considered only in the case of two patients with malignant infarction, but their critical condition contraindicated the potential surgical intervention.

Stroke care has entered into a new era.

In order to prevent persistent brain damage in an acute ischemic stroke, early restoration of cerebral blood flow is necessary.

In 1996 the US FDA approved intravenous thrombolysis with rt-PA for treatment of acute ischemic stroke. Intravenous rt-PA has become the "holy grail" of acute stroke treatment and is still the standard treatment for eligible stroke patients presenting within 4,5 hours after symptom onset.

However, it may produce recanalization and reperfusion in 5-10% of patients. Reperfusion rates are higher in the M2 segment of the MCA, in small vessels and in microvascular structures. In contrast, it is ineffective in the majority of patients with large thrombi and in patients with large vessel occlusions.

Intravenous thrombolysis has a limited effectiveness in large vessel occlusion.

Mechanical thrombectomy determined high rates of recanalization in proximal artery occlusion.

When a cerebral vessel is obstructed, there are two compartments in its respective territory: core and penumbra.

Inside the core, brain tissue is already dead, while in the penumbra neurons are structurally intact, only their functionality being affected. The goal of stroke treatment is to save the penumbra because the center of the infarction extends in the penumbra, while the latter shrinks progressively until the entire vascular territory becomes infarcted.

The infarction's evolution is dependent on the occlusion time and the state of collateral blood flow. In some patients with poor collateral circulation, the progression is faster, while in the case of good collateral flow, the progression is slower (19).

Khartri et al state that every 30 minutes of reperfusion delay is associated with a relative 10% reduction of good outcome probability (mRS = 0-2) (20).

Endovascular mechanical thrombectomy is an important advance for those patients with large vessel occlusion and stroke located in the anterior circulation.

The criteria presented in the new guidelines for mechanical thrombectomy are:

•pre-stroke mRS score = 0-1

•acute ischemic stroke that received i.v. t-PA within 4,5 hours of symptom onset.

•causative occlusion of the internal carotid artery or proximal (M1) middle cerebral artery (MCA)

•age of 18 years or older

•NIHSS score ≥ 6

•Alberta Stroke Program Early CT (ASPECTS) score ≥ 6

•treatment that can be initiated within 6 hours of symptom onset (21)

Selection of patients for endovascular treatment of acute ischemic stroke can be performed with the help of CT or MRI imaging.

Diffusion weighted magnetic resonance imaging is the gold standard for estimating the ischemic core. It provides full brain coverage and detects smaller lesions (22).

Perfusion CT evaluates cerebral blood volume and cerebral blood flow, but does not provide any information in cases with critical blood flow in preceding hours, that remitted with subsequent reperfusion.

The continued evolution of various therapies and technologies (such as aspiration and stent retrievers) will play an important role in the successful treatment of stroke patients.

Stroke patients have to be treated as quickly as possible. Today, the time windows has been extended beyond 6 hours from time last know well. The DAWN trial has shown a 73% reduction in disability in stroke patients treated within 24 hours. (23)

Conclusions

A part of patients with ischemic stroke are admitted to emergency hospitals in Neurosurgical or Intensive Care Departments, units that are not all specialized in performing thrombolysis or thrombectomy.

In this retrospective study we have analyzed the treatment received by these patients, that frequently included glucose 10% infusions, indicated from the first day of hospitalization even in the case of hyperglycemia and we have found a high rate of mortality in these cases.

Raising awareness upon the fact that glucose infusions administered to hyperglycemic patients in the first 24 hours after stroke onset could have a negative effect on their outcome and should not be prescribed routinely is of significant importance. This could be achieved with the help of CME courses for all physicians that are currently involved in the management of stroke patients.

Patients with acute ischemic stroke must be treated in stroke units, with proper equipment and specialists, where they should arrive in good time in order to benefit from a modern, efficient treatment provided by neurologists or neurointerventional radiologists. An increase in number and capacity of these medical units specialized in the treatment of ischemic stroke is imperative.

Results of our analysis are intended to correct routine treatment strategies of stroke patients and to raise the awareness of national public health institutions. The necessary measures should be taken in order to ensure that patients get to the best facility in order to receive the right therapy in the right amount of time.

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