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EC PHARMACOLOGY AND TOXICOLOGY
Research Article

Levels of Potassium, Chloride and Glucosis in Cerebrospinal Fluid and Blood in Patients with Infections of the Central Nervous System

Brankica Dupanovic[1]*, Snezana Pantovic[2], Snezana Dragas[1], Zeljko Mijailovic[3], Olgica Gajovic[3], Branko Jakovljevic[4] and Danko Zivkovic[1]

[1]Faculty of Medicine, University of Montenegro Clinics for Infectious Diseases, Clinical Centre of Montenegro, Podgorica, Montenegro

[2]Department of Biochemistry, Faculty of Medicine, University of Montenegro, Podgorica, Montenegro

[3]Department of Infectious diseases, Faculty of Medical Sciences, University of Kragujevac, Serbia

[4]Institute for Hygiene and Medical Ecology, School of Medicine, University of Belgrade, Belgrade, Serbia

***Corresponding Author**: Brankica Dupanovic, Faculty of Medicine, University of Montenegro Clinics for Infectious Diseases, Clinical Centre of Montenegro, Krusevac bb, Podgorica, Montenegro.

Received: April 18, 2019; **Published:** March 31, 2020

Abstract

Introduction/Objective: Infections of the central nervous system (CNS) are very common diseases. We wanted to show the importance of detecting potassium, chloride and glucose levels in the cerebrospinal fluid (CSF) and blood for diagnosis of these diseases.

Methods: Study included 120 patients where the control group were patients with meningism. Levels of potassium, chloride and glucose were measured on first, third and seventh day, except in control group.

Results: We had 66 male and 54 females patients. Patients suffering from bacterial infection (BI) had kalemia in range from 2,6 to 7,4 mmol/l, whilst the control group had levels in the normal range. Those suffering from purulent meningoecephalitis (PME) had the lowest kalemia, while those with viral encephalitis (VE) had the highest. All groups showed increasing levels of potassium, while in the control group that trend was not followed. Levels of potassium in CSF on first day were lower in patients suffering from BI than in the control group. PME group had the lowest CSF potassium levels. We noticed that the levels of chlorides on the seventh day are increasing in all groups, except in control group. Levels of chlorides in CSF are lower in group of patients suffering of BI comparing to those suffering from viral infections (VI). Patients suffering from BI had the highest glycaemia while patients with meningism had the lowest. The group of patients suffering from BI had hypoglycorrachia. Lowest levels of CSF glycosis were measured in group of patients suffering from BI, while both groups showed increasing values of CSF glucose levels during measurements.

Conclusion: Our study showed the importance of measuring levels of glucose, potassium and chlorides in CSF and blood during CNS infections.

Keywords: *CNS Infections; Potassium; Chloride; Glucose; Cerebrospinal Fluid; Blood; Diagnosis*

Introduction

Infections of the central nervous system (CNS) are severe, life-threatening diseases that have a significant place in medicine because of their serious clinical presentation and the recovering rates. They are divided according to the cause on bacterial, parasitic, fungal,

viral and prion infection and according to the place of pathological process on meningitis, encephalitis, meningoencephalitis, cerebritis, abscessus and myelitis. The diagnosis of inflammatory diseases of the central nervous system is based on historical data, objective neurological and somatic findings, indicators of tissue inflammation in serum and cerebrospinal fluid, cellular, biochemical, microbiological, serological and immune views of cerebrospinal fluid, radiological examination (computerized tomography and magnetic resonance imaging of the brain) etc.

Cerebrospinal fluid (CSF) finds its place in the cerebral chambers and subarachnoid space. The choroid plexus epithelium using mechanisms of filtration and active transport produces CSF at rate of 0.4 ml/min per gram of tissue and the total volume of the CSF in the entire human CNS amounts to 150 ml, in 24 hours 500 - 600 ml are produced thus the CSF is replaced three to four times per day [1]. The blood-brain barrier (BBB) separates blood from interstitial fluid and cells of the brain parenchyma. The BBB restricts movement of many substances between brain and blood, but also it is placed to deliver substrates for brain cell metabolism and to remove corresponding wastes. It has crucial role in regulating interstitial fluid ionic composition.

Glucose transport across the BBB is passive but mediated by specific GLUT1 transporters. Pathways of K^+ transport are via Na^+, K^+-ATPase located primarily in the abluminal (brain) side membrane and via Na^+, K^+, $2Cl^-$ cotransporters across the luminal (blood) side. The transport of Cl^- is linked to the HCO_3^-, because the only known route for net entry of Cl^- from the blood is an exchange of Cl^- for HCO_3^- via AE2 [2].

Evaluation of CSF is essential for suspected CNS infection. Analysis includes examining of the opening pressure, appearance of the liquid, cell count, glucose and protein concentration, CSF culture and polymerase chain reaction (PCR) [3].

Meningismus is condition when the meningeal syndrome is present, followed by normal cytobiochemical analysis results of CSF. The cause of this entity is the congestion and hyperaemia of leptomeningeal. It is not followed by migration of the blood cells from blood to the CSF. The hyperaemia of the meningeal causes the clinical presentation of meningismus (signs of increased intracranial pressure). The meningismus occurs after insolation, but also after digestive tract infections, pneumonia, morbilli, otitis, sinusitis, etc. Symptoms and signs are: headache, vomiting, nuchal rigidity, positive Kerning's and Brudzinski's sign, photophobia, hyperacusis. Also bradycardia, constipation and dermographism can be present [4,5].

The intention of this research is to show the importance of potassium, chloride and glucose levels in the CSF and blood for early diagnosis and differential diagnosis of diseases of the central nervous system.

Materials and Methods

The research was a clinical and prospective study that included a total of 120 patients hospitalized in the Clinical Centre of Montenegro in the period from 2000. to 2010. The test group included patients with central nervous system infections (meningitis, meningoencephalitis, encephalitis). The control group was consisted of patients with meningism or patients with infectious disease of CNS which has not been proven by any test. All patients included in this study signed an informed consent form. Also, this study was approved by Ethical Committee of Faculty of Medicine, University of Kragujevac. All patients were classified in five groups: purulent meningoencephalitis (PME); purulent meningitis (PM); tuberculous meningitis (TM); viral encephalitis (VE) and viral meningitis (VM) and control group (meningism). In all groups blood and cerebrospinal fluid levels of potassium, chloride and glucose were measured on first, third and seventh day of the disease, except patients with meningismus whose CSF analysis on third and seventh day were not made because of the ethical reasons. Concentration of potassium and chlorides was determined by ion-selective electrodes, while glycaemia and glycorrachia were determined by spectrofotometry. To reach the conclusions in relation to the hypotheses obtained data numerical characteristics are shown in the tables that contain the relevant local statistical parameters. Also, attribute characteristics are tabulated in two-dimensional

tables with absolute and relative frequencies. Statistical parameters used in this article are: measure of central tendency (mean), measures of variability (standard deviation, standard error, rank, minimum, maximum, variance) as well as tests to evaluate the distribution, χ^2 test, T test for related samples, t test for independent samples and ANOVA.

Results

There was a statistically highly significant fact that the average age is the highest in patients suffering from viral encephalitis (48.70 years) and purulent encephalitis (46.25 years), and the lowest in the group of patients with viral meningitis (12.05 years). There were 66 male patients affected (55%) and 54 female patients (45%) with no significant difference (Table 1).

Groups of diseases	N	Mean SD	SD	Min	Max.
Bacterial purulent meningoencephalitis	20	46.25	20.82	3	78
Purulent meningitis	20	22.35	16.03	2	53
Tuberculous meningitis	20	40.40	22.14	1	75
Viral encephalitis	20	48.70	21.99	3	78
Viral meningitis	20	12.05	7.80	3	32
Meningismus	20	25.60	23.03	2	84
Total	120	32.82	21.19	1	84
F = 8,613; p < 0,001					

Table 1: *Age of patients between groups.*

Regarding levels of potassium in blood, patients suffering from bacterial infection of CNS had levels in range from hypokalemia to hyperkalemia (2,6 - 7,4 mmol/l), whilst the control group had levels in the normal range (3,5 - 5,0 mmol/l). There is statistically significant difference regarding values of potassium measured on first and third day among groups, while on the seventh day samples the difference among groups does not exist. Group with PME had the lowest potassium blood levels in all mesaurments, while group with VE had highest potassium levels in blood in all mesaurments. All groups showed increasing levels of potassium during the three mesaurements, while in the control group that trend was not followed, adding to the fact that the levels of blood potassium were lower in every measurement (Table 2).

Disease (groups)	Number	Median value			SD			Min.			Max.		
		K1	K2	K3	K1	K2	K3	K1	K2	K3	K1	K2	K3
Bacterial infection	60	4,093	4,195	4,300	1.035	0.950	1.224	2,6	2,9	3,1	7,4	6,6	6,5
Viral infection	40	4,260	4,300	4,630	0.569	0.501	5.030	3,4	3,4	3,6	5,1	5,3	5,1
Meningism	20	4,186	4,130	4,270	0.457	0.372	0.332	3,7	3,5	3,7	5,0	5,0	4,9
Total	120	4,164	4,219	4,405	0,783	0,706	2,344	3,05	3,166	3,366	6,316	5,9	5,766

Table 2: *Potassium blood levels.*

ANOVA $F^1 = 2,213, p < 0,05; F^2 = 2,003, p < 0,05; F^3 = 1,464, p = 0,174.$

Levels of potassium in CSF on first day were lower in samples belonging to patients suffering from bacterial CNS infections (2,86 mmol/l) comparing to the control group (3,07 mmol/l). Levels of potassium in group of patients suffering from bacterial infection are the lowest in all measurements, while patients from both groups show tendency of CSF potassium level growth. PME group had the lowest

CSF potassium levels in all mesaurements and the highest levels on first day were in TM and VE group (3,01 mmol/l both), on the third day the highest levels were in group with PM, and on seventh day in group with TM (Table 3 and 4).

CNS disease (Groups)	n	Median value			Min.			Max.			SD		
		K1	K2	K3	K1	K2	K3	K1	K2	K3	K1	K2	K3
Bacterial infection	60	2,86	3,15	3,30	2,00	2,30	2,50	3,90	3,90	4,10	0.41	0.40	0.39
Viral infection	40	3,00	3,10	3,18	2,60	2,60	2,80	3,40	3,50	3,50	0.15	0.20	0.15
Meningism	20	3,07	-	-	2,90	-	-	3,30	-	-	0.13	-	-
Total	120	2,94	3,13	3,1	2,35	2,42	2,62	3,63	3,74	3,86	0,27	0,32	0,29

Table 3: *Potassium CSF levels.*

ANOVA $F^1 = 13.034$, $p < 0,001$; $F^2 = 3.060$, $p = 0,008$; $F^3 = 4.968$, $p < 0,001$.

Disease (Groups)	N	Median blood potassium level			N	Median CSF potassium level		
		K1	K2	K3		K1	K2	K3
PME	20	3,81	4,12	4,43	20	2,63	2,92	3,03
PM	20	4,32	4,29	4,62	20	2,94	3,28	3,39
TM	20	4,14	4,16	4,29	17	3,01	3,24	3,46
VE	20	4,29	4,29	4,70	20	3,01	3,13	3,21
VM	20	4,23	4,31	4,56	20	2,98	3,08	3,14
∑	100	4,16	4,24	4,52	93	2,92	3,13	3,25
p		0.384	0.923	0.537		0.003	0.010	< 0,001

Table 4: *Levels of potassium in blood and CSF according to the type of disease.*

Median levels of blood chlorides in all groups are in normal range (98 - 108 mmol/l). During illness it is noticed that the mean levels of chlorides on the seventh day are increasing in all groups. There is significant difference among levels of chloride among groups of diseases in first, and high difference in third sample of blood. The patients suffering from bacterial CNS infections had the lowest levels of chlorides in blood during all measurements. Both groups with patient suffering of viral and bacterial infection showed increasing tendency of chlorides level in blood, unlike patients from control group. The lowest levels of blood chlorides were in TM group in all mesaurements (Table 5).

Disease (Groups)	Number	Median value			SD			Min.			Max.		
		Cl1	Cl2	Cl3	Cl1	Cl2	Cl3	Cl1	Cl2	Cl3	Cl1	Cl2	Cl3
Bacterial infections	60	98,36	99,15	102,11	7.596	6.251	16.336	88	90	90	110	109	109
Viral infections	40	101,35	101,5	102,80	4.861	4.315	4.192	90	90	92	110	109	108
Meningism	20	101,80	101,95	101,25	3.071	5.145	2,.21	97	97	98	107	106	105
Total	120	99,93	100,4	102,19	5,93	5,421	9,93	90,16	91,16	92	109,5	108,5	108

Table 5: *Chlorides blood levels.*

ANOVA $F^1 = 0.019$, $p < 0,05$; $F^2 = 1.781$, $p > 0,05$; $F^3 = 7.115$, $p < 0,001$.

The levels of CSF chlorides on first and third day (106,88 mmol/l and 112,00 mmol/l respectively) in group of patients suffering from bacterial CNS infections were below normal range (118 - 132 mmol/l). During first and third day there is statistically significant differnce in CSF chlorides levels among groups, while the diffenece in levels on seventh day is not statistically significant. Levels of chlorides in CSF are lower in group of patients suffering from bacterial comparing to patients suffering from viral CNS infection. Unlike group with viral infection, group with bacterial infection shows increasing values of chlorides in CSF during all three measurements (Table 6 and 7).

CNS diseases (groups)	Number	Median value			Min.			Max.			SD		
		Cl1	Cl2	Cl3	Cl1	Cl2	Cl3	Cl1	Cl2	Cl3	Cl1	Cl2	Cl3
Bacterial infections	60	106,88	112,00	118,98	90	93	90	116	129	130	6.49	6.90	7.24
Viral infections	40	121,90	123,70	123,10	115	113	119	133	133	135	4.63	4.79	14.65
Meningism	20	123,90	-	-	117	-	-	131		-	4.06	-	-
Total	120	114,28	116,68	120,62	102,8	101	101,6	124,16	130,6	132	5,46	6,05	10,2

Table 6: *Chlorides CSF levels.*
ANOVA $F^1 = 46.611$, $p < 0,001$; $F^2 = 24.168$, $p<0,001$; $F^3 = 2.187$, $p > 0,05$.

Disease (groups)	N	Median chlorides blood level			N	Median CSF chlorides level		
		Cl1	Cl2	Cl3		Cl1	Cl2	Cl3
PME	20	98,90	99,65	101,95	20	105,75	110,05	115,30
GM	20	99,00	99,45	102,10	20	109,50	115,40	121,10
TM	20	97,20	98,35	100,80	17	105,40	110,45	120,53
VE	20	100,50	101,55	102,35	20	120,05	122,25	124,65
VM	20	102,20	101,45	103,25	20	123,75	125,15	121,55
∑	100	99,56	100,09	102,09	93	112,89	116,66	120,63
p		0,181	0,309	0,715		<0,001	<0,001	0,192

Table 7: *Levels of chlorides in blood and CSF according to the type of disease.*

Patients suffering from bacterial CNS infections had the highest median levels of glycaemia (7,1 mmol/l). At the same time patients with meningism had the lowest levels of glycaemia (5,3 mmol/l). Patients with viral infections had median value of glycaemia 5,6 mmol/l.

The group of patients suffering from bacterial CNS infection had hypoglycorrachia (1,29 mmol/l) with minimal value of 0.00 mmol/l and maximum of 2,80 mmol/l. Statistically significant difference in CSF glucose levels among groups in all three samples is noticed. Lowest levels of CSF glycosis were measured in group of patients suffering from bacterial infection, while both groups showed increasing values of CSF glucose levels during measurements (Table 8).

CNS diseases (Groups)	H	Median value			Min.			Max.			SD		
		G1	G2	G3	G1	G2	G3	G1	G2	G3	G1	G2	G3
Bacterial infections	60	1,29	1,58	2,90	0,00	0,00	0,60	2,80	3,00	6,00	0.72	0.69	0.94
Viral infections	40	2,88	2,91	3,39	0,70	0,80	1,80	4,50	4,40	5,2	0.57	0.58	0.71
Meningism	20	2,86	-	-	2,60	-	-	3,30	-	-	0.21	-	-
Total	120	2,08	2,11	3,09	0,66	0,32	1,08	3,45	3,56	5,68	0,58	0,64	0,85

Table 8: *Glucose CSF levels.*

Discussion

Our study showed the importance of measuring levels of glucose, potassium and chlorides in CSF and blood during CNS infections. Many studies have examined the levels of glucose in CSF and blood during CNS infections, but as far as our research goes no study has followed the potassium and chlorides levels in CSF and blood during CNS infections. Many other biomarkers have been examined such as lactate, procalcitonin, ferritin, CRP, etc. [6] but none of studies included potassium and chloride [7-10].

Our study showed that the patients with bacterial CNS infections had the lowest CSF glucose levels which correlates with other studies [11-13]. The reason of the low CSF glucose levels are inhibition of glucose entry into the subarachnoid spaces due to alternations in BBB, increased glycolysis by leucocytes and bacteria and increased rate of metabolism in the brain and spinal cord [11]. But also beside that our study showed that within the first week the levels of glucose increase in both patients with viral and bacterial infections of CNS. This finding opens wide space for new researches regarding the prediction of disease outcome based on the changes of glucose CSF levels during the time.

It is known that potassium and chloride are transported together in the choroid plexus [14] and the changes in transport during inflammation happen, so the study showed that the following of potassium and chlorides both in serum and CSF are important for differential diagnosis, because the statistically important difference was found among groups. Patients with PME had the lowest and patients with VE had the highest blood potassium levels and the levels in CSF were the lowest in group of patients with PME. All groups showed the tendency of increasing potassium levels in CSF, which can be used in new studies in the means of following the disease and predicting its outcome.

Chlorides both in blood were in normal range in all groups, but the levels in CSF on first and third day were lower than normal in group of patients with bacterial CNS infection which can be explained with altered BBB transport during inflammation [15], so far the CSF chlorides levels were examined in various studies regarding tuberculous meningitis [16], but our study showed that the both groups with viral and bacterial infection showed increasing in chloride blood concentration during time, while the CSF levels in group with bacterial CNS infection did follow the increasing trend, the group with viral CNS infections did not show the same, which can be used in differential diagnosis.

Conclusion

Our study showed the importance of measuring levels of glucose, potassium and chlorides in CSF and blood during CNS infections.

Conflicts of Interest

None.

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