

RE. Mazo]. Minsk: Navuka i tehnika, 1991, 383 p.

10. Ocenna i vedenie bolevogo sindoma u detey [Assessment and management of pain syndrome in children]: Kratkiy kurs komputernogo obuchenia, vkluchaushiy rekomendacii VOZ 2012 goda po obezbolivaniyu [A short course of computer training, including WHO recommendations for 2012 on anesthesia]. Moscow: R. Valent, 2014, 88 p.

11. Prahov A.V. Klinicheskaya elektrokardiografiya v praktice detskogo vracha: rukovodstvo dlya vrachey [Clinical electrocardiography in the practice of a pediatrician: a guide for doctors]. N. Novgorod: NizhGMA, 2009, 156 p.

12. Rodovye povredeniya [Birth injuries] Elektronny resurs [Electronic resource]. Moscow: GEOTAR-Media, 2011. Access mode: <http://www.studmedlib.ru/en/book/970406793V0055.html> (the circulation

date is June 9, 2016).

13. Shkolnikova M.A. Normativnye pokazateli EKG u detey i podrostkov [Normative parameters of ECG in children and adolescents]. Moscow: Association of Children's Cardiology of Russia, 2010, 232 p.

14. Yakovlev V.N. Normalnaya fisiologiya [Normal physiology]. Voronezh: N.N. Burdenko VGMA, 2005, 528 p.

15. Ruelas-Orozco G, Vargas-Origel A. Assessment of therapy for arterial hypotension in critically ill preterm infants / G. Ruelas-Orozco // Amer. Perinatol. - 2000. - Vol. 17 (2). - P.95.

The authors

1. Vecherkin Vladimir Alexandrovich - MD, professor, head of the department of pediatric surgery GBOU «N.N. Burdenko Voronezh State Medical University», Voronezh, Russia;

2. Chekmareva Darya Vladimirovna - assistant of the Department of Pediatric

Surgery, State Institution «N.N. Burdenko Voronezh State Medical University», the children's surgeon of the surgical department for newborns VODKB №1, Voronezh, Russia;

3. Shcherbinin Roman Leonidovich - children's surgeon, head of Department of Neonatal Surgery VODKB №1 Voronezh, Russia;

4. Ptitsyn Vladimir Alexandrovich - Candidate of Medical Sciences, Associate Professor of the Department of Pediatric Surgery of the N.N. Burdenko VSMU, Voronezh, Russia.

Responsible for correspondence, organizational moments:

Chekmareva Daria Vladimirovna

E-mail: tcchekmareva.dasha@yandex.ru

Mobile phone: +7 (950) 759-59-86

Home address: 394016, Voronezh, st. Begovaya, 219/3, sq. M. 44.

R.L.Shcherbinin, V.A.Vecherkin, S.G.Rezvan, V. A. Ptitsyn

EARLY DIAGNOSIS OF NECROTIZING ENTEROCOLITIS IN THE NEWBORNS

ABSTRACT

Necrotizing enterocolitis (NEC) today hasn't objective reliable laboratory markers for early diagnosis. The article presents the results of studying structural and functional properties of erythrocyte membranes (structural-functional state - SFS) using original method for automatic registration of acidic and osmotic erythrogram (ARAOE) in 50 healthy newborns and 90 suffering from NEC. The study highlighted two laboratory markers, significantly changing their values depending on the stage of the disease.

Keywords: necrotizing enterocolitis, NEC, newborns, hemolysis, erythrocytes.

Objective: to identify the dependence of erythrocyte membranes structural-functional properties from clinical stages of NEC in newborns and to assess their diagnostic value.

Tasks

1. To evaluate structural-functional state of erythrocyte membranes in healthy newborns and NEK newborns with the help of automatic registration of acidic and osmotic erythrogram method.

2. To identify significantly changing of SFS in neonates with NEC depending on the stages of the disease.

MATERIAL AND METHODS

The study included 140 infants. The control group consisted of 50 healthy children (group A) and a group of 90

infants with NEC at different stages (group B).

Group A included 50 healthy newborns with a gestational age of 38-40 weeks, weighing 3500-3850g.

In group B 70% of the newborns were premature. Among concomitant pathology dominated brain ischemia of different severity (100% of cases). Intrauterine infection and septic state was accompanied by the incidence in

93.3% of cases. 74.4% of infants in group B had a weight less 2500 g., including at least 1000g. – 10%.

The study of the SFS method (ARAOE) was carried out according to the method developed at the Department of biophysics and biology faculty FGBOU VPO «Voronezh state University». Equipment: 56M FEK with integrated differential amplifier, two-coordinate recorder 4 LKD – 003, digital voltmeter

Table 1

Distribution on disease stages in the group "B" (n 90)

NEC stages (Walsh & Kliegman)	Стадии НЭК, по Walsh и Kliegman					
	IA	IB	IIA	IIB	IIIА	IIIБ
Total (n 90)	22	20	18	10	12	8

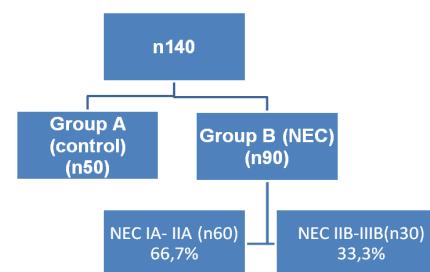


Fig.1 The structure of research.

Table 2
Distribution on gestational age in the group "B" (n=90)

Gestational age, (weeks)	Value, %
26-30	24
31-36	46
37-42	30

Table 3
Distribution of newborns on weight in the group "B"

Weight	Value, %
< 1 кг (n9)	10,0
1-2,4 кг (n58)	64,40
2,5-3,2 кг (n23)	25,60

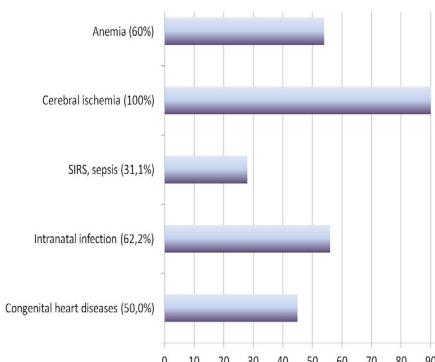


Fig.2 Complementary pathology in the B gr. (n=90)

type B7-20, thermostat UTU-6 and personal computer.

The principle of the method ARAOE is a photometric check of the process of erythrocytes hemolysis. Kinetic curves (erythrogramma) are graphic display of the sequential joining of red blood cells of various degrees of resistance to the stage of hemolysis.

The phases of research execution:

1. Blood sampling and preparation of erythrocyte suspension.

2. The study of hemolysis of red blood cells.

3. Check results.

Statistical data processing was carried

Table 4
Results of the surgical treatment in the group "B"

Results of the surgical treatment	Absolute quantity	Relative value, %
Surgery	30	100
Survived	26	86,6
Lethality	4	13,4

out on a personal computer using the statistical software package STATISTICA of StatSoft company, Inc., (USA) BIOSTAT version of 3.03 of the company Mc Graw-Hill, Inc. (USA).

THE RESULTS OF RESEARCH AND DISCUSSION

The obtained data demonstrates the growth of the constant maximum speed of hemolysis (Cmax) and the decrease in the acid resistance of the membranes (tlat) in the cases of clinical deterioration.

CONCLUSIONS

1. All investigated parameters of SFS method (ARAOE) is statistically significantly associated with the stages of NEC in newborns.

Table 6

The comparative characteristic of the average values of the measured indicators in researching groups

Researching group	G120, %	G30, %	Gmax, %	Kmax, o.e.	t lat, sek
Control gr. (n=50)	0,76±0,04	36,54±0,57	46±0,71	0,27±0,01	155,1±5,05
NEC IA-IIA	1,45±0,16	52,12±1,27	65,3±1,38	0,5±0	84,9±2,91
NEC IIB-IIIB	-2,25±0,32	45,0±0,45	65,57±1,3	0,97±0,27	66,67±1,52
Coefficients of reliability of differences between groups with the Student's criterion					
Control gr. - NEC IA-IIA	0,000011	0,000002	0,000001	0,000011	0,000001
Control gr.- NEC IIB-IIIB	0,000001	0,000001	0,000004	0,000001	0,000001
NEC IA-IIA - NEC IIB-IIIB	0,000000	0,000001	0,938322	0,000001	0,000001

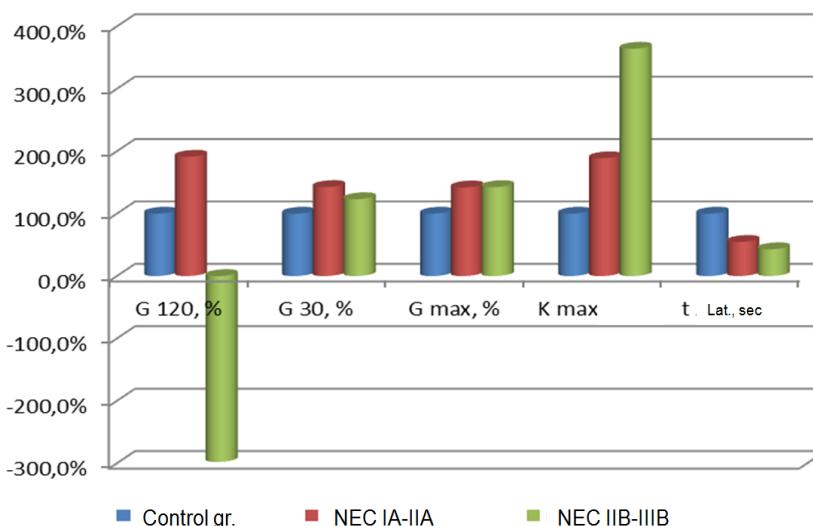


Fig.3 The units values of the APKOЭ- method

Table 5
The studied indicators with APKOЭ method

Unit	Value
G 120, %	Hypoosmotic hemolysis (the largest part of destroyed erythrocytes, placed in S.NaCl 0,55% during 2 min.).
G 30, %	Hypoosmotic hemolysis (the largest part of destroyed erythrocytes, placed in S.NaCl 0,55% during 30 min.).
G max, %	The largest part of the destroyed erythrocytes with hemolysis.
K max	Constant of the maximum speed of hemolysis.
t lat, sec.	The acid resistance of the erythrocytes.

2. The highest correlation coefficients are characteristic of the constant maximum speed of hemolysis (Cmax) (direct) and acid resistance (tlat) (reverse).

3. Newborns with the most severe NEC have the highest value of the indicator Cmax the smallest tlat.

4. There is a high statistically significant correlation between Cmax and tlat with the stages of NEC in newborns, that in combination with the low cost and ease of process definition allows to consider them as a promising additional markers for early diagnosis of this disease.

REFERENCES

1. Gitelzon I.I. Sostav krasnoy krovi v norme i patologii [The composition of red blood in normal and pathology]. Tomsk, 1960, P. 187.

2. Gitelzon I.I. Terskov I.A. Issledovanie funktsionalnogo sostoyaniya eritrona metodom eritrogramm [Research of the erythron functional state by the erythrogram method] Voprosy biofiziki, biohimii i patologii eritrotsitov [Questions of biophysics, biochemistry and pathology of erythrocytes].

Table 7

The correlation coefficients (NEC clinical gravity vs structural properties of the erythrocytes)

Unit	The correlation coefficient value	p
G 120, %	-0,60141	0,005
G 30, %	0,441241	0,032
G max, %	0,723849	0,001
Kmax, o.e.	0,840725	0,001
tlat, c.	-0,81557	0,001

Krasnoyarsk, 1960, P. 85 -99.

3. Karavaeva S.A. Diagnostika i osobennosti klinicheskogo techeniya nekroticheskogo enterokolita u detey [Diagnostics and features of the clinical course of necrotizing enterocolitis in children] Vestnik hirurgii [Herald of surgery]. 2002, v.161, №4, p.41-46.

4. Karavaeva S.A. Hirurgicheskoe lechenie nekroticheskogo enterokolita [Surgical treatment of necrotic enterocolitis]: avtoref. Dis. d-ra med. nauk [author's abstract. dis. Dr. med. Sciences]. St. Petersburg, 2002, 291 p.

5. Karavaeva S.A., Bairov V.G., Kotin A.N., Nemilova T.K. Tkanevaya gipoksiya kak prichina nekroticheskogo enterokolita u novorozhdennyih [Tissue hypoxia as the cause of necrotizing enterocolitis in newborns]. Materiali III Mezhdunarodnogo Kongressa Severnyih stran i regionov [Materials of the III International Congress of Nordic Countries and Regions]. Petrozavodsk-Paris, 1999, p. 154.

6. Mokrushina O.G., Golodenko N.V., Levitskaya M.V. Lechenie yazvenno-nekroticheskogo enterokolita u novorozhdennyih s nizkoy i ekstremalnoy massoy tela pri rozhdennii [Treatment of ulcerative-necrotic enterocolitis in newborns with low and extreme body weight at birth]. Materialy VI Rossiyskogo Kongressa «Sovremennye tehnologii v pediatrii i detskoj hirurgii» [Materials of the VI Russian Congress «Modern technologies in pediatrics and pediatric surgery»], Moscow, 2009.

7. Karavaeva S.A., Bairov V.G., Nemilova T.K. [et al.]. Nekroticheskiy enterokolit kak problema hirurgicheskoye neonatologii: 19-letniy opyt lecheniya [Necrotizing enterocolitis as a problem of surgical neonatology: a 19-year experience of treatment]. Vtoroy Mezhdunarodnyiy Kongress Severnyih Stran i Regionov [The II nd International Congress of the Nordic Countries and Regions of Ions], Kondopoga, p. 74-75.

8. Kozlov Yu.A. Novozhilov V.A., Kovalkov K.A., Chubko D.M. [et al.]. Nekrotiziruyuschiy enterokolit u novorozhdennyih: novyye vzglyady i tendentsii [Necrotizing enterocolitis in newborns: new views and trends]. Detskaya hirurgiya [Pediatric surgery]. 2016, No. 20 (4), p.188-194.

9. Neonatologiya. Natsionalnoe rukovodstvo [Neonatology. National leadership] / ed. N.N. Volodin. Moscow: GEOTAR-Media, 2008, P.451.

10. Rezvan S.G. Analiz molekulyarniyh mehanizmov vzaimodeystviya sinteticheskikh gomologov retinola s komponentami

Table 8

The regression model of influence of the NEC clinical gravity on erythrocytes properties

Unit	Coefficient	Standard error	T-statistics	Significance value
Constant	0,574221	0,237469	2,41809	0,0172
G120	0,00514457	0,0189083	0,27208	0,7860
G30	0,0137278	0,00273114	5,02642	0,0000
Gmax	0,0133121	0,00274893	4,84263	0,0000
Kmax	0,123543	0,0093605	13,1983	0,0000
T lat	-0,00407331	0,000768043	-5,30349	0,0000

Note. Determination coefficient R²=92,69%. Standard error = 0,216124. Average absolute percentage error of forecasting = 0,165798. eritrocytarnoy membrany i svobodnym gemoglobinom [Analysis of molecular mechanisms of interaction of synthetic homologs of retinol with components of the erythrocyte membrane and free hemoglobin]: PhD diss. Voronezh, 1996, 240 p.

11. Mokrushina O.G., Dronov A.F., Smirnov A.N., Golodenko N.V., Levitskaya M.V. Rol laparoskopii v diagnostike enterokolita u novorozhdennyih [The role of laparoscopy in the diagnosis of enterocolitis in newborns]. Materialy VI Rossiyskogo Kongressa «Sovremennye tehnologii v pediatrii i detskoj hirurgii» [Materials of the VI Russian Congress «Modern technologies in pediatrics and pediatric surgery»], Moscow, 2007, p. 280.

12. Studenikin M.Ya. Evdokimova A. I. Gemoliticheskie anemii u detey [Hemolytic anemia in children]. Tashkent: Medicine, 1979, 285 p.

13. Shabalov N.P. Neonatologiya : ucheb. posobie v 2 t. [Neonatology: Textbook in 2 v.]. 3rd ed., Rev. and additional, Moscow: MEDPress-Inform, 2004, 608 p.

14. Shumikhin V.S., Derunova V.I. Materialy VIII Rossiyskogo Kongressa «Sovremennye tehnologii v pediatrii i detskoj hirurgii» [Proceedings of the VIII Russian Congress «Modern Technologies in Pediatrics and Pediatric Surgery»], Moscow. 2009, 307 - 308 p.

15. Helwicz E. Epidemiology of infections in very low birth weight infants. Polish Neonatology Network research/ E.Helwicz [et al.] // Med Wieku Rozwoj. – 2013. – Vol. 17, N 3. –P. 224-231.

16. Olivier Abbo, Luke Harper, Jean-Luc Michel, Dushka Ramful, Audrey Breden, Frederique Sauvat. Necrotizing Enterocolitis in Full Term Neonates: Is There Always an Underlying Cause? Vol 2, No 3 (2013): Journal of Neonatal Surgery .

17. Anand Pandey, Shailendra P Singh,

Vipin Gupta, Rajesh Verma.

Conservative Management of Pneumoperitoneum in Necrotising Enterocolitis- Is it Possible? Vol 5, No 2 (2016): Journal of Neonatal Surgery.

18. Nilkant Phad, Amit Trivedi, David Todd, Anil Lakkundi.

Intestinal Strictures Post-Necrotising Enterocolitis: Clinical Profile and Risk Factors. Vol 3, No 4 (2014): Journal of Neonatal Surgery.

The authors

1. Shcherbinin Roman Leonidovich - head of the department of surgery of newborn children at the Vodkar Hospital No. 1 in Voronezh.

2. Vecherkin Vladimir Aleksandrovich - MD, associate professor, head of the Department of Pediatric Surgery FGBOU V «VSMU named after N.N. Burdenko »

3. Rezvan Sergey Grigorievich - Candidate of Biological Sciences, Associate Professor of the Department of Biophysics of the Biology and Soil Faculty of the Federal State Educational Establishment of Higher Professional Education in the VSU.

4. Vladimir A. Ptitsyn - Ph.D., associate professor, associate professor of the Department of Pediatric Surgery of the State Pediatric University of VSMU named after N.N. Burdenko ».

Responsible for correspondence: Shcherbinin Roman Leonidovich. Email neonatalsurgery@inbox.ru. Contact phone +7 (909) 210 36 00. Home address: 394 077, city of Voronezh, ul. Marshal Zhukov, 24, Apt. 26.

