

## Research Article

<https://doi.org/10.23934/2223-9022-2022-11-1-12-21>

# The Possibilities of Thromboelastography in Assessing Safety of Neuroaxial Blocks in Gestational Thrombocytopenia (Clinical Study)

EN Plakhotina <sup>1</sup>✉, TN Belousova <sup>1</sup>, NB Kuzina <sup>1</sup>, AN Kuzovlev <sup>2</sup>, EV Bryantsev <sup>1</sup>

Department of Anesthesiology and Intensive Care

<sup>1</sup>Vidnovsky Perinatal Center

17 Zavodskaya St., Moscow Region, Vidnoye, 142700, Russian Federation

<sup>2</sup>Federal Scientific and Clinical Center for Resuscitation and Rehabilitation, VA Negovsky Research Institute of General Resuscitation  
25, bld 2 Petrovka St., Moscow, 107031, Russian Federation

✉ **Contacts:** Elena N. Plakhotina, Doctor of Medical Sciences, Head of the Department of Anesthesiology and Intensive Care, Vidnovsky Perinatal Center.

Email: enp2004@inbox.ru

**ABSTRACT** Gestational thrombocytopenia (GT) is the most common type of thrombocytopenia during pregnancy. Unlike other types of thrombocytopenia, it is not accompanied by dysfunction of the cellular component of hemostasis. Currently, a quantitative decrease in platelets in GT is a contraindication to neuraxial blockades (NAB), which significantly reduces the quality of care in childbirth.

The aim of the study is to determine the possibility of safe use of neuraxial blockades in gestational thrombocytopenia.

A retrospective prospective study involved 70 patients who were performed delivery, depending on obstetric indications, either conservatively or surgically. The patients were divided into two groups. The main group (group No. 1) included 35 patients with gestational thrombocytopenia. The comparison group (group No. 2) clustered of 35 patients with a platelet content above  $150 \times 10^9 / L$ . A comparative intergroup analysis of indicators of a general blood test, coagulogram, thromboelastography with a test for functional fibrinogen before childbirth and 2 days after delivery. The change in platelet content and its effect on the coagulation status of patients during pregnancy were retrospectively analyzed. A comparative assessment of the volume of blood loss during childbirth and the early postpartum period and the risk of complications of neuraxial blockade in patients with and without gestational thrombocytopenia was carried out.

It was found that during gestational thrombocytopenia in the perinatal period, there is no decrease in coagulation potential, assessed by the results of coagulography and thromboelastography at a platelet level above  $49 \times 10^9 / L$ . The indicators of hemostasis did not have significant intergroup differences during pregnancy and childbirth. In the group of patients with gestational thrombocytopenia, the volume of blood loss during labor and the postpartum period did not differ from the group without thrombocytopenia, regardless of the method of delivery. The median blood loss after vaginal delivery in group 1 was 225 ml, in group 2 – 250 ml, with abdominal delivery – 572 ml and 386 ml – respectively. In this study, no complications of neuraxial blockade were observed in any of the groups.

The results obtained suggest that in patients with gestational thrombocytopenia, even with a significant decrease in platelet content, it is possible to perform neuraxial blockades during labor, taking into account the clinical picture and the absence of coagulation disorders confirmed by thromboelastography.

**Keywords:** gestational thrombocytopenia, neuraxial blockade, thromboelastogram, functional fibrinogen, epidural hematoma

**For quote** Plakhotina EN, Belousova TN, Kuzina NB, Kuzovlev AN, Bryantsev EV. The Possibilities of Thromboelastography in Assessing Safety of Neuraxial Blocks in Gestational Thrombocytopenia (Clinical Study). *Russian Sklifosovsky Journal of Emergency Medical Care.* 2022;11(1):12–21. <https://doi.org/10.23934/2223-9022-2022-11-1-12-21> (in Russ.)

**Conflict of interest** Authors declare lack of the conflicts of interests

**Acknowledgments, sponsorship** The study has no sponsorship

### Affiliations

Elena N. Plakhotina	Doctor of Medical Sciences, Head of the Department of Anesthesiology and Intensive Care, Vidnovsky Perinatal Center; <a href="https://orcid.org/0000-0002-6793-2318">https://orcid.org/0000-0002-6793-2318</a> , enp2004@inbox.ru; 45%, development of research design, analysis of the data obtained, description and presentation of research results, writing an article
Tamara N. Belousova	Candidate of Medical Sciences, Chief Physician of Vidnovsky Perinatal Center; <a href="https://orcid.org/0000-0003-3804-7691">https://orcid.org/0000-0003-3804-7691</a> , beltamara1@mail.ru; 20%, study design development and approval, patient selection, manuscript revision
Natalia B. Kuzina	Anesthesiologist-resuscitator of the Department of Anesthesiology and Resuscitation of the Vidnovsky Perinatal Center; <a href="https://orcid.org/0000-0002-1223-8740">https://orcid.org/0000-0002-1223-8740</a> , natal/kuzina2010@yandex.ru; 20%, implementation of the practical part of the work, documentation, statistical analysis of data
Artyom N. Kuzovlev	Doctor of Medical Sciences, Head of VA Negovsky Research Institute of General Resuscitation of the Federal State Budgetary Scientific Institution Federal Scientific and Clinical Center for Resuscitation and Rehabilitation, Head of the Laboratory of Clinical Pathophysiology of Critical Conditions; <a href="https://orcid.org/0000-0002-5930-0118">https://orcid.org/0000-0002-5930-0118</a> , artem_kuzovlev@mail.ru; 10%, study design development, manuscript revision

Evgeny V. Bryantsev	Anesthesiologist-resuscitator of the Department of Anesthesiology and Resuscitation of the Vidnovsky Perinatal Center; <a href="https://orcid.org/0000-0001-6155-9404">https://orcid.org/0000-0001-6155-9404</a> , <a href="mailto:evgeniyvla8@gmail.com">evgeniyvla8@gmail.com</a> ; 5%: implementation of the practical part of the work, collection of material, documentation
---------------------	---

$\alpha$ -angle	– clot formation kinetics
ALV	– artificial lung ventilation
APTT	– activated partial thromboplastin time
BP	– blood pressure
BMI	– body mass index
CI	– coagulation index
F <sub>LEV</sub>	– functional fibrinogen level
G	– clot density
GT	– gestational thrombocytopenia
HR	– heart rate
K	– clot formation time from R to 20 mm
LY	– clot lysis index
MA	– maximum amplitude
MAp	– maximum platelet amplitude
MFF	– maximum amplitude without the participation of platelets
NAB	– neuraxial block
NAH	– neuraxial hematoma
PTI	– prothrombin index
R	– reaction time
TEG	– thromboelastography

## INTRODUCTION

Gestational thrombocytopenia (GT) is the most common type of thrombocytopenia in pregnancy. Its frequency by the end of pregnancy reaches 6.6–11.6% and accounts for 70–80% of all cases of thrombocytopenia revealed during pregnancy. According to modern concepts, GT is physiological [1–7]. Despite this, the detection of GT is the reason for the refusal to perform neuraxial analgesia/anesthesia during delivery [8], which not only worsens the quality of care, but can also makes a threat to the life and health of the patient. For example, in the case of an emergency operative delivery of a patient with a "difficult airway" or "full stomach".

The main reason for refusal of neuraxial block (NAB) in labor with thrombocytopenia is the risk of developing neuraxial hematoma (NAH). However, according to the literature, the incidence of post-puncture NAH in the general population ranges from 1:3 600 to 1:775 000 and does not correlate with thrombocytopenia [9–15]. In obstetric practice, the incidence of NAH is so low that, in general population studies, obstetric patients are usually excluded from the analysis or analyzed in a separate sample. The risk of developing NAH after epidural analgesia in obstetric patients is estimated 1:168 000. Data on the development of this complication after subarachnoid anesthesia in obstetric patients are not available in the available literature. At the same time, as in the general population, no correlation was found between the development of NAH and thrombocytopenia [9–11, 16–22].

The historical roots of attempts to determine the threshold content of platelets in the blood during NAB are associated with the period when there was no possibility of an integral assessment of hemostasis with the allocation of its functional links: coagulation and cellular, as well as the possibility of separate analysis of the contribution of platelets and fibrinogen to clot formation. Probably, in those conditions, the only guideline in determining contraindications to NAB was a quantitative platelet count.

At present, the permissible lower limits of platelet count during NAB in the global medical community have not been determined. Despite the fact that in the Russian clinical guidelines the level of platelets  $100 \times 10^9/l$  is borderline for epidural anesthesia, and  $70 \times 10^9/l$  – for subarachnoid, the clinical recommendations of various countries for the most part do not include thrombocytopenia without clinical manifestations as a criterion that must be assessed during neuraxial anesthesia [1, 8, 21, 23–27]. At the same time, there is growing interest in the possibility of assessing the functional activity of platelets in thrombocytopenia, including integral elastometric tests. Studies have shown that in pregnant women with a platelet level above  $55 \times 10^9/l$ , the

coagulation and cellular components of hemostasis remain within the limits of normocoagulation and, therefore, the conditions for safe NAB are preserved [27, 28]. However, it should be noted that the possibilities of integral tests for assessing hemostasis in thrombocytopenia in obstetric practice in order to assess the safety of NAB have not been studied enough, which in most cases leads to an unjustified refusal to conduct them and a decrease in the quality of anesthetic care.

**Aim of the study:** to determine the possibility of safe use of NAB in GT.

Research objectives:

1. To study the dynamics of changes in the content of platelets and hemostasis parameters in the perinatal period in patients with the development of GT in comparison with the group of patients without thrombocytopenia.
2. To conduct a comparative intergroup assessment of the state of plasma and cellular components of hemostasis before delivery and in the postpartum period according to thromboelastography — TEG.
3. To investigate the functional activity of platelets in patients with GT and normal platelet count in the peripartum period using a test for functional fibrinogen.
4. To perform a comparative assessment of the volume of blood loss and complications of NAB during conservative and abdominal delivery in patients with and without GT.

## MATERIAL AND METHODS

In order to assess the effect of GT on the parameters of coagulation and cellular hemostasis and the safety of neuraxial blocks, a retrospective-prospective clinical study was conducted on the basis of the Vidnovsky Perinatal Center in the period from 2015 to 2020 with the participation of 70 patients who underwent conservative or surgical delivery in accordance with obstetric indications. The patients were divided into two groups depending on the content of platelets before the delivery. Group 1 (main) included 35 patients with GT. The criterion for inclusion in study group No. 1 was the presence of confirmed GT with a platelet count of less than  $100 \times 10^9/l$ . The exclusion criterion was thrombocytopenia of any etiology other than gestational. The diagnosis of GT was a diagnosis of exclusion and was made on the basis of anamnesis, prenatal record data on the dynamics of platelet count by trimesters of pregnancy, in the absence of thrombocytopenia before pregnancy, any clinical manifestations or changes in laboratory parameters after the exclusion of hepatitis C, HIV, immune thrombocytopenia, lymphoproliferative diseases, as well as complications of pregnancy, which may be accompanied by thrombotic thrombocytopenic purpura.

Group 2 (comparison) included 35 patients without thrombocytopenia. The criterion for inclusion in this group was the level of platelets not lower than  $150 \times 10^9/l$ . GT was included in the exclusion criteria. Also, the criterion for exclusion from both groups was refusal to participate in the study.

The conduct of the scientific study was approved by the ethical committee of V.A. Negovsky Research Institute of General Resuscitation, protocol No. 2/20/3 dated June 10, 2020.

For a comparative assessment of the coagulation potential of patients in both groups, a complete blood count was performed with the counting of the number of platelets in a stained smear according to the Fonio method; coagulograms; a comprehensive assessment of hemostasis was performed using a TEG 5000 thromboelastograph (Heamonetics, USA) on the day of delivery (immediately before caesarean section or during delivery) and on the 2<sup>nd</sup> day after delivery. In order to determine the contribution of coagulation and platelet hemostasis to the process of thrombosis, an assessment of total coagulation was performed with a test for functional fibrinogen. At the same time, the following thromboelastogram indicators were analyzed: reaction time (R), clot formation time from R to 20 mm (K), clot formation kinetics ( $\alpha$  -angle), maximum amplitude (MA), percentage of lysis 30 minutes after reaching MA (L30), coagulation index (CI), clot density (G), maximum platelet amplitude (MAp), maximum amplitude without platelet involvement (MAFF) and functional fibrinogen level ( $F_{LEV}$ ).

To assess the dynamics of platelet count and changes in coagulation during the development of GT during pregnancy, a retrospective analysis of laboratory data on the prenatal records of pregnant women was carried out. The volume of blood loss in childbirth and the risk of developing NAB complications in GT were analyzed in comparison with the control group.

Statistical analysis of the study results was performed using the Statistica 10 program (StatSoftInc., USA). The distribution was not tested for normality in the studied groups. Descriptive statistics are presented as median (Me), 25% and 75% percentiles (P25 and P75). Nonparametric criteria were used for comparison.

Comparison of quantitative data in two unrelated groups was performed using the Mann-Whitney U-test . Friedman test and Wilcoxon test were used to compare quantitative data in related groups. For the analysis of qualitative features, Pearson's  $\chi^2$  criterion was used. Differences were considered statistically significant with a significance level of less than 0.05.

## RESULTS

The studied groups were comparable in terms of age and delivery time (Table 1).

Table 1

### Evaluation of the representativeness of the study groups

Indicator, Me (R <sub>25</sub> ; R <sub>75</sub> )	Group 1, n =35	Group 2, n =35	P (Mann-Whitney U-test)
Age, years	30.5 (27; 32)	29 (25; 32)	0.34
Delivery time, weeks	39 (39; 40)	39 (39; 40)	0.66
Body mass index, kg/m <sup>2</sup>	26 (24.4; 28.7)	27.3 (25.5; 30.8)	0.049

The exception was the body mass index (BMI), which was statistically significantly higher in group 2, which, however, could not significantly affect the results of the study. When comparing the frequency and nature of concomitant pathology and methods of delivery, no intergroup differences were found:  $p > 0.05$  (criterion  $\chi^2$ ).

A study of the dynamics of platelet count during pregnancy showed that thrombocytopenia in Group 1 (unlike the comparison group) is determined already in the first trimester, followed by a statistically significant decrease in this indicator as pregnancy progresses (Table 2).

Table 2

### Intergroup analysis of the dynamics of the platelets content, $\times 10^9/l$

Stage	Group 1, n =35 Me ( P <sub>25</sub> ; P <sub>75</sub> )	Group 2, n =35 Me ( P <sub>25</sub> ; P <sub>75</sub> )	P (Mann-Whitney U-test)
trimester 1	147 (126; 179)	223.5 (198; 286.3)	0.001
trimester 2	135 (114.5; 158.1)*	218 (190.5; 263.5)	0.001
trimester 3	115 (98; 124)*	235 (203; 274)	0.001
childbirth	84 (80; 90)*	194 (175.5; 232)	0.001
2 <sup>nd</sup> day after delivery	105 (96; 112)*	214 (194; 234.5)	0.001
P (Friedman test)	0.008	0.097	

Note: \* –  $p < 0.05$  (Wilcoxon-test)

The platelet content in Group 1 reached its minimum values by the time of delivery. However, already by the 2<sup>nd</sup> day of the postpartum period in the group of patients with GT, there was a significant increase in the concentration of platelets to the level of this indicator in the third trimester.

In Group 2, the platelet count during pregnancy remained constant. There was a trend towards a decrease in this indicator by the time of delivery. Such changes are physiological in nature, reflecting the maximum increase in the volume of circulating plasma during this period, associated with the development of hemodilution.

Despite a statistically significant decrease in the platelet count in Group 1 as pregnancy progressed, no differences in coagulogram parameters were obtained at the same stages (Fig. 1).

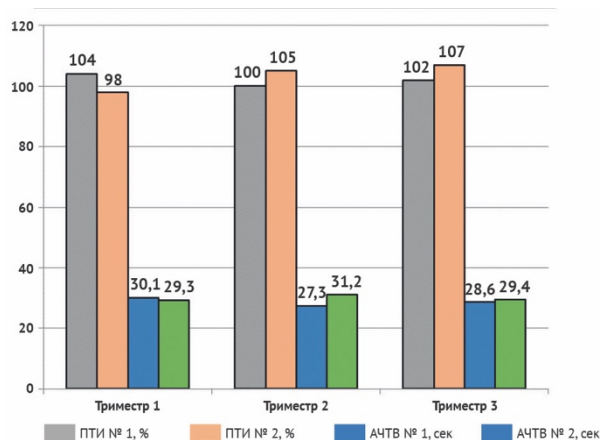


Fig. 1. Comparative analysis of coagulogram parameters by trimesters of pregnancy (Mann-Whitney U-test >0.05; Friedman-test >0.05)

Notes: APTT – activated partial thromboplastin time; PTI – prothrombin index

At the stages of the study, coagulography results were obtained in both groups, indicating normal coagulation throughout pregnancy.

Before delivery, when the platelet count reached the minimum values in Group 1, all coagulographic parameters remained within normal values and did not undergo statistically significant changes in comparison with the period of pregnancy (Table 3).

Table 3

**Dynamics of coagulogram indicators in the peripartum period**

Indicators coagulogram Me (P <sub>25</sub> ; P <sub>75</sub> )	Group 1, n =35		P *	Group 2, n =35		P *
	childbirth	2nd day after birth		childbirth	2nd day after birth	
APTT, sec	29 (26.4; 31)	27.7 (24.5; 28.95)	0.06	28.8 (26.9; 29.9)	28 (25.9; 30.6)	0.64
PTI, %	102 (93.3; 114)	105 (98.4; 115.2)	0.017	104.3 (92.9; 118.2)	107.9 (99.3; 119.1)	0.028
Thrombin time, sec	16.95 (16; 17.6)	16.95 (16.3; 17.5)	0.8	17 (16.5; 17.95)	17.3 (16.6; 17.9)	0.6
Fibrinogen, g/l	4.4 (3.9; 4.95)	4.5 (4.05; 4.9)	0.9	4.1 (3.7; 4.5)	4.3 (3.6; 4.9)	0.2

Note: \* - Wilcoxon-test; p>0.05, Mann-Whitney U-test. APTT, activated partial thromboplastin time; PTI, prothrombin index

In both groups, there was a statistically significant increase in the prothrombin index (PTI) in the postpartum period, while an intergroup analysis of coagulographic parameters during and after childbirth did not reveal statistically significant differences (Mann-Whitney U-test, p >0.05). It should be noted that immediately after delivery in the GT group, there was a significant increase in platelet count, although it didn't reach normal values during this period (Table 2). A statistically significant increase in PTI in both groups in the postpartum period indicated the activation of coagulation processes at this stage, which didn't depend on the content of platelets.

Taking into account the fact that the coagulographic parameters do not give an idea of the state of the hemostasis system as a whole and do not reflect changes in its cellular (platelet) link, TEG was analyzed using a functional fibrinogen test on the day of delivery and on the second day of the postpartum period.

The main indicators of TEG, reflecting the state of the plasma link of hemostasis (R, K, angle  $\alpha$ ), in patients with GT on the day of delivery, statistically significantly differed from those of patients in the comparison group, but remained within normal values. MA (FF) and F<sub>LEV</sub>, correlated with the concentration of fibrinogen, before delivery in both groups exceeded normal general population values and had no significant intergroup differences. After childbirth, these indicators increased significantly in the GT group and statistically significantly exceeded these indicators in the comparison group. Calculated indicators such as coagulation index (CI) and clot density (G) did not undergo statistically significant changes at the stages of the study in both groups. Despite the fact that clot density (G) and coagulation index (CI) during the delivery in the GT group were statistically significantly lower, the values of these calculated indicators remained above the population

norm during and after labor in both groups. In general, in the postpartum period, statistically significant changes in the main parameters of the plasma link of hemostasis were noted, mainly in the group of gestational thrombocytopenia, indicating the development of a trend towards hypercoagulability, which is normal for the postpartum period (Table 4).

Table 4

**Comparative analysis of thromboelastography parameters in the perinatal period**

Indicators TEG Me (R <sub>25</sub> ; R <sub>75</sub> )	Group 1, n =35		P **	Group 2, n =35		P **	Norm
	Before childbirth	2 days postpartum		Before childbirth	2 days postpartum		
R, min	11.1 (9.8; 12.7)*	10.7 (7.8; 12.5)	0.33	8.1 (6.75; 10.2)*	9.7 (6.5; 12.1)	0.58	9–27
K, min	2.9 (2.3; 4.1)*	2.2 (1.8; 3)	0.007	2.2 (1.8; 2.8)*	2 (1.8; 2.5)	0.06	2–9
Angle $\alpha$ , degrees	54.6 (44.7; 8.8)*	59.6 (52.9; 63.7)	0.062	59.8 (53.5; 64.7)*	58.1 (42.2; 67.7)	0.8	22–58
MA mm	64.5 (59.4; 68.9)	69.3 (63.6; 71.6)	0.104	67.9 (64.3; 70.3)	69.6 (65.1; 75)	0.02	44–64
G, units	8.7 (6.9; 10.5)*	10.3 (7.2; 12.1)	0.14	10.5 (8.93; 11.8)*	10.9 (9.5; 14.6)	0.09	3.6–8.5
CI	1.6 (0.7; 2.2)*	2.4 (1.1; 3)	0.12	2.6 (1.7; 3.1)*	2.6 (2; 3.6)	0.12	(-3)–(+3)
LY 30%	0 (0; 1)	0.2 (0; 2.2)	0.009	0.1 (0; 0.8)	0.8 (0; 1.3)	0.035	0–8
MA (FF) , mm	30.9 (27.6; 33.9)	34.5 (27.7; 37)*	0.005	31.2 (27.3; 33.8)	31 (29.2; 34.8)*	0.8	11–24
MApl , mm	35.3 (28.8; 37.7)	35.5 (26.8; 38.95)	0.7	34.6 (28.2; 40.2)	37.3 (33.7; 40.1)	0.32	25–35
F <sub>LEV</sub> , g/l	5.5 (5; 6.1)	6.3 (5; 6.9)*	0.002	5.6 (4.85; 6.1)	5.7 (5.3; 6.3)*	0.46	2–4

Note: \* - Mann-Whitney U-test :  $p < 0.05$ ; \*\* – Wilcoxon-test. TEG – thromboelastography, R – time gap between the initiation of the test and the formation of the first fibrin strands; K – the time from the moment the clot starts to form until the strength of the clot with an amplitude of 20 mm is reached;  $\alpha$  is the angle representing the growth rate of the fibrin network and the increase in clot strength; MA – maximum amplitude, an indicator of the maximum strength of the clot; CI – indicator of the overall assessment of the coagulation system in the direction of hypercoagulation or hypocoagulation; LY 30 – indicator of clot lysis during the 30 minutes following the achievement of MA; MA (FF) – indicator of the maximum strength of the clot without the participation of platelets; MApl – difference between MA and MA (FF) characterizes platelet function; F<sub>LEV</sub> – fibrinogen level

Despite the decrease in the platelet count in patients of group No. 1, the parameters of the cellular hemostasis link: MA (maximum amplitude in a sample with citrated blood) and Mapl (maximum amplitude obtained only with the participation of platelets) on the day of delivery were within the normal range, didn't change statistically significantly in the postnatal period and did not differ from those in the comparison group. Thus, at the stages of the study, platelet function in patients with GT remained intact (Table 4).

Two days after delivery, both groups showed a statistically significant increase in fibrinolysis activity, which did not go beyond the reference values, which can be regarded as an adequate response of the hemostasis system to postpartum hypercoagulation.

All anesthesia during childbirth was carried out according to obstetric indications after clinical and laboratory confirmation of the absence of coagulation disorders in patients according to the coagulogram and TEG with a test for functional fibrinogen. The frequency and nature of anesthesia during the delivery are shown in Fig. 2. In Group 1, epidural analgesia for pain relief through the birth canal was used much less frequently than in the comparison group, which was due to the lack of indications for its implementation and the desire of patients.

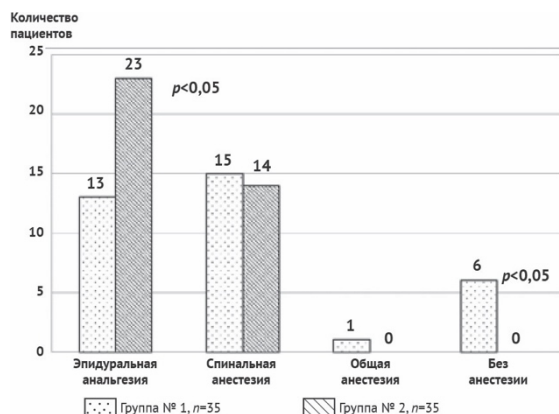


Fig. 2. The frequency and type of anesthetic aids during delivery (Mann-Whitney U-test)

Spinal anesthesia was performed if a caesarean section was necessary; there were no statistically significant intergroup differences in the frequency of performing this type of anesthesia. One patient from group No. 1 required general anesthesia with artificial lung ventilation (ALV) due to the onset of premature detachment of a normally located placenta lobule, ongoing bleeding, which was an indication for emergency abdominal delivery.

For a comparative assessment of the volume of blood loss during childbirth, the study groups were divided into two subgroups: vaginal delivery and caesarean section (Fig. 3).

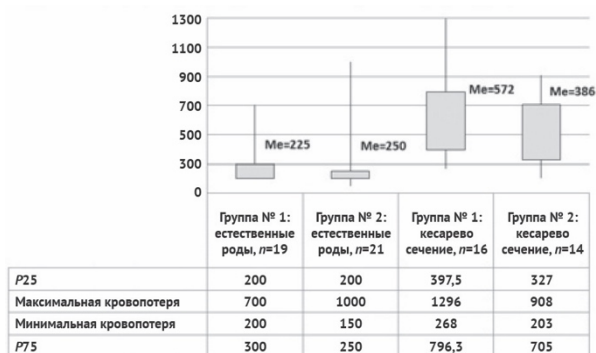


Fig. 3. Comparative analysis of the volume of blood loss during childbirth (Mann-Whitney U-test,  $p>0.05$ )

Intergroup analysis of blood loss volumes, taking into account the method of delivery, did not reveal statistically significant differences. All cases of blood loss exceeding physiological amount during vaginal and operative delivery in both groups were associated with uterine hypotension. The absence of coagulopathy was confirmed by TEG results. Correlation analysis between the volume of blood loss and platelet count during caesarean section and during vaginal delivery did not reveal a statistically significant relationship.

In the early postnatal period, there were no complications of anesthesia in the study groups.

As a clinical example, we report an extract from the medical record of 34-year-old patient L., BMI — 32.1 kg/m<sup>2</sup>, who was admitted to the Vidnovsky Perinatal Center with a diagnosis: “First pregnancy, 39.3 weeks. First stage of delivery. Gestational thrombocytopenia. Lipid metabolism disorder of 1<sup>st</sup> degree. Gestational diabetes. Gestational arterial hypertension. Upon admission, the patient complained of severe pain associated with the onset of delivery. Objectively, the patient's condition was satisfactory, the skin was of normal color and moisture. The petechial rash on the skin and mucous membranes was not revealed during examination. Blood pressure (BP) — 135/85 mm Hg, heart rate (HR) — 88/min outside of contractions. During contractions, blood pressure increased to 180/110 mm Hg, heart rate — 92–98/min. Laboratory parameters upon admission: hemoglobin — 112 g/l, RBC —  $3.2 \times 10^{12}/l$ , WBC —  $16 \times 10^9/l$ , platelets —  $49 \times 10^9/l$  (Fonio method), APTT — 26 sec, PTI — 104%, fibrinogen — 5.4 g/l. Taking into account gestational hypertension and a significant increase in blood pressure during labor, the patient was recommended to deliver under epidural analgesia. To assess the state of plasma and cellular components of hemostasis, the participation of platelets in the formation of a clot, the patient underwent TEG with a test for functional fibrinogen (Fig. 4). TEG data indicated moderate

hypercoagulability in the plasma component, characteristic of the third trimester of pregnancy, normal coagulation in the cellular component, normal clot density and coagulation index, and the absence of fibrinolysis activation. The test for functional fibrinogen showed the preserved function of platelets and their participation in the clot formation (MApl =31.6 mm). The study allowed to perform catheterization of the epidural space and deliver under conditions of prolonged epidural analgesia. The further course of childbirth proceeded without complications. The total blood loss during childbirth was 268 ml.

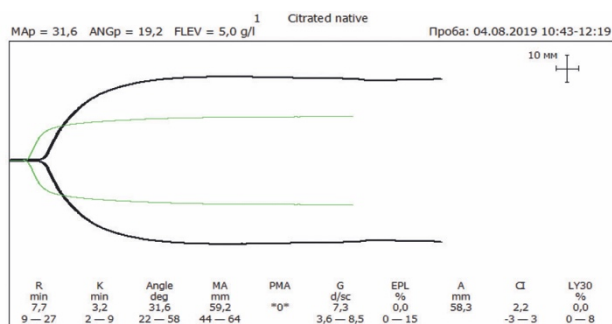


Fig. 4. Thromboelastography with a test for functional fibrinogen of patient L., platelet concentration —  $49 \times 10^9/l$ . First stage of delivery

The postpartum period proceeded without complications. On the 2<sup>nd</sup> day, according to laboratory data, there was an increase in platelet concentration up to  $78 \times 10^9/l$ , APTT — 26 sec, PTI — 108%, fibrinogen — 4.8 g/l. The performed TEG (Fig. 5) indicated an increase in coagulation potential (increased hypercoagulation in the plasma component and hypercoagulation in the cellular component, an increase in the contribution of platelets to thrombus formation, an increase in clot density and coagulation index), as well as a moderate activation of fibrinolysis. The early postpartum period proceeded without complications. On the 3<sup>rd</sup> day after delivery, the patient with the newborn was discharged home in a satisfactory condition, the platelet count upon discharge was  $156 \times 10^9/l$ .

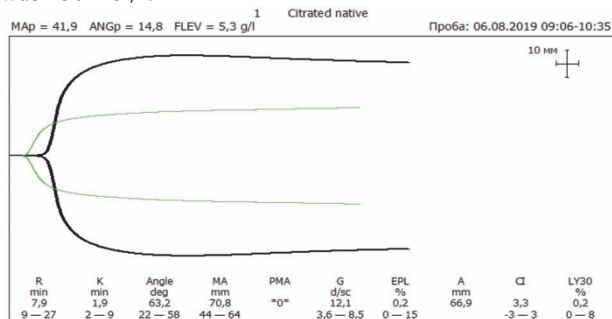


Fig. 5. Thromboelastography with functional fibrinogen test of patient L., platelet concentration —  $78 \times 10^9/l$ . Day 2 after childbirth

## DISCUSSION

The results of the study indicate the preservation of the coagulation component of hemostasis in pregnant women with GT at different gestation periods. The progression of GT during pregnancy is not accompanied by coagulation disorders. The data obtained are consistent with the results of studies by other authors, showing the absence of coagulation disorders and hemorrhagic complications in patients with GT, even with a decrease in platelet count below  $50 \times 10^9/l$  [24, 29, 30].

The use of TEG with a test for functional fibrinogen for a comprehensive assessment of hemostasis and determination of the contribution of platelets to thrombus formation did not reveal hypocoagulation disorders in the plasma and cellular components of hemostasis in patients with GT in the peripartum period. Despite the fact that during childbirth in the GT group, the indicators of plasma hemostasis, thrombus density and coagulation index were statistically significantly lower than in the group without thrombocytopenia at this stage, all indicators remained within the normal range. There were no differences in the indicators responsible for the cellular link of hemostasis. In both study groups, there was an increase in the activity of the plasma link



of hemostasis with activation of fibrinolysis in the postpartum period, which was more pronounced in patients with gestational thrombocytopenia, and the absence of significant changes in the cellular component. The significantly greater increase in the participation of fibrinogen should be noted in the formation of a thrombus in the group of patients with thrombocytopenia in the postpartum period, which may indicate compensatory, mutually substituting capabilities of the components of the hemostasis system. Thus, the coagulation status of patients with GT should not be assessed by individual indicators, such as platelet count, prothrombin time, or APTT, but based on a comprehensive assessment of the interaction of various hemostasis links and their participation in clot formation. In particular, the possibilities of using TEG to assess the state of the hemostasis system at very low platelet concentrations in pregnant women were investigated by C. Orlikowski et al., 1996; J. Huang, 2016 [25, 26]. The works of these authors also showed the absence of disturbances in the plasma and cellular components of hemostasis in gestational thrombocytopenia.

Modern international guidelines determine the possibility of NAB in pregnant women with thrombocytopenia in the absence of laboratory and clinical signs of hypocoagulation [1, 3, 23–26], which was the basis for the use of these methods of pain relief during childbirth in this study. The safety of using neuraxial methods of anesthesia in patients with GT in this study was confirmed in all cases by the absence of any clinical and laboratory disorders of coagulation. Gestational thrombocytopenia did not lead to an increase in blood loss during the delivery and in the early postpartum period, both with conservative and abdominal delivery. When observing patients in the early postnatal period, no complications of anesthesia were revealed in any of the groups. Similar results were obtained in studies by W. Ruppen 2006, M. Tanaka (2009), R. D'Angelo (2014) [18–22], which showed no correlation between thrombocytopenia and the development of NAH.

## CONCLUSION

The results of the study and the data of the analyzed literature suggest that in patients with gestational thrombocytopenia, even with a significant decrease in the blood platelet count, it is possible to perform neuraxial blocks during childbirth in the absence of clinical and laboratory signs of hemostasis disorders. Such an approach to assessing the possibility of performing neuraxial blocks during childbirth will not only improve the quality of anesthetic care for obstetric patients, but also increase its safety. However, this problem requires, on the one hand, further study to determine the capabilities of modern methods for assessing hemostasis to assess the safety of neuraxial blockades in patients with gestational thrombocytopenia. On the other hand, it should be noted that the use of neuraxial blocks in pregnant women with thrombocytopenia at the present stage is possible only in perinatal centers equipped with modern laboratory equipment for conducting tests for a comprehensive assessment of hemostasis.

1. The study confirmed the data on the dynamics of gestational thrombocytopenia during the progression of pregnancy with a maximum decrease in platelet count by the day of delivery. At the same time, it was shown that the decrease in the content of platelets during pregnancy is not accompanied by coagulation disorders.

2. The indicators of thromboelastogram in patients with gestational thrombocytopenia during childbirth and in the postpartum period indicate moderate hypercoagulability in the plasma and cellular levels, as well as in the comparison group.

3. Thromboelastography with a test for functional fibrinogen in patients with gestational thrombocytopenia did not reveal disorders of the functional activity of platelets in the peripartum period and statistically significant differences from these patients from the comparison group.

4. Confirmation of the preservation of normal hemostatic potential in patients with gestational thrombocytopenia in the study is the absence of complications of neuraxial blocks and bleeding associated with thrombocytopenia.

## REFERENCES

1. Cines DB, Levine LD. Thrombocytopenia in pregnancy. *Blood*. 2017;131(21):2271–2277. <https://doi.org/10.1182/blood-2017-05-781971>. PMID: 28637667
2. Umazume T, Yamada T, Morikawa M, Ishikawa S, Furuta I, Koyama T, et al. Platelet reactivity in twin pregnancies. *Thromb Res*. 2016;138:43–48. PMID: 26826507 <https://doi.org/10.1016/j.thromres.2015.12.019>
3. Kasai J, Aoki S, Kamiya N, Hasegawa Y, Kurasawa K, Takahashi T, et al. Clinical features of gestational thrombocytopenia difficult to differentiate from immune thrombocytopenia diagnosed during pregnancy. *J Obstet Gynaecol*. 2014;41(1):44–49. PMID: 25163390 <https://doi.org/10.1111/jog.12496>
4. Asif N, Hassan K. Thrombocytopenia in Pregnancy. *Hematol Transfus Int J*. 2017;5(5):307–309. <https://doi.org/10.15406/htij.2017.05.00133>

5. Fogerty AE Thrombocytopenia in pregnancy: mechanisms and management. *Transfus Med Rev.* 2018;32(4):225–229. PMID: 30177431 <https://doi.org/10.1016/j.tmr.2018.08.004>
6. Grandone E, Mingalimov MA, Grigoryeva KN, Bitsadze VO, Shkoda AS, Khizroeva DKh, et al. Thrombocytopenic syndromes during pregnancy. *Obstetrics and gynecology.* 2019;10:5–12. (in Russ.). <https://doi.org/10.18565/aig.2019.10.5-12>
7. Palta A, Dhiman P. Thrombocytopenia in pregnancy. *J Obstet Gynaecol.* 2016;36(2):146–52. PMID: 26431056. <https://doi.org/10.3109/01443615.2015.1041893>
8. Kulikova AV, Shifman EM, Sokolovskiy SV, Levit AL, Nedashkovskiy EV, Zabolotskikh IB, et al. Neyroaktsial'nye metody obezbolivaniya rodov. Klinicheskie rekomendatsii. Protokoly treatment. In: Kulikov AV, Shifman EM (eds.). *Anesthesiologiya, intensivnaya terapiya i reanimatsiya v akusherstve i ginekologii. Klinicheskie rekomendatsii. Protokoly treatment.* Moscow: Meditsina Publ.; 2017:153–169. (in Russ.) <https://doi.org/10.18821/9785225100384>
9. Lagerkranser M. Review of Neuraxial blocks and spinal haematoma: Review of 166 case re-ports published 1994–2015. Part 1: Demographics and risk factors. *Scand J Pain.* 2017;15:118–129. PMID: 28850335 <https://doi.org/10.1016/j.sjpain.2016.11.008>
10. Lagerkranser M, Lindquist Ch. Neuraxial blocks and spinal haematoma: Review of 166 cas-es published 1994–2015. Part 2: diagnosis, treatment, and outcome. *Scand J Pain.* 2017;15(1):130–136. PMID: 28850336 <https://doi.org/10.1016/j.sjpain.2016.11.009>
11. Bateman BT, Mhyre JM, Ehrenfeld J, Kheterpal S, Abbey KR, Argalious M, et al. The Risk and Outcomes of Epidural Hematomas After Perioperative and Obstetric Epidural Catheterization: A Report from the Multicenter Perioperative. *Anesth Analg.* 2013;116(6):1380–1385. PMID: 22504213 <https://doi.org/10.1213/ANE.0b013e318251daed>
12. Gulur P., Tsui B., Pathak R., Koury KM, Lee H. Retrospective analysis of the incidence of epiduralhaematoma in patients with epidural catheters and abnormal coagulation parameters. *Br J Anaesth.* 2015;114(5):808–811. PMID: 25614136 <https://doi.org/10.1093/bja/aeu461>
13. Ehrenfeld JM, Agarwal AK, Henneman JP, Sandberg WS. Estimating the Incidence of Suspect-ed Epidural Hematoma and the Hidden Imaging Cost of Epidural Catheterization: A Retrospective Review of 43,200 Cases. *Reg Anesth Pain Med.* 2013;38(5):409–414. PMID: 23924685 <https://doi.org/10.1097/AAP.0b013e31829ecfa6>
14. Pitkänen MT, Aromaa U, Cozanitis DA, Förster JG. Serious complications associated with spinal and epidural anaesthesia in Finland from 2000 to 2009. *Acta Anaesthesiol Scand.* 2013;57:553–564. PMID: 23305109 <https://doi.org/10.1111/aas.12064>
15. Van Veen JJ, Nokes TJ, Makris M. The risk of spinal haematoma following neuraxial anaesthesia or lumbar puncture in thrombocytopenic individuals. *Br J Haematol.* 2010;148(1):15–25. PMID: 19775301 <https://doi.org/10.1111/j.1365-2141.2009.07899.x>
16. Cuyper V, Van de Velde M, Devroe S. Intracranial subdural haematoma following neuraxial anaesthesia in the obstetric population: a literature review with analysis of 56 reported cases. *Int J Obstet Anesth.* 2016;25:58–65. PMID: 26597409 <https://doi.org/10.1016/j.ijoa.2015.09.003>
17. Goodier CG, Lu JT, Hebbard L, Segal BS, Goetzl L. Neuraxial Anesthesia in Parturients with Thrombocytopenia: A Multisite Retrospective Cohort Study. *Anesth Analg.* 2015;121(4):988–991. PMID: 26378701 <https://doi.org/10.1213/ANE.0000000000000882>
18. Ruppen W, Derry S, McQuay H, Moore RA. Incidence of Epidural Hematoma, Infection, and Neurologic Injury in Obstetric Patients with Epidural Analgesia/Anesthesia. *Anesthesiology.* 2006;105(2):394–399. PMID: 16871074 <https://doi.org/10.1097/00000542-200608000-00023>
19. D'Angelo R, Smiley RM, Riley ET, Segal S. Serious Complications Related to Obstetric Anesthesia The Serious Complication Repository Project of the Society for Obstetric Anesthesia and Perinatology. *Anesthesiology.* 2014;120(6):1505–1512. PMID: 24845921 <https://doi.org/10.1097/ALN.0000000000000253>
20. Bernstein J, Hua B, Kahana M, Shaparin N, Yu S, Davila-Velazquez J. Neuraxial Anesthesia in Parturients with Low Platelet Counts. *Anesth Analg.* 2016;123(1):165–167. PMID: 27159067 <https://doi.org/10.1213/ANE.0000000000001312>
21. Tanaka M, Balki M, McLeod A, Carvalho JCA. Anestesia Regional e Trombocitopenia Não Pré-Ecláptica; Hora de Repensar o Nível Seguro de Plaquetas. *Revista Brasileira de Anestesiologia.* 2009;59(2):142–153. PMID: 19488526 <https://doi.org/10.1590/S0034-70942009000200002>
22. Ray NP Can We Continue to Deny Neuraxial Anesthesia to Otherwise-Healthy Parturients With Thrombocytopenia? *Anesth Analg.* 2017;124(2):704–705. PMID: 28098703 <https://doi.org/10.1213/ANE.0000000000001785>
23. Bergmann F, Rath W. The Differential Diagnosis of Thrombocytopenia in Pregnancy. *Dtsch Arztebl Int.* 2015;112(47):795–802. PMID: 26634939 <https://doi.org/10.3238/arztebl.2015.0795>
24. Wang X, Xu Y, Luo W, Feng H, Luo Y, Wang Y, et al. Thrombocytopenia in pregnancy with different diagnoses Differential clinical features, treatments, and outcomes. *Medicine (Baltimore).* 2017;96(29):e7561. PMID: 28723784 <https://doi.org/10.1097/MD.00000000000007561>
25. Camann W. Obstetric Neuraxial Anesthesia Contraindicated? Really? Time to Rethink Old Dogma. *Anesth Analg.* 2015;121(4):846–848. PMID: 26378695 <https://doi.org/10.1213/ANE.0000000000000925>
26. Lee LO, Bateman BT, Kheterpal S, Klumpner TT, Housey M, Aziz MF, et al. Risk of Epidural Hematoma after Neuraxial Techniques in Thrombocytopenic Parturients. A Report from the Multi-center Perioperative Outcomes Group. *Anesthesiology.* 2017;126(6):1053–1064. PMID: 28383323 <https://doi.org/10.1097/ALN.0000000000001630>
27. Orlikowski CE, Roche DA, Murray WB, Gouws E, Moodley J, Kenoyer DG, et al. Thromboelastography changes in pre-eclampsia and eclampsia. *Br J Anaesth.* 1996;77(2):157–161. PMID: 8881617 <https://doi.org/10.1093/bja/77.2.157>
28. Huang J, McKenna N, Babins N. Utility of Thromboelastography During Neuraxial Blockade in the Parturient with Thrombocytopenia. *AANA J.* 2014;82(2):127–130. PMID: 24902455
29. Katz D, Beilin Y. Disorders of coagulation in pregnancy. *Br J Anaesth.* 2015;115(2):75–88. PMID: 26658204 <https://doi.org/10.1093/bja/aeu374>
30. Reese JA, Peck JD, Deschamps DR, McIntosh JJ, Knudtson EJ, Terrell DR, et al. Platelet counts during pregnancy. *N Engl J Med.* 2018;379:32–43. <https://doi.org/10.1056/NEJMoa1802897>

**Received on Mar 26, 2021**

**Review completed on Dec 22, 2021**

**Accepted on Dec 27, 2021**