ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Functional Activity Of Primary Hemostasis In Calves During The First Year Of Life.

Zavalishina S Yu*.

Russian State Social University, st. V. Pika, 4, Moscow, Russia, 129226.

ABSTRACT

The normal development of the functional capabilities of the body and its hemostasis is largely due to the optimal functional activity of platelets, causing the state of blood rheology, optimal blood flow to the tissues, optimum cardiac activity, a high level of resistance and intensive metabolism. For calves during early ontogenesis, a gradual increase in the functional activity of platelets was revealed. This was manifested by a reduction in their platelet aggregation time. Its increase with increasing chronological age can be seen due to the growth of exogenous effects on platelets, combined with an increase in villebrand factor blood concentration. The revealed increase in platelet activity inevitably leads to an increase in the number of aggregates of various sizes circulating in their blood during the first year of life. This is obviously an important adaptive value for maintaining homeostasis in the body of a growing animal. The regular dynamics of indicators of primary hemostasis during their early ontogenesis is associated with an increase in platelet activity, an increase in their active forms in the blood, which inevitably leads to an increase in the number of aggregates of various sizes circulating in the vessels. These changes should be considered very important for maintaining homeostasis in the context of increasing environmental effects on the animal organism.

Keywords: platelets, calves, functional early ontogenesis.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Of great importance in the adequate physiological development of calves a significant place is occupied by the age dynamics of the functional state of their primary hemostasis system [1,2,3]. There is no doubt that the normal development of the functional capabilities of the body and the entire hemostasis [4,5] is largely determined by the optimal functional activity of platelets [6,7], which determines the state of blood rheology [8,9], the optimal blood flow to the tissues [10,11], good cardiac activity [12,13], high level of resistance to respiratory diseases [14,15] and sufficient metabolic rate [16,17].

However, in early ontogenesis in calves, the state of lipid peroxidation of plasma and platelets and the activity of antioxidant enzymes of blood platelets [18,19], which largely determine the level of functional ability of blood plates [20,21], has not been clarified. Changes in the ontogenesis of calves of the aggregation function of platelets under the influence of various inductors and their combinations that are present in real blood flow conditions have not been elucidated [22,23]. They have not evaluated the age dynamics of the degree of morphological activity of platelets in the lumen of blood vessels. Based on this, the goal of the present study was formulated: to clarify the dynamics of the parameters of platelet functions in healthy calves during the first year of life.

MATERIALS AND METHODS

Research was conducted in strict accordance with ethical principles established by the European Convent on protection of the vertebrata used for experimental and other scientific purposes (adopted in Strasbourg March 18, 1986, and confirmed in Strasbourg June 15, 2006) and approved by the local ethic committee of Russian State Social University (Record №12 dated December 3, 2015).

Healthy calves were observed: 267 newborn calves, 22 calves of 30 day old, 21 calves of 3 months of age and 23 calves of one-year-old. The intra thrombocytic lipid peroxidation (LPO) was evaluated by the concentration of the basal level of malondialdehyde (MDA) in the reduction reaction with thiobarbituric acid and by the level of acyl hydroperoxides (AHP). The number of platelets in capillary blood in the Goryaev chamber was counted. The products of platelet-induced phospholipid-coagulation activators (F3-platelets) labilization were traditionally evaluated by calculating the platelet activity index. Platelet aggregation (AP) was studied by a visual micromethod using as inducers ADP (0.5×10^{-4} M), collagen (dilution 1: 2 of the main suspension), thrombin (0.125 units / ml), ristomycin (0.8) mg / ml), adrenaline (5×10^{-6} M), as well as combinations of ADP and adrenaline, ADP and collagen, adrenaline and collagen to simulate real blood flow conditions. Intravascular platelet activity was determined visually using a phase contrast microscope. Statistical processing of the results obtained was carried out using Student's t-test.

RESEARCH RESULTS

All calves included in the study were under constant surveillance. Before each study during the entire neonatal period and in the subsequent periods of examination, they determined the main physiological parameters, carried out morphological and biochemical blood tests. The results of these studies showed that the estimated total functional and biochemical values (temperature, heart rate, respiration rate, white blood cell count, protein concentration and blood thickening level) in the examined calves during all observation periods were within the physiological age norm.

The content of primary products of LPO-AHP in platelets of healthy calves aged 1-2 days was at the level of 2.90±0.02 $D_{233}/10^9$ platelets, not changing significantly during the entire neonatal phase, averaging 2.87±0.04 $D_{233}/10^9$ platelets. At the same time, the level of basal MDA in platelets - the end product of POL in 1-2 days of life in calves reached a level of 0.86±0.05 nmol/10^9 platelets, also without changing during the first 10 days of life, averaging over the neonatal phase 0.89±0.02 nmol/10^9 platelets.

The level of catalase and superoxide dismutase activity in the blood plates under the supervision of healthy calves did not have reliable dynamics, averaging over the estimated period 10500.0±11.05 IU/10^9 platelets and 1780.0±2.06 IU/10^9 platelets, respectively.

In older animals, an increase in the activity of catalase and superoxide dismutase was noted (on 30 days 10550.0±14.20 IU/10^9 platelets, 1810.0±2.18 IU/10^9 platelets, 3 months - 10620.0±11.50 IU/10^9 platelets, 1830.0±1.82 IU/10^9 platelets, 1 year - 10710.0±14.20 IU/10^9 platelets, 1880.0±2.80 IU/10^9 platelets, respectively), which caused a tendency to weakening of the LPO in the blood plates, which amounted to 1 year of life (basal MDA 0.63±0.04 nmol/10^9 platelets, AHP 2.52±0.02 D_{233}/10^9 platelets).

The platelet activity index in the first two days of life of the calves was 25.3±0.05%, remaining at this level during the entire neonatal phase. This indicated the stability during the given age period in the blood plates of healthy calves of the level of the products of labilization of platelet phospholipids - coagulation activators. An assessment of the platelet activity index of older calves showed its tendency to increase - 30 days 25.6±0.02%, 3 months - 26.0±0.06%, having reached 27.2±0.07% of the reliable level by year 1 ($p<0.05$).

In calves at 1–2 days old, the time of AP development under the influence of collagen was 29.4 ± 0.26 s, being at a fairly low level during the newborn. Similar AP dynamics in healthy newborns were observed under the influence of ADP (mean 39.0 ± 0.28 s) and ristomycin (mean 41.0 ± 0.26 s). Later, thrombin and adrenaline antibodies developed, also in the absence of their reliable dynamics during the neonatal phase, averaging 54.0±0.2s and 97.0±0.45 s during the first 10 days of life, respectively. The established absence of AP dynamics in newborn calves with an isolated application of inductors was consistent with the stability of their AP development time against the background of a combination of inductors that averaged: for ADP + adrenaline - 36.0±0.50 s, for ADF + collagen - 27.0± 0.09s, for adrenaline + collagen - 30.1±0.12 s.

The combination of aggregation inducers that occur in real blood flow conditions in animals has made it possible to more closely approximate our understanding of in vivo in healthy animals to the platelet aggregation process that actually occurs in their bloodstream during the entire neonatal period. At the end of the neonatal period in calves, a tendency to accelerate AP was noted by 30 days, and by 3 months already. its significant gain, fixed by one year old.

The revealed patterns were confirmed by the study of intravascular platelet activity. The level of discocytes in the blood of healthy newborn calves in the first 1-2 days of life was 76.1±0.03%, not changing significantly throughout the entire neonatal period (on average - 82.0±0.16%). The number of disco-echinocytes, spherocytes, sphero-echinocytes and bipolar forms of platelets also remained stable in the bloodstream throughout the neonatal phase. As a result, the sum of the active forms of platelets also did not change significantly, averaging 18.0±0.2%. In the blood of newborn calves, the levels of free-circulating small and large platelet aggregates did not have reliable dynamics, amounting to 3.4±0.06 and 0.15±0.03 per 100 free platelets at the beginning of the neonatal period and 3.8±0.06 at its end, and 0.13±0.02 per 100 free-lying platelets, respectively. The number of platelets involved in the aggregation process in healthy calves at the beginning of the neonatal phase was 5.3±0.08%, at its end 5.3±0.02%. By 30 days of age in healthy calves, there was a tendency to increase, and for a number of indicators a slight significant increase in the intravascular activity of platelets, which increased by 3 months. and especially to 1 year of life (the sum of the active forms is 19.6±0.03%, 21.6±0.04% and 23.9±0.05%, respectively). These data indicate the stability of intravascular platelet activity in vivo in the neonatal phase in healthy calves, providing them with optimal microcirculation during adaptation to extrauterine life with subsequent enhancement of the intravascular platelet activity under the influence of environmental influences necessary for adequate hemostasis aimed at maintaining the growing organism of the animal.

DISCUSSION

The state of body reactivity is largely formed under the action of an adequate supply of nutrients due to the rheology of blood [24] and changes during ontogenesis [25], maturation of organs and improvement of their functions [26,27]. An important role in the dynamics of its state is played by the level of LPO of platelets [28,29].

In healthy physiologically mature newborn calves, there is stability for 10 days of antioxidant activity of platelets, the level of LPO in them, which causes the stability of the activity of primary hemostasis, rather weakly stimulating platelets [30,31]. This largely contributes to a stable low activity of blood platelets in calves in the neonatal phase [32,33].

During ontogenesis in calves, a gradual increase in the functional activity of platelets is revealed [34]. Thus, in newborn calves, AP was rather low, gradually increasing with increasing chronological age [35]. This is obviously due to the growth of exogenous effects on platelets, including an increase in the concentration of von Willebrand factor in the blood - a platelet adhesion cofactor [37,38] with a simultaneous increase in the number of receptors to it on the surface of platelets [39,40]. Receptor rearrangements on the surface of the blood plates caused by the maturation of the hemostatic system are the result of complex adaptive reactions in animals and membrane changes in platelets, which ultimately result in optimal adaptation of platelet hemostasis in the postnatal period [41].

Evaluation of antibodies with a variety of inductors and their combinations confirmed in calves during ontogenesis, an increase in the aggregative function of blood plates [42]. Acceleration of antibodies with strong agonists of aggregation - collagen and thrombin with receptors on the platelet membrane is caused by the activation of phospholipase C [43], which stimulates the phosphoinositol pathway through diacylglycerol and protein kinase C with phosphorylation of proteins of the contractile system [44]. Inositol triphosphate promotes the release of Ca^{2+} from intra platelet depots [45]. The implementation of these mechanisms leads to the intensification of actomyosin contraction [46].

It is likely that maturation of platelet enzyme systems plays a role in enhancing this process, leading to an earlier reaction of platelets to stimuli.Similar reactions were noted for weak agonists of platelet aggregation - ADP and adrenaline interacting with their membrane receptors and causing the expression of fibrinogen receptors stimulating phospholipase A_2, regulating the release of phospholipids of arachidonic acid with increased formation of thromboxane A_2 [47].

The simultaneous use of several inductors showed their mutually potentiating action, confirming the patterns found in the study of antibodies with isolated inducers [48].

The increase in intravascular platelet activity during ontogenesis indirectly indicates an increase in the physiological level of aggregation inducers (thrombin, ADP, adrenaline) in the vascular bed, increasing the baseline level of platelet activity [49]. At the same time, in healthy calves to 3 months and 1 year in the blood there is a tendency to a decrease in the number of intact discoid forms of platelets, indicating a higher basal activity [50-51]. An increase in the level of disco-echinocytes and other active forms coincides with an increase in the hemostatic activity of platelets, associated with the expression of fibrinogen receptors on their membrane [52-53].

CONCLUSION

During the ontogeny of calves, as they grow, platelet activity increases, increasing the content of their active forms in the bloodstream, inevitably leading to an increase in the number of circulating aggregates of various sizes, which is obviously of adaptive importance for maintaining homeostasis, resulting from an increase in environmental effects on animals.

REFERENCES

[1] Medvedev IN. (2018) The State Of Aggregation Properties Of Neutrophils In Patients With Abdominal Obesity And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 1985-1989.
[2] Medvedev IN. (2018) Severity Of Erythrocyte Aggregation In Patients With Hyperuricemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2025-2030.
[3] Medvedev IN. (2018) Activity Of Aggregation Properties Of Neutrophils In Patients With Arterial Hypertension With Type 2 Diabetes Mellitus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2043-2047.
[4] Medvedev IN. (2018) Increased Aggregation Properties Of Platelets In Patients With Hyperuricemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :2048-2053.
[5] Medvedev IN. (2018) Severity Of Aggregation Properties Of Neutrophils In Patients With Hyperuricemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2088-2093.
[6] Medvedev IN. (2018) Aggregation Of Erythrocytes In Patients With Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 1676-1681.

[7] Medvedev IN. (2018) Platelet Aggregation Activity In Patients With Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :1738-1743.
[8] Medvedev IN. (2018) Intensity Of Neutrophil Aggregation In Patients With Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :1778-1783.
[9] Medvedev IN. (2018) Aggregational Properties Of Erythrocytes In Patients With Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 1803-1808.
[10] Medvedev IN. (2018) Aggregation Of Thrombocytes In Patients With Arterial Hypertension And Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 1604-1609.
[11] Medvedev IN. (2018) Severity Of Neutrophil Aggregation In Patients With Arterial Hypertension With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :1647-1651.
[12] Medvedev IN. (2018) Aggregational Capacity Of Platelets In Patients With Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :1830-1835.
[13] Medvedev IN. (2018) The Ability To Aggregate Neutrophils In Patients With Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 1861-1866.
[14] Medvedev IN. (2018) Intensity Of Spontaneous Aggregation Of Erythrocytes In Patients With Abdominal Obesity And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :1919-1924.
[15] Medvedev IN. (2018) Expression Of Aggregation Capacity Of Platelets In Abdominal Obesity And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :1941-1946.
[16] Medvedev IN. (2018) The Level Of Erythrocyte Aggregation In Patients With Type 2 Diabetes Mellitus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2115-2120.
[17] Medvedev IN. (2018) Aggregational Activity Of Thrombocytes In Patients With Type 2 Diabetes Mellitus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :2137-2142.
[18] Medvedev IN. (2018) Severity Of Aggregation Neutrophils In Patients With Type 2 Diabetes Mellitus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :2162-2167.
[19] Medvedev IN. (2018) Intensity Of Spontaneous Aggregation Of Erythrocytes In Patients With Impaired Glucose Tolerance And Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2173-2178.
[20] Medvedev IN. (2018) Activity Of Platelet Aggregation In Patients With Impaired Glucose Tolerance And Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2183-2188.
[21] Medvedev IN. (2018) Severity Of Aggregation By Neutrophils In Patients With Impaired Glucose Tolerance And Abdominal Obesity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2194-2199.
[22] Medvedev IN. (2018) Features Of Erythrocyte Aggregation In Patients With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :2210-2215.
[23] Medvedev IN. (2018) Aggregation Of Platelets In Patients With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) :2226-2231.
[24] Medvedev IN. (2018) Aggregational Capabilities Of Neutrophils In Patients With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2248-2253.
[25] Medvedev IN. (2018) Spontaneous Aggregation Of Erythrocytes In Patients With Arterial Hypertension With Impaired Glucose Tolerance. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 2275-2280.
[26] Apanasyuk LA, Soldatov AA. (2017) Socio-Psychological Conditions for Optimizing Intercultural Interaction in the Educational Space of the University. Scientific Notes of Russian State Social University. 16(5-144) : 143-150. doi: 10.17922/2071-5323- 2017-16-5-143-150.
[27] Maloletko AN, Yudina TN.(2017) (Un)Making Europe: Capitalism, Solidarities, Subjectivities. Contemporary problems of social work. 3 (3-11) : 4-5.
[28] Pozdnyakova ML, Soldatov AA. (2017) The Essential and Forms of the Approaches to Control the Documents Execution. Contemporary problems of social work. 3 (1-9): 39-46. doi: 10.17922/2412-5466-2017-3-1-39-46.
[29] Oshurkova JuL, Medvedev IN, Fomina LL. (2018) Physiological Indices of Platelet-Coagulation Hemostasis in Purebred Ireshire Cows in The Course of Lactation. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2) : 419-426.

[30] Oshurkova JuL, Medvedev IN, Fomina LL. (2018) Physiological features of platelet aggregation in calves of Ayrshire breed during the phase of plant nutrition. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2) : 1008-1013.
[31] Oshurkova JuL, Medvedev IN, Tkacheva ES. (2018) Functional Features Of Platelet Aggregation In Heifers Of The Ayrshire Breed, Which Are Being Prepared For Insemination. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(3) : 1155-1160.
[32] Glagoleva TI, Medvedev IN. (2018) Physiological Features Of Anti-aggregational Control Of Blood Vessels Over The Shaped Elements Of Blood In Calves At The Onset Of Ontogenesis. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 440-447.
[33] Vorobyeva NV, Mal GS, Skripleva EV, Skriplev AV, Skoblikova TV. (2018) The Combined Impact Of Amlodipin And Regular Physical Exercises On Platelet And Inflammatory Markers In Patients With Arterial Hypertension. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(4) : 1186-1192.
[34] Oshurkova JuL, Medvedev IN, Fomina LL. (2018) Physiological features of platelet aggregation in calves of Ayrshire breed during the phase of plant nutrition. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2) : 1008-1013.
[35] Skorjatina IA. (2018) Therapeutic Possibilities Of Rosuvastatin In The Medical Complex In Relation To Disaggregation Vascular Control Over Erythrocytes In Persons With Arterial Hypertension And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2) : 977-983.
[36] Bikbulatova AA, Pochinok NB, Matraeva LV, Erokhin SG, Makeeva DR, Karplyuk AV.(2018) Formation Of International Practice Of Holding Competitions Of Professional Skills Among Professionals With Disabilities. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 296-302.
[37] Bikbulatova AA, Pochinok NB, Matraeva LV, Erokhin SG, Makeeva DR, Karplyuk AV. (2018) The Russian Historical Aspect Of The Development Of The International Federation Of Abilimpix. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 329-335.
[38] Bikbulatova AA, Pochinok NB, Soldatov AA, Matraeva LV, Erokhin SG. (2018) Organization Of International Competitions Of Professional Skill Among People With Disabilities. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 379-387.
[39] Bikbulatova AA. (2018) Technology Implementation Of Competitions Of Professional Skill. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 407-419.
[40] Bikbulatova AA, Kartoshkin SA, Pochinok NB. (2018) Schemes Of Competitions Of Professional Skills Among People With Disabilities In Russia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 357-362.
[41] Bikbulatova AA, Matraeva LV, Erokhin SG, Makeeva DR, Karplyuk AV. (2018) Methodical Foundations Of Carrying Out Competitions Of Professional Skill Among People With Disabilities. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 243-247.
[42] Bikbulatova AA, Karplyuk AA, Parshin GN, Dzhafar-Zade DA, Serebryakov AG. (2018) Technique for Measuring Vocational Interests and Inclinations in High-School Students with Disabilities. Psikhologicheskaya nauka i obrazovanie-psychological science and education. 23(2) : 50-58.doi: 10.17759/pse.2018230206
[43] Makhova AV. (2018) Physiology Of The Hypothalamus In The Human Body. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 478-484.
[44] Makhov AS. (2018) The Importance Of The Needs Arising In People When Organizing Classes Rink Bandy (Mini Hockey). Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 96-101.
[45] Makhov AS. (2018) The Basic Needs Of Hearing Impaired People In Organizing Football Training. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 121-126.
[46] Makhov AS. (2018) Perspectives Of Rink-Bendi Development Among People With Hearing Impairment In Russia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 139-146.
[47] Makhov AS. (2018) Specificity Of Requirements Of Russian And Foreign Hockey Players With Hearing Impairment To The Process Of Training And Competition. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 157-163.
[48] Makhov AS. (2018) Motivational Field Of Disabled People With Musculoskeletal Injury To Participation In Training On Russian Press. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(5) : 211-217.
[49] Bespalov DV, Medvedev IN, Mal GS, Polyakova OV. (2018) Physiological Capabilities Of The Vascular Endothelium With The Developing Arterial Hypertension In People Of Different Ages Who Had Long Had

Low Physical Activity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2) : 972-976.

[50] Bespalov DV, Medvedev IN, Mal GS, Makurina ON. (2018) Functional activity of the vascular endothelium in patients with initial signs of atherosclerosis against the background of regularly dose-related exercise stress. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2) : 1020-1024.

[51] Bikbulatova AA, Andreeva EG, Medvedev IN. (2018) Hematological Features Of Patients With Osteochondrosis Of The Spine. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2018; 9(3) : 1089-1095.

[52] Bikbulatova AA, Karplyuk AV, Medvedev IN. (2018) Methodical Bases Of The Help To Young Invalids In A Choice Of Sphere Of Their Future Professional Activity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(4) : 571-577.

[53] Bikbulatova AA, Karplyuk AV, Medvedev IN. (2018) The Problem Of Vocational Guidance Work With Young People, Who Have Limited Health Opportunities In Modern Russia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(4) : 586-590.