Thrombophilia and thrombotic disorders in newborns

Keywords: venous thromboembolic disease, arterial ischemic events, neonatal intensive care units, central venous system

Abbreviations: VTE, venous thromboembolic disease; NICU, neonatal intensive care units; AIS, arterial ischemic events; CVS, central venous system;

Editorial

Thromboembolic disease is rare in childhood. The annual incidence in children is estimated at about 0.7 cases of venous thrombosis per 100,000 population, 1.0 of stroke and 0.1 of myocardial infarction, while in adults the incidence reported is 74.2, 45.4 and 175.6 cases respectively. The lower incidence of venous thromboembolic disease (VTE) in children compared to adults is mainly due to the integrity of the vessels and the enhanced anticoagulant activity of the endothelium, and additionally to the reduced capacity of thrombin generation, inactivation of thrombin by α2-macroglobulin, the increased concentration of which, counterbalances the physiological deficiency of antithrombin and protein C/S, to the decreased levels of tissue factor in cord blood and concentration of eicosanoids and proteoglycans, depending on age. The incidence of thromboembolic events (VTE) is higher in infants than in older children. About 10% of VTE occur in the first four weeks of life, frequently in critically ill neonates (2.4 symptomatic VTE cases per 1000 admissions in Neonatal Intensive Care Units-NICU). The incidence of symptomatic venous thrombosis (VTE) in newborns is 5.1/100,000 live births. Although it is considered that the thromboembolic events are under diagnosed, newborns are nearly 40 times more likely to suffer a VTE than during the entire childhood, but certainly the above probability is significantly less than that referred in adults.

The hemostatic system both in preterm and full-term newborns differs significantly from that of older children and much more than that of adults, however, normally in newborns there is a balance in between bleeding or thrombosis diathesis. The increased incidence of VTE in critically ill infants is attributed to the derangement of equilibrium of the hemostatic mechanism, because of the lower concentrations of natural inhibitors and impaired fibrinolytic activity and also due to elevated levels of factor von Willebrand. The combination of the above with both the high viscosity of blood due to the high hematocrit and the small vascular diameter of newborns results in low capillary flow, especially on coexistence of dehydration or hypercoagulable state because of infection or prematurity. Furthermore, the use of venous or arterial catheters is one of the major risk factors for thrombosis in neonatal period. Nowadays, 15% of infants in NICU and at least 50% of preterm infants of birth weight <1000 gr have catheter in umbilical vein. Thrombosis in children is a multifactorial event and the result of acquired (>90% of cases) or congenital risk factors. For the manifestation of VTE in neonates, several coincidental risk factors (variety of underlying diseases or triggering events of the child or maternal) are required. Studies so far, have not revealed thrombophilic factors contributing to the occurrence of asymptomatic or symptomatic VTE. Genetic factors are related to the risk of VTE in children and newborns but no causal relationship is established for most of them. The frequency of presence of thrombophilic factors in children with VTE is reported 13-79% in several studies. The huge discrepancy is attributed mainly to variation in the design of the trials, the difficulty in the definition of related prothrombotic disorders, and also to the small number and different patient populations. Regarding thromboembolic events of central venous system (CNS), and although the high frequency of idiopathic arterial ischemic events (AIS), the prevalence of thrombophilic factors varies in different studies from 20 to 50%, while increased appears the possibility of the presence of congenital thrombophilia in neonates with renal, hepatic or portal vein thrombosis. Furthermore, maternal thrombophilia has been associated with the occurrence of perinatal AIS, venous sinus thrombosis or renal vein thrombosis. However, in neonates there is scepticism about the interpretation of results of the various studies due to the complexity of the mechanism of hemostasis and the interaction of several acquired factors. Thrombosis in neonates is generally a multifactorial process. Future studies may clarify both causative background and therapeutic choices in this group of patients.

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References

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