Reg. No: 2016/21/N/NZ5/01442; Principal Investigator: lek. Alina Agnieszka Sobczak

A new microscopic insight into the thrombogenicity and other complications of umbilical catheters use

Obtaining a central vascular access is the fundamental principle of intensive care. The presence of a catheter in a central vein allows administration of hyperosmolar parenteral nutrition (TPN), long-term hydration and close to the heart intake of resuscitation drugs. A catheter in a central artery permits painless blood sampling and continuous blood pressure monitoring. Neonatology has a unique vascular central access in a form of a patent umbilical vessels visible after birth in the umbilical stump - two arteries and one vein. A catheter in the umbilical vein (UVC) passes the liver through the left branch of a portal vein and ductus venosus, ending close to the right atrium. A catheter in the umbilical artery (UAC) passes the internal iliac artery, the common iliac artery and ascends in the aorta in the upstream direction, ending properly above the diaphragm. In case of premature children as well as children in need of intensive monitoring, umbilical catheterization is a quick and painless procedure often performed already in the delivery room. However, umbilical vessels differ anatomically and functionally from other central vessels, therefore generate potentially life-threatening complications seen nowhere else. That is why umbilical catheters among all central accesses are kept the shortest time in the patient, although the exact mechanism responsible for the complications is not known.

The complications generated by the catheter – blood-acquired infections, cardiac tamponade due to catheter's immobilization and tissue irritation from the TPN, ischemic events - lead to its possible thrombotic nature. According to the literature data, 90% of thrombotic events in a neonatal population are related with the presence of an intravascular catheter. Our preliminary data have shown that the thrombi can form already on the day 2. of catheterization, while the international guidelines allow keeping the UAC up to 5 days and UVC up to 14 days of use. The correlation between thrombotic events and catheter presence suggests a possible role of the catheter microstructure in clotting initiation. The catheter microstructure changes with time due to the exposition to the body fluids; the changes will be observed using scanning electron microscopy (SEM) and chemical analysis of the precipitates (EDS, energy dispersive spectroscopy). A possibility of catheter microbial colonization and biofilm formation will be evaluated with microbial cultures and smears of the catheters removed from the patients. In our preliminary research we observed a considerable roughness of the catheter due to a radiopaque polymer (barium sulfate) which turned out to comprise up to <sup>3</sup>/<sub>4</sub> of the catheter's circumference. The barium sulfate is present in order to visualize the catheter in the X-ray scans. However, popularization of ultrasonography as an alternative method to X-ray means the thrombogenic radioopaque material may not be needed in the future.

Among all pediatric patients, neonates are most prone to develop thrombosis which for neonates particularly can be a life-threatening situation. The presence of patent fetal circulation (patent ductus arteriosus, patent foramen ovale) generates the risk of paradoxical embolism; thrombi dissolvent is impaired due to the immature fibrinolysis. Additionally, small-diameter vessels, immature hemostasis, inability to surgically remove the thrombus nor give pharmacological treatment (higher risk of intraventricular hemorrhage) contribute to the lack of therapeutic management when complications occur.

The subject of iatrogenic umbilical catheter-related complications in the neonatal population is poorly understood. There is a lack of publications regarding this topic, lack of explicit guidelines regarding umbilical catheters use & monitoring and lack of research on the microstructure of the catheters. This project will contribute to the basic research concerning issues mentioned above and hopefully can be applied to a wider range of vascular catheters & indwelling devices. Understanding the mechanism underlying umbilical complications can enable to create a universal algorithm of catheters' use, and there is a great need for it since umbilical catheters are used worldwide.