REVIEWS

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Ewa Barczykowska[1, A, C, D], Marzena Szwed-Kolińska[2, B, C],
Agnieszka Wróbel-Bania[1, B, C], Robert Ślusarz[3, E, F]

The Use of Central Venous Lines in the Treatment of Chronically Ill Children

[1] Department of Pediatric Nursing, L. Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland
[2] Clinical Training Specialist, Becton Dickinson Polska Sp. z o.o.
[3] Department of Neurological and Neurosurgical Nursing, L. Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland

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Abstract

Treatment of chronic diseases in children is a special medical problem. Maintaining constant access to the central vascular system is necessary for long-term hemato-oncological and nephrological therapies as well as parenteral nutrition. Providing such access enables chemotherapic treatment, complete parenteral nutrition, long-term antibiotic therapy, hemodialysis, treatment of intensive care unit patients, monitoring blood pressure in the pulmonary artery and stimulation of heart rate in emergency situations as well as treatment of patients suffering from complications, especially when chances of access into peripheral veins are exhausted. Continuous access to the central vascular system is desirable in the treatment of chronically ill children. Insertion of a central venous catheter line eliminates the unnecessary pain and stress to a child patient accompanying injection into peripheral vessels. In order to gain long-term and secure access to the central venous system, respecting the guidelines of the Center for Disease Control and Prevention contained in the updated 'Guidelines for the Prevention of Intravascular Catheter-Related Infections' is necessary (**Adv Clin Exp Med 2014, 23, 6, 1001–1009**).

Key words: central venous lines, chronic disease, children.

Chronic disease is considered to be a stressor straining human body and mind for a long term. A combination of various biological, mental and social factors determines how big of a stressor a chronic disease is for a child and how it can cope with the strain.

A chronically ill child is exposed to a number of strains, resulting from the essence of a given illness: discomfort, organ and system dysfunctions, pain, fear, suffering, necessity of self-control and limitation to psychomotor activity. The treatment process triggers stressful experiences for a child, as well. Treatment frequently requires compulsory immobilization, observing rules which apply to a certain medical procedure and sometimes separation from the family and isolation in hospital as well as contact with strangers working as medical staff. The tedious and unpleasant medical procedures being performed are also stressful [1]. Pain accompanying medical procedures is known as iatrogenic. The problem of iatrogenic pain involves not only the medical procedures causing pain, but all other situations causing fear and anxiety as well [2]. Stressful experiences lead to a mental demobilization in a child patient, weaken its motivation to participate in the process of treatment and trigger irrational defensive behavior. Repeated and long-term stress can result in relatively permanent damage to the child's immunity as well as its nervous and emotional balance [1].

According to the European Charter for Children in Hospital '(…) steps should be taken to mitigate and avoid unnecessary physical and emotional stress experienced by a child in connection with his/her stay in hospital (…)' [3]. Actions undertaken to improve the comfort and mental health of

patients and their families play an important role in the modern approach to long-term treatment of children. Medical procedures limiting unnecessary physical and mental suffering of a patient are being introduced to pediatric practice. Inserting a permanent central vascular line eliminates the unnecessary pain and stress accompanying acquiring access to peripheral vessels. Introducing the procedure of central vein cannulation is particularly desirable in the comprehensive treatment of chronic diseases in children [4].

Catheterization of Central Veins

Catheterization of central veins is performed not only on children, but also on adults. It is an invasive procedure which requires insertion of a catheter into one of the large veins (central venous catheters – CVC) [5, 6] or a pulmonary artery [6]. The catheter is inserted through jugular anterior veins, subclavian veins or femoral veins in such a way that its end is placed in the inferior caval vein below the ostium of renal veins or in the superior caval vein at the ostium to the right atrium [7].

Current recommendations concerning the choice of intravascular catheters, points of insertion, preparing the skin, nursing and rules of changing the dressing on the site of insertion, are contained in 'Guidelines for the Prevention of Intravascular Catheter-Related Infections' of the Center for Disease Control and Prevention. This publication categorizes recommendations on the basis of existing and credible scientific data, theoretical rationale, applicability and economic impact. Additionally, the publication takes into consideration the statutory and legal requirements – Table 1. The publication is addressed to medical staff responsible for inserting intravascular catheters, people responsible for supervising and monitoring infections in hospitals and outpatient clinics as well as catheter patients treated in their own homes [8].

Indications for CVC Use

Placing a central catheter in the caval vein provides constant access to the venous system and, owing to a substantial internal cross-section of the catheter, enables fast transfusion of fluids and blood and instant dilution of administered preparations which minimizes their irritating effect on the vascular wall and improves the comfort of treatment [9].

Inserting a central venous catheter is necessary with respect to planned long-term therapies. It enables:

- parenteral nutrition [10–14],
- chemotherapy [5, 15],
- use of antibiotics,
- use of analgesics,
- transfusion of blood and blood products,
- collection of blood [5],
- hemodialysis [16],
- intensive therapy [6], monitoring of blood pressure in the pulmonary artery and stimulation of the heart rate in emergency situations [11],
- administration of clotting factors [17],
- long-term treatment of patients suffering from complications, especially when it is no longer possible to access peripheral veins [11].

Parenteral Nutrition

Parenteral nutrition (PN) is made possible through access to central veins [11]. In 1968 S.J. Dudrick et al. comprehensively presented for the first time a description of long-term parenteral

Table 1. Classification system of recommendations specified in the guidelines pertaining to prevention of intravascular catheter-related infections [8]

Category	Meaning
Category IA	strongly recommended for implementation and strongly supported by well-designed experimental, clinical or epidemiologic studies
Category IB	strongly recommended for implementation and supported by some experimental, clinical or epidemiologic studies and a strong theoretical rationale; or an accepted practice (e.g. aseptic technique) supported by limited evidence
Category IC	required by state or federal regulations, rules or standards
Category II	suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale
Unresolved issue	represents an unresolved issue for which evidence is insufficient or no consensus regarding efficacy exists

nutrition through a catheter placed in the caval vein after subcutaneous puncture of the jugular vein [10]. According to Dudrick, parenteral nutrition is advisable for treating patients who cannot, would not, or should not take food the regular way or who are undernourished [13]. In long-term parenteral nutrition, the best possible venous access is provided by tunneled central catheters, regardless of a child's age [12, 15]. A central venous catheter is required to administer high osmotic concentration mixtures satisfying total requirements for nutrients [14].

The most frequent indications for parenteral nutrition include:

– in newborns: functional immaturity of the gastrointestinal tract, developmental anomalies including necrotizing enterocolitis, perioperative period [12, 13, 18],

– in infants and older children: status *post* bowel resection, acute phase of Crohn's disease, intestinal pseudo-obstruction, acute pancreatitis, status *post* multiple organ injuries, neoplastic disease [12].

Properly conducted parenteral nutrition belongs to the most important elements of treating infants of very low birth weight and infants with extremely low birth weight in the first weeks of their life [18]. Parenteral nutrition of neonatals can be performed through a peripheral venous catheter or a central vein catheter and, in some cases, through the umbilical artery for a limited period of time [12, 18, 19].

CVC also enables total parenteral nutrition of patients who do not tolerate oral nutrition due to chemotherapy's toxic influence on the mucous membrane of the gastrointestinal tract [5].

No recommendations for using any particular lumen in parenteral nutrition have been given – unresolved issue [20].

Antineoplastic Therapy

Antineoplastic therapy involves cyclical and long-term administration of cytostatic agents, antibiotics and other medicine as well as multiple performance of numerous and repetitive examinations for diagnosis and control. The treatment requires blood sampling which causes not only problems resulting from repeated venipuncture, but also problems of a psychological nature [4, 21].

CVC usage, especially for children treated for hematologic neoplasms, involves a risk of catheter-related complications, including infections, thromboses, mechanical complications and obstructions [22]. During chemotherapy, apart from adverse reactions, other side effects can occur. Serious complications include, among others, rupture of blood vessels and extravasation of cytostatic agents into surrounding tissues. No precise data concerning the frequency of this complication's occurrence is available [23]. The authors claim that the calculations point to extravasation of a medicine into the perivascular space as occurring in 0.01–0.45% to 6.4–7% of patients [23, 24].

Extravasation should be looked upon as an acute complication to oncological treatment. In the area under extravasation, various lesions may occur, from minor redness, edema and discomfort, to irreversible damage to the tissue in the form of ulceration with possible damage to muscles, tendons and nerves, accompanied by extreme pain [23].

Using CVC enables safe administration of chemotherapeutic agents, even those which cause burning and cannot be administered safely into peripheral veins [5, 24]. Due to comfortable and long-term access to the venous system, CVCs are currently a device of primary importance in the treatment of patients suffering from malignant neoplasms [5], as well as a factor increasing comfort in cancer treatment [22].

Blood Sampling

No contraindication to performing routine blood sampling from children through a properly inserted central catheter is known [25].

Hemodialysis

Hemodialysis is a method of extracorporeal elimination of toxins, recognized as one of the most significant achievements in modern medicine. This method is used to treat, among other patients, children suffering from renal failure after poisoning. The results of treating children with repeated hemodialysis are comparable to data from European or American registers [16].

Vascular access in hemodialized children is problematic, mainly due to their vessel anatomy. The choice of a catheter is individualized and connected with a particular institution's experience as well as with the child's weight [16]. In child patients, CVC is the most frequent choice [26].

In treatment of patients undergoing hemodialysis and those suffering from advanced nephropathy, subclavicular access should be avoided to eliminate the risk of subclavian vein stenosis – Category IA. Patients suffering from chronic renal failure, should have an arteriovenous fistula or vascular prosthesis inserted instead of a CVC – Category IA.

Antiseptic unguents are applied following each catheter introduction for hemodialysis, and following the completion of each dialysis, only if a given unguent does not interact with the material from which the hemodialysic catheter is constructed, according to the producer's information – Category IB [8].

Administering Clotting Agents

One of the basic ways of treating patients suffering from severe hemophilia is prophylactic administration of the missing clotting factors. The use of central catheters makes it possible to introduce preventive measures in children with severe hemophilia with difficult access to peripheral veins, as well to proceed with immunotolerance in patients with an inhibitor through regular, daily administration of factor VIII or IX, depending on the type of hemophilia [17, 27]. The experiments performed by the Clinic of Pediatrics, Hematology and Oncology of the University of Medicine in Warsaw show that using CVC makes it possible to perform effortless, painless and safe intravenous treatment of patients who require recurrent transfusion of clotting agents. In children suffering from severe plasmatic hemorrhagic diathesis (hemophilia A, hemophilia B, type 3 von Willebrand disease), PORT-A-CATH ports were used to administer clotting agents.

In most cases, administration of clotting agents is performed at home. It is very important to prepare parents for the task of administering the clotting agent by themselves, discussing the problems of maintaining hygiene, observing rules, duration of leaving the catheter in and of the child's safety. Parents are permitted to operate a catheter independently of a nurse after passing an examination [17].

Choosing a Central Catheter and Site of Insertion

In 1973 the first central venous catheter was used. A team of scientists under the direction of J.W. Broviac designed a silicone catheter with an attached Dacron tube. The catheter was inserted into the superior caval vein, leading out of the body following subcutaneous tunneling of the chest wall. It was used for long-term home parenteral nutrition. In 1979 Hickman modified Broviac's catheter by thickening the wall and increasing lumen. Whereas a double lumen silicone catheter with a Dacron tube was used for long-term parenteral nutrition and chemotherapy, a triple-lumen catherer enabled blood sampling during infusion [11].

Catherization of central venous vessels is a difficult procedure with regard to child patients due to the small diameter of such vessels and the thinness of the catheters adapted for this purpose [15].

In neonatals, insertion of a central venous line can be performed through various methods. In practice, due to the lack of venous valves, percutaneous central catheters are the most frequently used: either cannulation of central veins through peripheral veins (Epicutaneo-Cava Catheter – ECC) or the Seldinger technique (Peripherally Inserted Central Catheter – PICC) [6, 7, 18, 28]. It is also possible to cannulate the umbilical vein and perform venesection [28]. The methods vary in performance techniques, indications, contraindications and complications. At present, there is no unambiguous data showing which method is the safest and the most effective for neonatals. When choosing a method, one should take into consideration: the neonatal's general condition, its weight and age, and the risk of complications as well as the skills and experience of the person performing the procedure. ECC and PICC are used for neonatals of a weight below 1800 g and thus requiring long-term parenteral nutrition [7].

Epicutaneo-Cava Catheter – ECC

Cannulation of central veins through peripheral veins is presently the most commonly used method as for neonatals [28]. It requires insertion of a long, soft catheter through the needle lumen into one of the peripheral veins (basilica vein, saphenous vein, axillary vein) and ducting it into the central vein [7, 18]. The procedure is short, simple and can be performed in conditions observed in a neonatal department. It is minimally invasive, and does not require general anesthesia. Moreover, it provides long-term venous access which is particularly important when treating child patients of a very low body mass, where cannulation of peripheral veins is highly limited. According to information found in references, this method is characterized by a scarce occurence of complications [28].

In neonatal treatment, inserting cannulas into the caval veins of the upper body – the cubital fossa vein, temporal vein, external jugular vein and axillary vein – is preferred. Cannulation of the veins of the lower body is bound with a greater risk of thrombotic complications [28].

Indications for ECC use in newborns include: necessity of maintaining long-term venous access, parenteral nutrition with a concentrated glucose solution and/or amino acids, monitoring central venous pressure (CVP), usage of medications which

cannot be administered through peripheral veins (e.g. catecholamine, hyperosmolar solutions) [28].

Once the ECC is inserted, one has to observe the following rules:

– strict aseptic techniques apply when changing the dressing or the infusion solutions,

– it is advisable to maintain constant flow of the infusion liquid through the cannula [18, 28],

– during parenteral nutrition, it is advisable to supplement the transfused solutions with heparin, in the amount of 0.25 IU/mL [28],

– blood products must not be transfused,

– blood sampling must not be performed [28].

Direct Cannulation of Central Veins

When selecting the central catheter insertion site, one should take into consideration primarily the patient's comfort, the possibility of securing the catheter and of maintaining aseptic conditions, as well as parameters specific for a given patient (e.g. catheters used previously, anatomical deformations, tendency to bleeding), the possibility of performing ultrasound examination at the patient's bed as well as the experience of the person responsible for inserting the catheter [20]. It is necessary to compare the risk of infectious complication occurrence with the risk of mechanical complications (pneumothorax, subclavian artery puncture, subclavian vein stenosis, thrombosis, air embolism, wrongfully sited insertion of a catheter) – Category IA [8, 20].

The catheter insertion site has a direct influence on the risk of catheter-related infection and inflammation of a vein. The influence of the catheter insertion site on the risk of infection is partially bound with the risk of thrombophlebitis and the density of the flora on the patient's skin [20].

Studies show that the subclavian vein, the jugular vein and the femoral vein are prioritized for catheter insertion, due to caution against infections and to the types of catheter-related infections. From the point of view of infection prevention, the subclavian vein should be selected as the primary site of insertion [20].

General Rules of Cannulating Central Veins

Catheter insertion must be performed under strict observance of aseptic techniques (in the conditions of an operating room) and with the use of an ultrasound or an X-ray [25, 29]. It is advisable to observe the central catherer insertion *via* ultrasound to minimize the number of cannulation attempts and mechanical complications. Insertion of a catheter with the use of an ultrasound should be performed only by staff fully trained in this technique – Category IB [20, 25].

The size of the catheter should be adjusted to the diameter of pediatric vessels.

While inserting a catheter or a driver into the vessel, one should not use excessive force to overcome resistance.

Proper positioning of the catherer must be confirmed by radiological examination.

Before using a catheter, one should verify the possibility of free outflow of blood through its lumen [29].

CVC with a minimum number of lumina and ports required in given circumstances, should be used – Category IB [20, 25].

An intravascular catheter which is no longer needed should be removed as soon as possible – Category IA [6, 18, 20, 25, 30, 31].

The presence of a catheter in a vessel always poses a risk. The more catheters and the longer they are used, the higher the risk of infection is posed [6].

If accordance with aseptic techniques is impossible (i.e. a catheter is inserted in a life-saving situation) the catheter thus inserted should be removed as soon as possible, i.e. within 48 h – Category IB [6, 20].

During daily maintenance of a CVC:

– the need of using the catheter should be assessed,

– the patency and proper positioning of the catheter must be verified [30],

– in order to avoid any damage to the catheter, a 10 mL syringe of 0.9% sodium chloride not containing preservatives, should be used for verifying patency [31],

– skin around the catheter should be observed for topical symptoms of infection and the parameters of the patient's condition should be monitored for signs of systemic infection [25, 30],

– sterile gauze dressings or sterile, transparent and semi-permeable dressings must be used in the catheter insertion site – Category IA [8, 30, 32],

– for dressing changes, clean or sterile gloves must be worn – Category IC. In the case of a transparent dressing, a visual inspection of the catherer insertion site must be performed. In the case of a non-transparent dressing, haptic examination of the site should be performed. Frequency of such evaluations depends on the patient's clinical condition. If reddening in the site of the catheter insertion, body temperature increase for no clear reason,

or other symptoms suggesting local or blood infection are observed, one should remove the dressing for a careful examination of the catherer insertion site – Category IB [8, 25].

The catheter port should be secured with a dressing.

Prior to the acquisition of venous access, the site of a planned catheter insertion should be treated with a disinfectant (while taking into consideration the time required for the disinfectant to act).

Prior to the administration of medicine, the performance of a catheter must be verified by aspiration of blood [25].

Unused ports and valves should be secured with plugs [25, 32]. The venous-access closing plugs are single-use (disposable once a plug is opened). A new plug should be taken out of its packaging and used to close the access in such a way as to avoid contaminating internal surfaces [25].

In case of needleless connectors being used, they should not be replaced more frequently than every 72 hours or as per the manufacturer's recommendations in order to minimize the risk of infection – Category II [33].

To minimize the risk of contamination, ports should be disinfected by being wiped with a proper disinfectant (chlorhexidine, povidone iodine, iodophor or 70% alcohol) and the port must be connected only with sterile equipment – Category IA [33].

In case of needleless systems being used in the vascular line, connectors with a valve divided by a partition are preferred, instead of ones with a mechanical valve, as using mechanical valves increases the risk of infectious complications – Category II [33].

The catheter, or the catherer insertion site must not be immersed under water. Patients are allowed to shower, provided that precautions are taken to minimize the possibility of microorganisms reaching the catheter (the catherer insertion site should be protected with a waterproof cover while showering) – Category IB [8].

Any additional manipulations such as booster injections and fluid mixing must be avoided [34].

Complications Connected with Cannulation of Central Veins

Complications accompanying catheterization of venous vessels of pediatric patients are not rare [15, 17, 22]. Patients bear a risk of:

– topical or general catheter-related infection [6, 7, 17],

– air or thrombotic pulmonary embolism,

– technical complications (catherer's dislocation or removal),

– catheter blockage [9, 18] and mechanical damage [9, 7, 35]. Catheter blockage can stem from many reasons: mechanical damage, infection, improper placement (e.g. dislocation of the catheter's tip from the central vein to the peripheral vein) and thrombosis [36],

– cardiac tamponades in neonatals under parenteral nutrition through a catheter inserted into the superior caval vein [37],

– travel of the parenteral nutrition mixture into the pulmonary cavity. This rare and dangerous complication was described by Jakubczyk et al. as causing respiratory failure. The hyperosmolar solution used in parenteral nutrition caused absorption of the serous fluid into the pulmonary cavity. As a superb nutrient, it also enabled multiplication of bacteria which, as a consequence, led to sepsis [15],

– infection-related complications, mechanical complications, catherer obstructions, thrombosis-related complications, skin lesions over the port's cavity, and other complications in pediatric treatment of neoplasms. Research by Panas et al. on the functioning of central catherers found no catherer-related complications were observed in 1/3 of patients [22].

Insertion of venous catheters is favorable to infections, as the method circumvents the natural immunity of the skin. Catheter-related infections usually occur during the insertion (if aseptic techniques are not applied), as a result of skin contamination around the catheter, due to infusion line infection, during fluid transfusion and as a result of a hematogenous infection [6].

Should a catheter-related infection be suspected, a blood sample must be drawn for blood culture and determination of fungal antigens. An antibiotic should be administered intravenously – the choice depends on the epidemiological situation in the ward [25].

Such infection can take the form of: 1) infection of the injection site and topical pain, reddening, hardening, purulent discharge; 2) infection of the catheter canal and pain, hardening, reddening along the subcutaneous canal; 3) subcutaneous pocket infection causing reddening, skin necrosis within the area of the subcutaneous tissue in which the reservoir of the vascular catheter is placed.

The most severe form of catheter-related infection is sepsis. Apart from the vascular line, factors increasing the risk of blood infection include invasive treatment and diagnostics as well as hemodialysis and peripheral venous catheters [6].

Catheter-related bloodstream infections (CRBSI) are infections directly connected with insertion of a catheter and with microorganisms present on the patient's skin and on the staff's hands. In 58–65%

of cases, patients are infected due to skin-colonizing bacteria: *Staphylococcus epidermidis*, other coagulase-negative *Staphylococcus and Staphylococcus aureus* as well as *Enterococcus* spp., *Acinetobacter* spp., *Klebsiella* spp., *and Candida* spp. [30, 38].

Infections related to vascular lines may also result from primarily or secondarily infected fluids administered intravenously. Such infections constitute 10% of overall catheter-related infections. The etiological factors of such infections often comprise gram-negative microorganisms: *Pseudomonas* spp., *Acinetobacter* spp., as well as coliform organisms (*Klebsiella* spp., *Enterobacter* spp., *E. coli, Serratia* spp.), fungi and HBV, HCV, HIV and B19 viruses [30]. Infections may also result from a lack of tightness of the connection with the packaging containing the infusion (contamination in the place of the reservoir connection), open vents in the transfusion device and improperly secured injection ports. Moreover, the risk of infections is increased by nonconformity with aseptic techniques during infusion preparations and the performance of all actions connected with the vascular system [6].

Preventing CVC-Related Infections

In order to minimize the risk of CVC-related infections, Mączyńska suggests implementing a 'central catheter bundle', i.e. a set of 5 key proper actions pertaining to a patient with a central venous catheter:

I. Hand hygiene of the staff inserting the catheter.

II. Observing the rules of asepsis around the patient.

III. Proper disinfection of skin with a proper agent (2 percent chlorhexidine).

IV. The proper choice of the insertion site.

V. Daily monitoring and evaluation of the need to use a catheter [6, 25, 39].

For the best possible effect, all recommendations should be followed completely. Results obtained in Michigan (the Keystone ICU Project) prove how successful respecting the recommendations stipulated in the 'central catheter bundle' is. Within 18 months from the implementation of the bundle, the frequency of catheter-related infections dropped from 7.7 to 1.4/1000 days with a catheter [39].

The priority role of education and the obligation to organize training courses for health service staff should be highlighted. Staff must be educated within the scope of indications for intravascular catheter use, proper insertion techniques, maintenance of intravascular catheters and appropriate infection control means, aimed at preventing catheter-related infections [8, 25, 30, 32]. Staff should be periodically verified for being responsible for inserting and maintaining intravascular catheters, as well as for knowing and observing the recommendations. It is necessary to appoint only trained employees who have confirmed their competence within the scope of inserting and maintaining peripheral and central catheters – Category IA, and employ appropriate nurses in intensive care units – Category IB [8].

The authors concluded that continuous access to the central vascular system is desirable in the treatment of chronically ill children. Inserting a central venous catheter line eliminates unnecessary pain and stress accompanying the action of inserting a needle into pediatric patients' peripheral vessels. In order to achieve long-term and safe access to the central venous system, respecting CDC guidelines contained in the current 'Guidelines for the Prevention of Intravascular Catheter-Related Infections' is necessary.

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Address for correspondence:

Ewa Barczykowska
L. Rydygier Collegium Medicum in Bydgoszcz
Nicolaus Copernicus University in Toruń
Techników 3
85-801 Bydgoszcz
Poland
Tel.: +48 525 852 193
E-mail: ebarczykowska@interia.pl

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