INTRODUCTION

The use of a peripherally inserted central catheter (PICC) is performed in newborns (NB) since the 1970s, initially for administration of parenteral nutrition1,2, but later as a routine procedure in neonatal intensive care units (NICUs). Complications associated with the use of PICC are similar to those of other central catheters, such as bleeding, catheter embolism, arrhythmias, infection of the insertion site and sepsis3,4. Pericardial effusion due to PICC may also occur, but it is even rarer than those related to other types of central catheter4,5. Some studies relate the accumulation of pericardial fluid associated with PICC to an erosion of the catheter tip through the wall of the right atrium, leading to pericardial effusion and tamponade. Other authors admit a local inflammatory reaction of the catheter tip in contact with the endocardium, leading to an inflammatory exudate6. Although early reports describe this complication in term children, its occurrence in preterm infants is well established6-10.

The objective of this study was to determine the incidence of pericardial effusion with cardiac tamponade in preterm infants in a pediatric intensive care unit, with emphasis on the relationship between pericardial effusion and peripherally inserted central catheter, and to evaluate the role of bedside ultrasound in approaching these cases.

METHODS

We conducted a retrospective analysis of a database of the Neonatal Intensive Care Unit Service of the Santa Isabel Hospital, Ubá, Minas Gerais, from July 2014 to December 2016. The criteria for inclusion of the patients in the study were prematurity, hospitalization in the NICU, episode of hemodynamic alteration or ventilatory difficulty during the NICU stay, age between

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0 and 28 days and having undergone bedside ultrasound (USG). The latter was performed by an intensivist pediatrician in all patients presenting with hemodynamic changes or ventilatory difficulties, with identification of cases of pericardial effusion, which were submitted to therapeutic and diagnostic pericardiocentesis.

The variables evaluated were gestational age at birth, corrected age, gender, weight, type of central catheter, duration of PICC use, catheter tip location, clinical manifestations, date of onset of symptoms, biochemical appearance and characteristics of the pericardial fluid, final diagnosis, treatment and outcome.

The study was approved by the Ethics in Research Committee under the certificate of presentation for ethical appreciation number 64217116.8.0000.5153.

**RESULTS**

The unit occupancy rate in the period was 100%, with 426 admissions. Functional echocardiography was performed in 285 patients by the same pediatric intensivist with training in bedside ultrasound. Six cases of pericardial effusion were identified, four of them with hemodynamic repercussion, characterized by obstructive shock and the need for emergency treatment, which consisted of pericardial puncture performed by the same thoracic surgeon (Table 1). The puncture was performed through the sub-xiphoid route with the aid of USG carried out by the intensivist pediatrician in all cases (Figure 1). In this group, three cases of cardiac tamponade were related to the implantation of PICC and one case related to congenital heart disease. The other two patients with unexplained effusion were just observed, with resolution of the pericardial effusion without the need for invasive procedures.

![Figure 1. Bedside ultrasonography in pericardial effusion. A- ultrasonographic aspect at the beginning of pericardiocentesis, showing right atrium collapse and large accumulation of fluid in the pericardial space; B- appearance at the end of pericardiocentesis, with restored right atrium diameter and discrete residual amount of pericardial fluid; C- catheter in the pericardial space for pericardiocentesis; AD- right atrium; VE- left ventricle.](image)

Among the patients studied, ie those with hemodynamic or ventilatory alterations who were submitted to bedside USG, the overall incidence of pericardial effusion was 2.1% (six patients in 285 USG exams), while the incidence of PICC-related effusion among patients with hemodynamic instability was 1.05% (three patients in 285 USG exams). Among the 426 newborns admitted in the study period, 194 used PICC, which allows us to say that the incidence of cardiac tamponade only among patients who

| Table 1. Biochemical characteristics of the pericardial fluid |
|------------------|----------------|----------------|----------------|----------------|
|                  | PTN (g/dl) | Glucose | TC | LDH | K⁺ | Na⁺ |
| NB 1 *           | 0.3        | 278     | 2  | 15  | 2.8 | 110 |
| NB 2 *           | 0.1        | 140     | 2  | 16  | 3   | 118 |
| NB 3 *           | 0.2        | 148     | 1  | 36  | 3   | 116 |
| NB 4 **          | 1          | 55      | 10 | 15  | NR  | NR  |

PTN: total protein; TC: total cellularity; LDH: lactic dehydrogenase; K⁺: potassium; Na⁺: sodium; NR: not measured. NB: newborn; * the NBs 1, 2 and 3 were in use of PICC with crystalloid infusion with biochemical characteristics very close to the pericardial fluid. ** the NR 4 featured heart disease due to coarctation of the aorta.
used PICC was 1.5% (three cases in 194 patients). Among the six patients with pericardial effusion in the evaluated period, four had cardiac tamponade. Considering that all patients with hemodynamic instability were submitted to bedside USG, 0.94% (four patients out of 426 admissions in the period) showed hemodynamic instability due to pericardial effusion. Among the four patients who presented instability, three patients had PICC-related pericardial effusion.

All patients with pericardial effusion had a gestational age ranging from 30 to 36 weeks (median of 33 weeks) and weight between 1680g and 3000g. Patients with PICC had the catheter implanted two to four days before clinical manifestations related to cardiac tamponade. Nevertheless, in all cases, ultrasound detected the tip of the catheter located in the right ventricle in close relation to its wall. Patients with catheters presented worsening of respiratory and hemodynamic conditions, with tachypnea and dyspnea, oxygen saturation, tachycardia, filiform pulses and poor peripheral perfusion, with the diagnosis of pericardial tamponade confirmed by bedside USG. One patient, born preterm and hospitalized in the NICU at 27 days of life in hemodynamic shock, presented an increase of the cardiac area at the radiography and was initially approached as cardiogenic shock due to probable cardiopathy. However, this diagnosis was changed to pericardial tamponade after functional echocardiography, with therapeutic pericardiocentesis. Analysis of the liquid revealed exudate without bacterial growth. This patient had unexplained biventricular hypertrophy and had not been submitted to PICC insertion at any time before or during the NICU stay. Only after evaluation of the pediatric cardiologist and the pediatric echocardiographer was the diagnosis of coarctation of the aorta established.

**DISCUSSION**

The mechanism of pericardial effusion associated with the central catheter in newborns may be due to cardiac perforation at the time of insertion, necrosis of the organ wall by infusion of hyperosmolar solution, or local inflammatory mechanism leading to transudation into the pericardial space\(^1\). In the experience reported here, we believe in the late cardiac perforation hypothesis, since the tamponade occurred in all cases between 48 and 96 hours after the catheter installation and, mainly, because the pericardial fluid had biochemical characteristics identical to the infused solution (Table 1).

Chest X-ray has been used as a method to identify the location of the central catheter. However, some studies have used ultrasound examination to demonstrate the incorrect positioning of catheters that the radiological examination showed to be ideally located\(^{10-12}\). We believe that the routine use of bedside USG presents advantages over the chest radiograph for the correct location of the catheter. There is no use of ionizing radiation, the USG device presents greater portability in relation to the radiographic apparatus, one obtains a real-time imaging, and the doctor can perform it at the bedside, with no need of a technician to operate the equipment. As a disadvantage, the USG requires specific training for its accomplishment and is a method dependent on the operator’s skills. All of our patients with PICC-associated pericardial effusion had the tip of the catheter in close contact with the wall of the right ventricle, detected by the bedside USG.
Hemodynamic changes in cardiac tamponade lead to severe obstructive shock and high lethality. Compensatory physiological mechanisms associated with an intensive medical support generally allow life maintenance for variable periods, usually hours and possibly days, but the effective drainage of the pericardial fluid is fundamental in the treatment of these patients. The increase in the number of vacancies in neonatal ICUs in Brazil has the potential to increase the absolute number of these complications. Most of the Brazilian hospitals do not have a team of pediatric cardiac surgery or thoracic surgery with operative training in children, making the treatment of pericardial tamponade in newborns a challenge for the assisting medical team. Although the pediatric surgery team is undoubtedly able to perform the procedure, it is not part of their routine to approach complications related to pericardiocentesis, such as the need for thoracotomy, pericardiotomy and cardiac raphy. Moreover, the surgical team to provide care in such cases, be it the pediatric, the cardiac or the thoracic surgery one, should be well defined, allowing the approach to the patient to quick and safe. In our institution, the thoracic surgery team performs procedures related to pericardial effusion, in agreement with the pediatric surgery team and neonatologists. The fact that this complication often occurs in premature and underweight children makes the procedure even more complex technically and delicate. In our study, all patients were surgically approached by the same thoracic surgeon, which is an important factor for the quality of care of the NICU.

Cardiac tamponade should be considered in every newborn who develop shock, especially in those who have undergone the insertion of any type of central catheter. The use of bedside USG facilitates the diagnosis of the type of shock, favoring the specific treatment. Some studies have shown that the time between insertion of PICC and the development of tamponade can occur from hours to days after the procedure. In the current study, this condition developed between the second and the fourth day after insertion of the PICC. One factor that we considered important for the rapid diagnosis and treatment of our patients was the availability of the bedside USG performed by a pediatric intensive care physician of the NICU itself.

Although there are few studies evaluating cardiac complications resulting from the use of PICC in newborns, there are works that suggest an incidence of tamponade between 0.4 and 3%. Our study confirmed this proportion, with 0.94% of patients admitted in the study period presenting tamponade. If we consider exclusively the patients who used PICC, the pericardial tamponade index in this population was 1.5%. A study that specifically evaluated PICC-related deaths in newborns found three fatal events resulting exclusively from cardiac tamponade in 390 catheter insertions. A study conducted by Beradshall et al. revealed a low incidence of cardiac tamponade associated with PICC, but with mortality directly related to tamponade or to the therapeutic procedure close to 50%. Ohki et al., in a study conducted in 19 NICUs in Japan, evaluated 975 patients who received PICC, with 2.9% of complications associated with this type of catheter, and 0.1% occurrence of cardiac tamponade. In our study, the mortality directly related to the tamponade or to the therapeutic intervention was 0%.
We believe that early diagnosis facilitated by the deliberate use of the bedside USG and the availability of thoracic surgery staff with training in the procedure were the main factors for good diagnostic and therapeutic outcome.

Some studies have shown that there is no difference in the risk of death from cardiac tamponade related to PICC for factors such as gestational age and weight. Regarding general mortality among newborns with this condition, Nowlen et al. performed a review, in 2002, that describes a tamponade-related mortality of 34%. Another review conducted by Askegard-Giesmann, in 2009, showed an overall mortality rate of 18.4%, while a third review by Kayashima, in 2015, revealed a 37% overall mortality. A randomized study conducted by Katheria et al. compared the PICC insertion in neonates with and without bedside USG. The group in which the insertion of the catheter was guided by this USG modality presented a shorter time of catheter insertion, a smaller number of catheter manipulations during the procedure, and a smaller number of radiographs to confirm the location of the catheter, confirming the usefulness of this bedside exam when installing this type of venous access and at confirming its correct positioning.

Treatment of cardiac tamponade associated with central catheters in newborns is well established. Pericardiocentesis plays a role both in the emergency and in the definitive treatment of this condition. Nowlen et al. showed a mortality rate of 8% in patients undergoing pericardiocentesis versus 75% when this procedure was not performed. Our study describes the experience of a single center, with the same assisting team and with homogeneity in the diagnostic and treatment routine, without mortality directly related to tamponade or to the therapeutic procedure. The only death occurred due to multiple organ failure, due to the patient's previous clinical conditions, about 15 days after the resolution of the patient's tamponade. This newborn presented coarctation of the aorta, and the effusion was not related to the PICC. In all our patients, hemodynamic parameters improved immediately after pericardiocentesis.

Until the mid-2000s, most studies evaluating pericardial effusion associated with various types of central catheter in newborns were case reports, reviews or meta-analyses. In the last 13 years, there have been original studies evaluating the complications related to the use of PICC. However, there are few Brazilian studies on the subject that are not case reports. Our work involves four cases, three of which proven to be related to PICC insertion and without mortality, which makes the work relevant considering the extreme rarity and lethality of this condition. It has, however, the limitation of evaluating a relatively short period of time (36 months) and a small number of patients with PICC-related cardiac tamponade.

We could verify that pericardial effusion related to peripherally inserted central catheter is a rare but extremely severe event. The use of bedside ultrasound in patients with acute hemodynamic or respiratory decompensation allows the accurate diagnosis of cardiac tamponade. The approach by means of pericardiocentesis at the moment of diagnosis allows the immediate hemodynamic improvement of the patient. Even in cases where there is suspicion of cardiac perforation by the central peripheral insertion catheter, only pericardiocentesis and the withdrawal or traction of the central catheter present excellent resolution of the condition.
RESUMO

Objetivo: determinar a incidência de derrame pericárdico com tamponamento cardíaco em recém-natos prematuros em uma unidade de terapia intensiva pediátrica, com ênfase na relação entre o derrame pericárdico e a inserção de cateter central de inserção periférica, e avaliar o papel da ultrassonografia à beira do leito na abordagem desses casos.

Métodos: análise retrospectiva dos pacientes internados em unidade de terapia intensiva pediátrica, entre julho de 2014 e dezembro de 2016, que apresentaram derrame pericárdico com repercussão hemodinâmica, avaliados por ultrassonografia. Resultados: foram estudados 426 pacientes admitidos na unidade neonatal de cinco leitos, com realização 285 ultrassonografias à beira do leito. Foram encontrados seis casos de derrame pericárdico, sendo quatro casos com choque obstrutivo e necessidade de realização de drenagem pericárdica, sem mortalidade relacionada ao procedimento e com melhora hemodinâmica em todos os pacientes após o procedimento. A incidência de derrame pericárdico foi de 2,4 casos por ano. Conclusão: a incidência de derrame pericárdico é baixa em neonatos, porém o diagnóstico precoce é fundamental devido à alta morbimortalidade, especialmente nos casos de instalação abrupta. Todos os casos foram diagnosticados pela ultrassonografia à beira do leito, demonstrando sua importância no rastreio desses casos, especialmente em nos quadros de choque de etiologia incerta e neonatos com instabilidade hemodinâmica de início súbito que estão em uso de acesso venoso central.


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