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REVIEW ARTICLE

Paraneumonic pleural effusion. Use of intraeural fibrinolytics in PICU and its possible complications

Derrame pleural paraneumónico. Uso de fibrinolíticos intraeural en UCIP y sus posibles complicaciones

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ABSTRACT

Introduction: An increase in the prevalence of parapneumonic pleural effusion has been observed in recent decades. Intrapleural fibrinolysis for treatment allows destruction of fibrin bridges facilitating drainage, but it is not without complications.
Objective: to describe the use of fibrinolytics and its possible hematologic complications in parapneumonic pleural effusion.
Methods: a bibliographic review on parapneumonic pleural effusion was carried out. Author criteria and research results available in SciELO, Medline, PubMED databases were expressed. A total of 30 bibliographic references were used, more than 75 % of the literature consulted corresponds to the last five years.
Development: Pleural effusion can range from the appearance of scarce serous fluid in the pleural cavity to an exudate mainly of bacterial origin. The clinical situation, the size of the effusion and its characteristics are determinants of decision making.
Conclusions: Pleural effusion in the last 10 years an increase in its incidence has been reported, specifically of pneumococcal and staphylococcal etiology. Treatment consists of antibiotic administration associated with fibrinolytics and/or surgical treatment. Among the fibrinolytics to be used is streptokinase. Its indication will be in complex effusion. The most frequent complication at pleural level is hemorrhage.

Keywords: Pleural Effusion; Streptokinase; Pneumonia.

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RESUMEN

Introducción: En las últimas décadas se ha observado un aumento de la prevalencia del derrame pleural paraneumónicos. La fibrinólisis intrapleural para el tratamiento permite destruir los puentes de fibrina facilitando el drenaje, pero no está exento de complicaciones.
Objetivo: describir el uso de fibrinolíticos y sus posibles complicaciones hematológicas en el derrame pleural paraneumónico.
Métodos: se realizó una revisión bibliográfica sobre el derrame pleural paraneumónico Se expresó criterios de autores y resultados de investigaciones disponibles en las bases de datos SciELO, Medline, PubMED. Se empleó un total de 30 referencias bibliográficas, más del 75 % de la literatura consultada corresponde a los últimos cinco años.
Desarrollo: El derrame pleural puede ir desde la aparición de escaso líquido seroso en la cavidad pleural, hasta un exudado fundamentalmente de origen bacteriano. La situación clínica, el tamaño del derrame y sus características son determinantes de la toma de decisiones.
Conclusiones: El derrame pleural en los últimos 10 años se ha reportado un aumento en su incidencia, específicamente de etiología neumocócica y estafilococcica. El tratamiento consiste en la administración de antibiótico asociado a fibrinolíticos y/o tratamiento quirúrgico. Entre los fibrinolíticos a emplear está la Estreptoquinasa. Su indicación será en el derrame complejo. La complicación más frecuente a nivel pleural es le hemorragia.

Palabras clave: Derrame Pleural; Estreptoquinasa; Neumonía.

INTRODUCTION

In recent years, an increase in pediatric hospitalizations for bacterial pneumonia and its complications, such as parapneumonic pleural effusion,[1] defined as a collection of fluid in the pleural space in association with pneumonia, has been reported.[2]

Classically, it goes through three stages: I) exudative, II) fibrinopurulent and III) organizing. Most of these effusions present in the exudative stage and resolve with antibiotics. When the infection progresses, fibrinopurulent material is deposited forming septa (stage II) and a thick layer of fibrin may appear on the visceral and parietal pleura, making lung expansion difficult (stage III).[3]

This entity affects 450 million people worldwide annually, of which 156 million new episodes occur in children under five years of age.[4]

The incidence of parapneumonic pleural effusions is estimated at 1-3,3 cases / 100 000 children and 28-40 % of those hospitalized for community-acquired pneumonia (CAP) present parapneumonic effusions.[5] Pleural empyema is a frequent manifestation of pleural disease in children from developing countries.[6]

In Latin America, 14 % of deaths under five years of age are due to pneumonia, for an approximate 60,000 deaths.[6,7,8]

In Cuba, influenza and pneumonia occupy the fourth place among the causes of infant mortality and are the main cause of death of infectious origin.[9,10] Of the pneumonias, 8,7 % are serious and cause the death of two million children in developing countries, 90 % of them are caused by Streptococcuspneumoniae (S. pneumoniae) and Haemophilusinfluenzae (Hib).[2,10]

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The initial treatment of this complication is associated with antimicrobials. Pleural tube drainage may fail due to viscous fluid and the presence of multiple pleural space septa, requiring video-assisted thoracoscopic surgery (VATS) or thoracotomy and decortication.[3]

Intrapleural fibrinolysis for the treatment of pleural effusions was described in 1949. Its early use decreases viscosity, breaks the septa and the early pleural shell, which facilitates drainage and avoids surgical procedures.[11,12]

At the Center for Genetic Engineering and Biotechnology (CIGB) in Havana, recombinant streptokinase (SKr; Heberkinase®), the first streptokinase molecule obtained by recombinant DNA techniques, was obtained in 1990.[12] It is a fibrinolytic agent that interacts with plasminogen and forms an active complex with protease activity.[13]

Instillation of these agents into the pleural space is indicated in situations in which there is a multiloculated effusion, whether of hematic, purulent, or complicated parapneumonic origin.[14,15]

Few studies on this subject have been performed in children, so in accordance with the above, we decided to carry out a literature review with the aim of describing the use of fibrinolytics and their possible hematologic complications in parapneumonic pleural effusion.

METHODS

A bibliographic review was carried out using national and international literature, in electronic and printed format, the parapneumonic pleural effusion and the use of fibrinolytics with its possible hematological complications, authors' criteria and research results on the subject were expressed.

The search for sources of information was carried out between October and December 2021. The literature used was taken from articles and texts available in the SciELO, Science Domain, Medline, PubMed databases, among others, and computer descriptors were used such as: pleural effusion, intrapleural fibrinolysis, complications due to the use of streptokinase, complicated pneumonia.

The empirical method was used for documentary observation, and the theoretical methods: historical-logical and analysis-synthesis, in the processing of data and criteria of authors of the literature consulted.

A total of 39 bibliographic references were used. As a criterion for the selection of the literatures, it was established that 75 % of the references used corresponded to the last five years.

DEVELOPMENT

Pleuropulmonary anatomy

For a better understanding of the different pathological alterations that can affect the pleura and pleural cavity, it is necessary to have basic knowledge of pleural anatomy and physiology.[16]

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The human organism has several devices and systems for its functioning, the respiratory system is one of them, which has as main organs the lungs, with its basic structural unit, which allows the obtaining of oxygen and the expulsion of carbon dioxide among other functions. Located in the thoracic cage, they are covered by the pleura, a thin membrane that covers the lungs with their fissures, the mediastinum, the diaphragm and the costal wall, separately in each hemithorax. Classically a distinction is made between the parietal and visceral pleura, but in reality it is a continuous membrane and the transition between the two pleurae is at the pulmonary hilum.[8]

The pleural vasculature is entirely derived from the systemic circulation in both the parietal and visceral pleura. The fluid produced in the pleura is reabsorbed primarily via the lymphatic circulation.[6,8]

Pleural fluid is a plasma ultrafiltrate from both pleural sheets, its volume does not exceed five to 15 ml in the adult without disease, its production is approximately 0,1 to 0,2 ml/kg body weight per day, its appearance is clear, it contains 1,5 g/dl of proteins and about 1 500 cells/ml with a predominance of monocytes and with a pH of 7,6. Pleural effusion occurs when there is an imbalance between pleural fluid production and reabsorption.[16,17,18]

As for the mechanism by which pleural effusion occurs, there are at least six mechanisms responsible:[5]

1. Increased hydrostatic pressures. This mechanism is especially important only when capillary pressures of the pulmonary circulation are elevated.
2. Decreased oncotic pressure in the microcirculation. This is rare, due to the great reabsorption capacity of the lymphatic circulation, which can reabsorb up to 30 times the volume of pleural fluid.
3. Increase in the negative pressure of the pleural space. It occurs exclusively when there is massive pulmonary atelectasis. It is doubtful that it alone will lead to a large effusion without superimposed cause.
4. Increased permeability in the microcirculation. It is a mechanism that occurs, above all, when the pleura is involved in the pathological process giving rise to exudates.
5. Impaired lymphatic drainage. It is one of the main mechanisms responsible for the persistence of pleural effusion. It constitutes the main mechanism of production of pleural effusion of tumor origin. It also occurs in the blockage or rupture of the thoracic duct, which will cause a chylothorax and can be secondary to tumors (lymphoma), trauma or infections (filariasis). Other causes with clear impairment of lymphatic drainage as the main mechanism are sarcoidosis and post-radiation effusion.
6. Movement of fluid from the peritoneum. This occurs through the lymphatics and small diaphragmatic defects. Examples are effusions secondary to ascites, urinary obstruction, peritoneal dialysis, Meigs syndrome and pancreatic processes.[15,19]

The presence of liquid in the thorax is among the oldest affections that humanity has had to face, correctly considered as a syndrome because it gathered a group of symptoms and clinical signs of diverse etiology, called pleural liquid interposition syndrome.[11,19]

Among the different causes that produce this syndrome, pleural effusion of infectious cause occupies an important place.[20]

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Pneumonia constitutes one of the most frequent causes of pleural effusion in children; an important percentage of those who require hospitalization develop it and within these, a significant group becomes complicated.[21]

Definition and classification

Pleural effusion: nosological entity that can range from the appearance of scarce serous fluid in the pleural cavity to a frankly purulent exudate of variable volume.[18]

Complicated pleural effusion: one in which the usual medical treatment fails and tends to loculation, requiring the use of fibrinolytic agents or pleural debridement surgery and sometimes even pulmonary decortication.[6]

For effusions associated with bacterial pneumonias, the following terminology has been used up to the present time:[7,22]

- Paraneumonic effusion or pleurisy: any effusion associated with bacterial pneumonia, lung abscess or bronchiectasis.
- Empyema: is defined as the accumulation in the pleural cavity of purulent, thick, creamy, often foul-smelling fluid. It can also be a cloudy or clear liquid, with predominance of polymorphonuclear containing toxic granulations and, frequently, with germs in the microscopic examination.

Whatever the origin of the infection, the evolution of empyema can be schematized in four successive phases: dry pleuritis phase, acute or exudative phase, fibrinopurulent, subacute or transitional phase and chronic or organizational phase.[6]

A.-Dry pleuritis: (< one week)
The inflammatory process of the pulmonary parenchyma extends to the adjacent pleura producing a local pleuritic reaction, without pleural effusion so many authors consider it as a preceding stage and not proper of pleural effusion. Clinically it corresponds to the appearance of pleuritic chest pain and the auscultation of a pleural friction rub.

B.- Acute or exudative: (one week)
In response to pleural inflammation and increased capillary permeability, the pleural space is occupied by a fluid liquid (in principle sterile in most cases) of low cellularity. The lung is still free of adhesions and the pleural fluid shows low levels of leukocytes and lactate dehydrogenase (LDH), as well as normal glucose and pH values.

At this stage, full anatomical restoration can be achieved with medical treatment, the effusion is reabsorbed and complete lung re-expansion is achieved. This period can be as short as 48 hours.

C.- Subacute or fibrinopurulent: (two-three week)
The fluid becomes more turbid due to the increase of polymorphonuclears, bacteria and fibrin. The latter covers both pleural sheets like sheets limiting lung expansion. If this stage progresses, loculations are formed by limiting membranes. The speed and intensity of this evolution is influenced by the type of germ and the efficacy of treatment. The pH and glucose in pleural fluid decrease and LDH increases.

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D.- Chronic or organizational: (four-six week)
It is characterized by the organization of the so-called pleural cortex by invasion of capillaries and fibroblasts. The pleural fluid is viscous and contains more than 65 % sediment, indicating that pleural symphysis has already occurred. The pH of the pleural fluid is less than seven and the glucose is less than 40 mg/dl. The cortex is fixed to the visceral pleura from which it will be inseparable, as well as to the parietal pleura, the diaphragm and the rest of the elements of the thoracic wall.[8,21,22,23]

A review of the medical literature shows that the logical sequence of these stages does not occur in the same way in all patients; it is influenced by the causative microorganisms, their biological variability and virulence and the diversity of forms of presentation.[22,19]

History

The presence of fluid in the thorax is among the oldest affections that mankind has had to face.

Until the early years of the 20th century, surgeons feared the opening of the pleural cavity. The experience gained in war wounds during the preceding centuries had repeatedly demonstrated the rapidly fatal effects that could occur when a wide opening of the chest wall.[8,24]

During the first decades of the 20th century, one of the problems most frequently encountered by the thoracic surgeon was pleural empyema. During World War I, the Empyema Commission was created, whose contribution to the current knowledge of its treatment was very outstanding.[23] At that time it was common for pneumonia to be complicated by empyema.

From the first description of pleural instillation of fibrinolytics by Trillett and Sherry in 1949 to the present time, few studies have been reported comparing the efficacy of this technique with conventional surgery and videothoracoscopy with debated results, but even today its usefulness is controversial by different authors and the benefits of this technique are compared with videothoracoscopy, thoracotomy and even with drainage tube placement, as the only procedure.[22]

The 1950s marked a new stage for this condition, due to the clinical use of newly created antibiotics, for which reason the incidence of the disease decreased notably and there was a change in the microorganisms that caused it.[14] Another important element was the existence of more precise radiological studies in the diagnosis and follow-up of patients: the bases of imaging were established, however this condition continued to be a health problem.[25]

As early as 1984, the use of catheters in the drainage of empyematous collections in which treatment with a conventional chest tube had failed was reported.[8]

After the first appendicectomy by laparoscopy was performed and in 1987 the first cholecystectomy, the world of treatments in these conditions was revolutionized after these events and it was possible to use them also in the thorax.[15,24]

In the literature consulted it is stated that since 1973, they wrote about the use of urokinase in the drainage of a hemothorax through a conventional drainage tube with good results and later, in 1987, they successfully reported the drainage of two infected extravascular hematomas, inserting a catheter and successive instillations of urokinase.[13,14]

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Later in other published works,[16,23] successes between 90 and 100% of cases were achieved in the treatment of multiloculated pleural effusions and hemothorax, with the intracavitary instillation of urokinase through percutaneous catheters placed under radioscopic control.

Epidemiology

Paraneumonic pleural effusion is becoming more frequent every day as a complication of pneumonia, which causes about 1.3 million deaths annually in children under five years of age, accounting for 18% of all deaths at this age, with 99% occurring in resource-poor countries.[2]

Acute lower respiratory infections in 2019 represented the fifth leading cause of infant mortality and the third leading cause of post-neonatal mortality.[9] It is estimated that during the first five years of life a child suffers from five to nine episodes of acute respiratory infection per year; and that two out of every 100 of these episodes develop pneumonia.[2,8]

In developed countries, such as North America, Europe, Oceania and Japan, it is estimated that up to 2,6 million cases of pneumonia occur annually in children under five years of age, causing 1,5 million hospitalizations and approximately 3,000 deaths from this cause, a figure higher than deaths from meningitis.[4]

Pneumonias are one of the most frequent causes of pleural effusion in children. Approximately 40 % of pneumonias requiring hospitalization in children have pleural effusion and 0,6-2 % of pneumonias are complicated by empyema.[4,6]

According to PAHO/WHO reports, acute respiratory infections in the Americas account for 30-40 % of hospitalizations, of which 60 % are due to pneumonia.[16]

In the United States, more than one million patients require hospital admission each year and the estimated cost of treatment of a patient with uncomplicated CAP admitted to a hospital is 20 times higher than outpatient treatment.[18,23]

In Latin America and the Caribbean, more than 80,000 children under five years of age die each year from respiratory tract infections, 85 % of them from pneumonia.[16]

Cuba is not exempt from this increase, acute respiratory diseases in children are increasing and although mortality due to pneumonia has decreased considerably in recent years, rates are similar to those of developed countries.[2,9]

A significant percentage of pneumonias evolve with DPPN, pulmonary and extrapulmonary complications derived from it increase and 0.6 - 2% are complicated with empyema.[6,9]

Diagnosis

The clinical situation, the size of the effusion and its characteristics are determinants of decision making.[14]

Pleural effusion is suspected when there is a worsening of the general condition, appearance of pleuritic pain, decreased mobility of the affected hemithorax, dullness on percussion, muffled or decreased breath sounds and if O2 saturation decreases. Plain radiography is used for diagnosis. The most useful radiological test is ultrasound, which provides superior information to computed tomography (CT) as to the nature of the effusion (simple or complicated).[5,25]

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In case of significant effusion, thoracentesis is performed. The biochemistry of the pleural fluid allows classifying the effusion as: uncomplicated, complicated or empyema. Treatment consists of the administration of intravenous antibiotics associated with fibrinolytics.[4]

The parameters will be assessed as follows:

- Measure PH unless the appearance of the fluid is frankly purulent.
- Glucose measurement is useful when there is doubt about the quality of the pH measurement.

Differential diagnosis between pleural fluid exudates and transudates.[23]

PARAMETERS	EXUDATES	TRANSUDATES
Proteins	> 3 g/l	< 3 g/l
Pleural/serum protein ratio	> 0.5	< 0.5
Ph	< 7.3	> 7.3
Glucose	< 3.33mml/l	> 3.33mml/l
Cholesterol	> 60 mg/ dl	< 60 mg/ dl
Leukocytes	> 1.000 / l	< 1.000 / l

Empyema should be considered in any patient on antibiotic treatment associated with high C-reactive protein (CRP) values (> 200 mg/l) and persistent fever after 48 hours. Up to 20 % of empyemas are complicated by necrotizing pneumonias; what used to be frequent for Staphylococcus aureus is now becoming frequent for pneumococcus.[26] The clinical situation and the size of the effusion are determinants of the decision making process. [6,23]

Paraneumonic Pleural Effusion [23]

	Simple	Complicated	Empyema
Ph	< 7.3	< 7.2	< 7.0
Leukocytes/mµ3	> 10.000	> 10.000	15.000
Glucose	< 60 mg/dL	< 40 mg/dL	< 40 mg/dL
Culture	Negative	Positive	Positive
LDH	< 1.000 UI/L	> 1.000 UI/L	> 1.000 UI/L

Treatment

In the evolution of parapneumonic empyema, three stages can be distinguished: exudative, fibrinopurulent and organized. In the exudative stage, it is usually easily evacuated by thoracentesis and chest drainage. In the organized stage, it is necessary to perform thoracotomy for decortication and in many cases atypical partial pneumonectomies'.[5]

In the fibrinopurulent stage, chest drainage is generally insufficient since it is frequently blocked and, if resolution does not occur rapidly, it is likely that thoracotomy and decortication will be required for the tabication. Some authors recommend performing this procedure early.[24,26] In contrast, others use intrapleural fibrinolytic instillation and videothoracoscopy as a way to prevent more aggressive surgery and decrease the morbidity and mortality associated with thoracotomy.[15]

The failure of these drains is mainly due to the septation or loculation of the pleural collection.[5,27]

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Current guidelines recommend early use of intrapleural fibrinolytics for the management of CPPD when loculations are present in the pleural cavity (resistant to pleural drainage) and in the context of empyema. Published studies have found great efficacy and minimal side effects with their use.[12,13]

In these cases the use of fibrinolytic substances has been recommended, in order to slow down the pathophysiological phenomenon and break the fibrin bridges and remove the accumulated fibrinoid material. Substances such as streptokinase, urokinase, and tissue plasminogen activator are used for this purpose. Few studies have been performed in children, but it has been seen that when comparing the use of these substances versus saline solution for empyema lavage or use of surgical techniques, hospital stay is reduced with the latter.[1,13]

Coagulation, fibrinolysis, fibrinolytics and adverse reactions

The physiology for the formation of fibrin clots is described in several studies. A thrombus or clot forms when blood cells become enclosed in a matrix of the protein fibrin, an enzyme that can act in dissolving clots. This process is known as thrombolysis or fibrinolysis. In the mammalian blood circulation, the enzyme responsible for this process is plasmin, a serum protease similar to trypsin.[11]

Plasmin is the fibrinolytically active form produced from inactive zymogen, called plasminogen, which is present in the blood circulation. The conversion of plasminogen to plasmin is mediated by proteolytic cleavage of the Arg 561-Val 562 bond, which is mediated by several plasminogen activators.[28] The plasminogen activators present in blood are tPA and uPA. Fibrinolytic activity in the circulation is modulated by inhibitors of plasminogen activators (including plasminogen activator inhibitor 1, PAI-1) and plasmin (a1-antiplasmin, a2-macroglobulin). [29]

Plasmin acts on the fibrin network and converts it into degradation products (PDF).[11]

Recombinant forms of human plasminogen activators (tPA and uPA) and also streptokinase (Sk), a protein isolated from the beta-hemolytic group C streptococcus bacteria, which is not found naturally in human circulation, appear in clinical treatment.[12]

Sk, tPA and uPA do not have direct fibrinolytic activity; their therapeutic action is exerted by activation of the plasminogen present in the blood and its conversion to plasmin.[22]

Sk, unlike tPA and uPA which are proteases, does not have its own enzymatic activity. This protein acquires its activating capacity through the formation of a complex with plasminogen or plasmin present in the blood circulation, thus degrading fibrinogen and fibrin clots and reducing the number of pleural septa.[29]

As with other thrombolytic drugs, the main complication of treatment with Sk is bleeding, which is related to the dose and duration of intravenous infusion. Respiratory failure has been described after the use of fibrinolytics.[4]

Due to its bacterial origin, Sk is antigenic and can therefore produce allergic reactions in addition to fever, chills, urticaria or rash. Anaphylactic shock is fortunately very rare (between 0,1 and 0,5 %); however, arterial hypotension requires resuscitation with fluid therapy in seven to 10 % of patients.[11,29]

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Urokinase is a plasminogen activator, which converts it into plasmin, therefore, it is not specific to act on fibrin. The destruction of the septa facilitates the drainage of the pleural effusion.[13]

Its thrombolytic activity is similar to that of Sk, but its clinical application is limited by its high costs and the lack of randomized studies proving its efficacy.[1]

There is a linear correlation between plasma thrombolytic activity and Uk dose, which may be due to its mechanism of action and the absence of neutralizing antibodies. Its main side effect is hemorrhage, and it lacks antigenic properties in humans.[13]

There is no clear and unanimous agreement on the most appropriate or precise doses of fibrinolytics. In all the studies published to date, the doses used were empirical.[12]

Controlled clinical trials in children are scarce, with an inadequate number of patients and insufficient statistical power to demonstrate a benefit of this treatment and to be able to recommend it in precise indications.

Contraindications

It is difficult to establish a standard since they vary among different authors. It is advisable to avoid its use in patients with suspected hypersensitivity to streptokinase, bronchopleural fistula, fibrothorax, large empyema with trapped lung, presence of multiple separated lobes, post-pneumonectomy or recent intrapleural hemorrhage (less than three days).[1] The presence of a bronchopleural fistula could produce pneumonitis in the contralateral lung and greater systemic absorption; however, there have been cases in which it was used two days after fistula closure or after pulmonary surgery without complications.[22]

Contraindications include a history of acute hemorrhagic stroke, surgery or head trauma in the previous two weeks, intracranial neoplasms, recent thoracic or abdominal surgery. However, these contraindications would be rather for the systemic use of fibrinolytics, but when instilled in the pleural cavity absorption is minimal and their use in patients with these pathologies does not seem to present an increased risk.[22,23]

Published studies have found high efficacy and minimal side effects in the use of fibrinolytic agents in certain pleural effusions.[30] The instillation of these agents within the pleural space is indicated in situations in which there is a multiloculated effusion.[4]

Indications.[1]

According to the experience developed by the aforementioned Medical Surgical Unit team in the instillation of intrapleural fibrinolytics, the criteria for indicating such procedure in patients with parapneumonic empyema are:

Persistence of fever (axillary temperature > 38°C) for more than 48 hours, poor general condition or dysfunction of the drainage tube or both, after placement of the chest drain.
Complex effusion, with septa, septa or suspended particles on chest ultrasound on admission, prior to drain placement.

Finding of fibrin in the operative act of placement of the chest drain.
In all these cases the minimum recommended time between the placement of the drain and the administration of the first dose of SK is 12 hours.

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Procedure: [1,4]

Hydrocortisone: 20 mg/kg i/v half an hour before the procedure.
Bupivacaine 0,25 %. Under 1 year old: 10 ml intrapleural. Older than 1 year: 20 ml intrapleural. In the case of children under 1 year with bupivacaine 0,25 %, or if bupivacaine 0,5 % is used, in both cases the dose is half, a total of 20 ml should be completed in the urological syringe by adding SSF.

Streptokinase (SK). Under 1 year old: 100,000units.

Older than 1 year: 200,000units intrapleural.

SK comes in powdered form in concentrations of 750,000 units or 1,500,000 units, and must be diluted with SSF. In both cases, 7,5 ml of SSF is added and the vial is shaken. If the SK is 750,000 units, 100,000 units remain per ml. If the SK is 1,500,000 units, 200,000 units remain per ml. After reconstituted with the serum, it should be kept in the refrigerator and can be stored for three days (which is the duration of the initial treatment) properly labeled.

Recommended size of pleural drainage tubes

Weight	Non-septated effusion	Septated effusion
< 3 kg	8 - 10	10 – 12
3-8 kg	10 – 12	12 - 16
9-15 kg	12 - 16	16 - 20
16-40 kg	16 – 20	20 - 28
> 40 kg	24 - 28	28 - 36

Technique: [1,23]

1. Correct hand hygiene of those involved in the procedure.
2. Nursing administers the dose of hydrocortisone to the patient.
3. The physician dresses in sterile clothing.
4. Preparation on the sterile field of the doses corresponding to the patient's age.
5. The dose of bupivacaine is loaded from the vial to a 20ml syringe, filling the total capacity of the syringe with SSF.
6. The dose of SK is loaded from the vial to a 50ml syringe, completing with SSF the total capacity of the syringe (1ml of diluted SK for each 50ml syringe in the case that the dose to be used is 2ml).
7. In the patient's bed, corroborating that the drainage under water does not bounce, the cure that has the thoracic drainage is removed (if it is not in the air), the patient is lateralized (he can be in the arms of the person who accompanies him).
8. The drainage tube is clamped and the bottle is removed, measuring the output and assessing the characteristics of the drained fluid.
9. The physician connects the syringe with the dilution of bupivacaine, unclamps and injects rapidly. Clamp again.
10. Attach the syringe, unclamp and inject the corresponding dose of SK, slowly. Clamp again.
11. The tube will remain clamped for four hours. During this time it is important to change the patient's position, lateralize him/her to both sides, Trendelemburg and seated position for periods of 1 hour in each position. In the case of the lateral position where the pleural drainage is located, if the patient is small, it is recommended to perform the procedure in the arms of the person accompanying the patient to avoid discomfort.

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12. Once this period has elapsed, the nurse connects the drainage again to a closed system under water.
13. Declamp, measure the output, the characteristics of the liquid and record in the clinical history. The few air bubbles that entered if the procedure was not done properly may come out, which do not contraindicate the procedure to be performed at 24 hours.
14. If at any time during the 4 hours, the patient manifests severe pain, installs respiratory difficulty, the drainage should be placed under water and immediately unclamped.

If there is no evidence of complications, it will be repeated once a day for 3 days. A control ultrasound will be performed 12 hours after the end of each dose to evaluate the application of the next dose; less than two doses are not recommended. It is not necessary to perform a chest X-ray, unless there is a clinical deterioration of the child or other indication outside the procedure itself.

CONCLUSIONS

Pleural effusion is a nosological entity that can range from the appearance of scarce serous fluid in the pleural cavity to a frankly purulent exudate of variable volume. In the last 10 years, an increase in complicated pleural effusions in children, specifically of pneumococcal and staphylococcal etiology, has been reported. The clinical situation, the size of the effusion and its characteristics are determinants of decision making. The biochemistry of the pleural fluid allows classifying the effusion as uncomplicated, complicated or empyema, which defines the treatment. Bronchopleural fistula is one of the most important contraindications due to the risk of greater systemic absorption and thus the appearance of complications at this level. The most frequent complication from the hematological point of view at pleural level is hemorrhage. It is a therapy that has proven to be effective in reducing the incidence of thoracic surgery and thus vital risk for the pediatric patient.

Conflict of interest:
The authors declare that there is no conflict of interest.

Authors' contribution:
All authors participated in the conceptualization, formal analysis, original draft-drafting, drafting-revising, editing, and approval of the final manuscript.

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