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Standard treatment regimen with and without dexamethasone on outcome of children aged 3–7 years with empyema: a randomized double blind clinical trial

Alireza Eshghi[1], Nasrin Hoseiny Nejad[1], Azar Mohammadzadeh[2,3], Farhad Mansouri[4] and Shabnam Aghajani[5*]

Abstract

Background Corticosteroids have an effective inhibitory effect on inflammatory factors and are used as adjunctive therapy for viral pneumonia. We conducted this study to compare the effects of a standard treatment regimen with and without dexamethasone on the outcomes of 3-7-year-old children with empyema.

Methods This randomized controlled trial was conducted at a university hospital in Iran from June 2023 to November 2024. Children aged 3–7 years with empyema were enrolled. All patients received standard antibiotic treatment (Vancomycin and Meropenem) and a fibrinolytic agent (alteplase). The dexamethasone group received additional intrapleural dexamethasone injections. Randomization was performed using block randomization with a block size of 4. Both children and outcome assessors were blinded to dexamethasone administration. The primary outcome was length of stay (LOS), with secondary outcomes including duration of fever, chest tube placement, oxygen saturation, and CRP levels.

Results Out of 47 patients (dexamethasone group = 23), 48.9% of the subjects ($n = 23$) were girls. The LOS in the dexamethasone group, with a median of 9.5 days and a range of 7–17 days, was significantly less than in the control group, with a median of 16 days and a range of 10–24 days. The duration of fever (median 5 vs. 11 days) and CRP level (median 12.5 vs. 21) in the dexamethasone group were significantly lower than in the control group. No significant difference was observed between the two groups in terms of PCR for COVID-19 and influenza, pleural fluid smear culture, blood culture, oxygen saturation, and duration of chest tube placement.

Conclusions Our findings showed that the use of dexamethasone decreases the duration of hospitalization, duration of fever, and CRP levels, leading to faster recovery in children with empyema. Dexamethasone can be a safe and effective adjunctive therapy for empyema in children.

Trial registration IRCT20240705062336N1, Retrospectively Registered (20241116).

Keywords Corticosteroid, Dexamethasone, Empyema, Pediatrics

*Correspondence:
Shabnam Aghajani
ali_phd203@yahoo.com

Full list of author information is available at the end of the article

Introduction

Empyema is a serious complication defined as the accumulation of pus in the pleural space. It occurs in 2–7% of children hospitalized with community-acquired pneumonia (CAP) [1, 2]. This disease is more prevalent in preschool-aged children [2]. Although the prevalence of empyema has decreased following pneumococcal vaccination and the use of various antibiotics, it remains a significant concern in pediatric pneumonia cases [3, 4].

Children are particularly susceptible to empyema due to their immature immune systems. In pediatric patients, empyema often manifests with more severe clinical symptoms compared to adults, including chest pain, high fever, cough, purulent sputum, and shortness of breath. Given the serious nature of empyema, early intervention is crucial in managing this complication. Prompt diagnosis and initiation of appropriate treatment can significantly improve patient outcomes and reduce the likelihood of complications [5, 6].

Treatment for empyema typically involves a combination of medication and surgical interventions. Common treatment modalities include intravenous antibiotics, intercostal chest tube drainage (ICD), video-assisted thoracoscopic surgery (VATS), thoracotomy decortication (TDC), and chest tube placement. The specific treatment approach is tailored to the individual patient's condition and the severity of the empyema [7–9].

Corticosteroids are effective in inhibiting inflammatory factors and are frequently utilized as adjunctive therapy for viral pneumonia [10]. Recent studies have indicated that corticosteroids can significantly reduce the length of hospitalization for patients with pneumococcal pneumonia and empyema. Additionally, early administration of corticosteroids has been shown to shorten the recovery time for these patients [11–13].

Physicians typically refrain from prescribing corticosteroids during active infections due to their immunosuppressive effects and potential long-term complications. However, a review of published randomized, double-blind trials comparing corticosteroids to placebo in various infections concluded that corticosteroids can be both effective and safe for a wide range of conditions. Specifically, McGee found that corticosteroids are safe for patients with bacterial meningitis, tuberculous meningitis, tuberculous pericarditis, severe typhoid fever, tetanus, and pneumocystis pneumonia with moderate to severe hypoxemia, as their use improves patient survival [10]. Given that prolonged hospitalization and infection duration can lead to irreversible complications in children, in addition to the significant burden of diagnostic and treatment costs, timely diagnosis and management of empyema are crucial. With this in mind, the present study aimed to compare the effect of the standard treatment regimen with and without dexamethasone on the length of hospital stay in 3-7-year-old children diagnosed with empyema.

Methods

Trial design

This study was designed as a randomized controlled trial with parallel groups. Recruitment began in June 2023 until November 2024. In preparing this manuscript, we followed the CONSORT (Consolidated Standards of Reporting Trials) guidelines to ensure transparent and accurate reporting of our clinical trial. The study protocol is available at the Iranian Registry of Clinical Trials with the ID number IRCT20240705062336N1.

Setting & participants

The study was conducted at a university hospital affiliated with Iran University of Medical Sciences in Iran. The sample consisted of children hospitalized at Aliasghar Children's Hospital between 2022 and 2024. Eligibility criteria included children aged 3 to 7 years with a diagnosis of empyema, confirmed by the presence of pus in the intrapleural fluid or a positive microbial culture of the pleural fluid. Critically ill and intubated patients, as well as those receiving corticosteroids for other conditions, were excluded.

Patients were closely monitored for potential adverse effects related to dexamethasone administration. Withdrawal criteria included any signs of sensitivity or complications attributable to dexamethasone, such as allergic reactions (e.g., urticaria, skin rash), gastrointestinal bleeding (e.g., hematemesis, melena), hyperglycemia, or hypertension. In such cases, dexamethasone administration was immediately discontinued, and the patient was withdrawn from the study.

Interventions

All patients in both groups received standard antibiotic treatment, including Vancomycin and Meropenem. Vancomycin was administered at 10 mg/kg/dose four times a day (QID), and Meropenem at 20 mg/kg/dose three times a day (TDS). Additionally, a fibrinolytic agent, alteplase, was injected into the pleural chest tube by a pediatric pulmonologist once daily for three days, mixed with 4 cc in 40 cc of normal saline. For patients in the dexamethasone group, they received an additional treatment of dexamethasone injected into the chest tube. The dexamethasone was administered in two doses every 48 h, with a total daily dosage of 0.2 mg/kg/day. The maximum total dosage of dexamethasone received by any patient was capped at 2 mg to ensure safety and minimize potential side effects. The control group received 0.5 cc of normal saline as a placebo injection.

Randomization, concealment & masking

Randomization was performed using the online platform Sealed Envelope with block randomization (block size of 4) by an individual outside the research team who held the randomization sequence and sealed envelopes containing unique codes. The principal investigator contacted this individual to obtain group assignments for each enrolled patient. Regarding blinding, children, parents, and outcome assessors remained blinded throughout the study. Since the children were between 3 and 7 years old, the intervention was indistinguishable from other treatments they received. Parents were not present in the ward or PICU at the time of the injections. The injections consisted of either 0.5 cc of normal saline (placebo) or dexamethasone, 0.5 cc of normal saline was injected alone in the control group, while dexamethasone was injected in the intervention group. While the principal investigator administered the injections, outcome assessments were conducted by an independent pediatrician who was not involved in the injections or intervention, ensuring that outcome assessors remained blinded to group assignments.

Primary and secondary outcomes

The primary outcome of the study was the length of stay (LOS), defined as the total number of days each participant stay in the hospital from admission to discharge. Secondary outcomes included the duration of fever and the duration of chest tube placement, measured in days from insertion to removal. Oxygen saturation (SO2) levels were assessed using pulse oximetry immediately prior to discharge and recorded as a percentage. Additionally, C-reactive protein (CRP) levels were measured by spectrophotometry before and 48 h after dexamethasone administration to evaluate the inflammatory response. Importantly, the incidence of complications and adverse events related to treatment was also monitored as a secondary outcome. This included systematic assessment of steroid-related side effects such as allergic reactions (e.g., urticaria, skin rash), gastrointestinal bleeding (e.g., hematemesis, melena), hyperglycemia, and hypertension. Blood glucose levels were checked every 12 h using a glucometer, and blood pressure was monitored every 6 h to promptly identify any adverse effects, ensuring patient safety throughout the study.

Sample size

The sample size was determined using PASS2021 software, referencing Tagarro's study [14]. We considered Type I and Type II errors of 0.05 and 0.20, respectively. Based on a mean length of hospitalization of 4.5 days for the intervention group and 7.5 days for the control group, with a standard deviation of 3.5, we calculated that a sample size of 23 participants was needed for each group.

Statistical analysis

Data were analyzed using SPSS software version 24. Quantitative variables were reported as median (range), depending on the distribution of the data. Categorical variables were expressed as frequency (percentage). To compare outcomes between the two groups, Mann-Whitney U test was utilized. Chi-square tests were applied to assess differences in categorical variables. A significance level of <0.05 was considered statistically significant.

Results

As illustrated in Figs. 1 and 52 children were assessed for eligibility, of whom 4 were excluded, including 2 due to prior cortisone use. A total of 48 patients aged 3 to 7 years with empyema were randomized equally into the intervention (dexamethasone) and control groups ($n=24$ each). All patients received the allocated intervention. One patient in the dexamethasone group was lost to follow-up due to chest tube removal, resulting in 23 patients analyzed in this group, while all 24 patients in the control group completed the study and were included in the analysis. Of the 47 patients analyzed, 23 were girls. The mean age of patients in the dexamethasone group was 6.16 years (SD = 3.25). There were no significant differences between the two groups regarding gender and age ($P=0.763$ and $P=0.786$, respectively) (Table 1).

One patient in each group had received the flu vaccine. Chest pain and shortness of breath were observed in all patients. PCR evaluation for Covid-19 infection resulted in two positive cases in the control group 17 patient in the dexamethasone group and 16 patients in the control group had positive PCR for influenza. (Table 2)

In Table 3 primary and secondary outcome variables evaluated between dexamethasone and control group. The LOS in the dexamethasone group with a median of 9.5 and a range of 7–17 days was significantly less than the control group with a median of 16 and a range of 10–24 days. The duration of fever (median 5 vs. 11) and CRP level (median 12.5 vs. 21) in the dexamethasone group was significantly lower than the control group. No significant difference was observed between the two groups in terms of PCR for covid-19 and influenza, pleural fluid smear culture, blood culture, oxygen saturation and duration of chest tube. (Tables 2 and 3)

Discussion

We evaluated the impact of a standard treatment regimen, both with and without dexamethasone, on the duration of hospitalization for children aged 3 to 7 years diagnosed with empyema. Our findings demonstrated that the addition of dexamethasone significantly shortened the LOS, reduced the duration of fever, and lowered blood CRP levels compared to the control group.

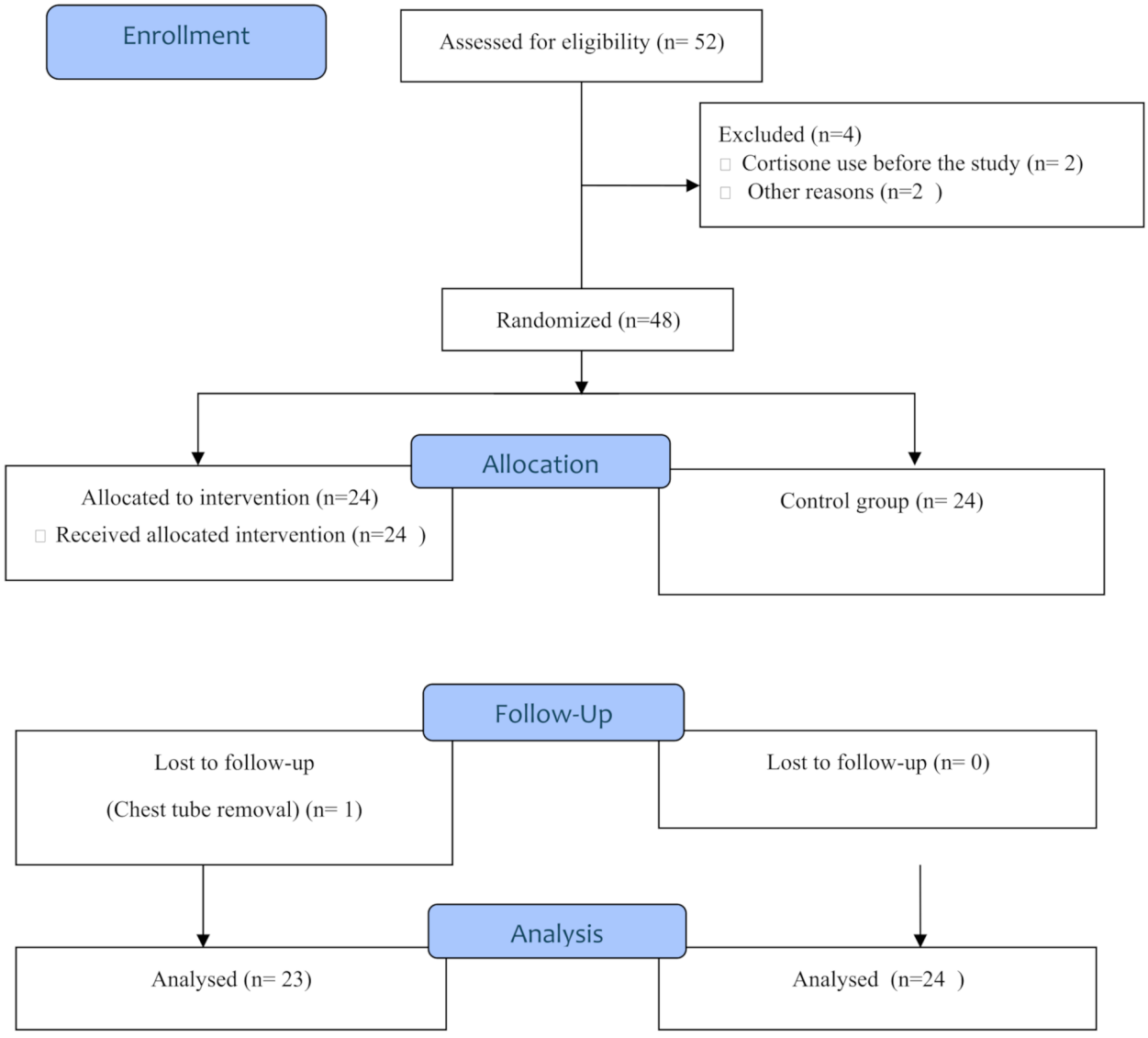

Fig. 1 Flow diagram of study participants

Table 1 Baseline Demographic characteristics of study participants by treatment group

	Dexamethasone group (*n* = 23)	**Control group (*n* = 24)**	***P*-value**
Age, Mean(SD)	6.16 (3.25)	6.43 (2.91)	0.786
Gender, N(%)			
girl	12 (54.5)	11 (45.8)	0.555
boy	11 (45.5)	13 (54.2)	

These differences are not only statistically significant but also clinically meaningful. A reduction in LOS from a median of 16 to 9.5 days represents a substantial decrease in hospitalization burden for both patients and healthcare systems, potentially lowering the risk of hospital-acquired complications and reducing costs. Similarly, the shortened duration of fever (median 5 vs. 11 days) reflects faster clinical recovery and improved patient comfort. The significant decrease in CRP levels in the dexamethasone group indicates a more rapid resolution of inflammation, which is consistent with corticosteroids'

Table 2 Comparative analysis of PCR and culture results in study groups

	Dexamethasone group		Control group		*P*-value
	Negative	Positive	Negative	Positive	
PCR covid-19	21 (100)	0	21 (52.2)	2 (8.70)	0.267
PCR Influenza	4 (19.0)	17 (81.0)	7 (30.4)	16 (69.6)	0.384
Pleural fluid smear	8 (57.1)	6 (42.9)	6 (42.9)	8 (57.1)	0.450
Blood Culture	19 (95.0)	1 (5.0)	41 (97.6)	1 (2.4)	0.476

Table 3 comparison of primary and secondary outcome between study groups

	Dexamethasone group ($n=23$)	Control group ($n=24$)	*P*-value*
	Median (range)	Median (range)	
LOS (day)	9 (7–17)	16 (10–24)	**< 0.001**
O2Sat at admission(%)	87.56 (61–96)	89.53 (80–96)	0.88
O2Sat at discharge (%)	96.06 (93–98)	95.58 (92–99)	0.31
Fever duration (day)	5 (3–13)	11 (4–17)	**< 0.001**
Chest tube duration (day)	7 (5–9)	8.00 (6–10)	0.33
CRP at admission (mg/L)	77.73 (56–94)	77.48 (27–94)	0.72
CRP at discharge (mg/L)	15.73 (4–61)	19.78 (8–35)	0.02

*U Mann Whitney

anti-inflammatory effects and supports their role in modulating the inflammatory response in empyema.

The antipyretic effect of dexamethasone likely contributes to the reduced fever duration. Corticosteroids exert their antipyretic action by influencing the hypothalamic set point, thereby lowering fever and associated symptoms. While corticosteroids are not primarily indicated for fever reduction alone, their anti-inflammatory properties help control systemic inflammation, which is reflected in the CRP decline. This accelerated resolution of fever and inflammation may facilitate earlier clinical stability and discharge, as observed in other respiratory infections treated with corticosteroids.

Regarding oxygen saturation and chest tube duration, no significant differences were observed between the dexamethasone and control groups. This finding can be explained by the pathophysiology of hypoxemia in empyema and pneumonia. Decreased oxygen saturation typically results from ventilation/perfusion mismatch, intrapulmonary shunting, increased dead space, or hypoventilation—mechanisms that corticosteroids do not directly modify. Consequently, dexamethasone's anti-inflammatory effects do not translate into measurable improvements in oxygenation in this context. Moreover, chest tube removal is generally determined by the volume and character of pleural fluid drainage, with removal criteria based on secretion volume thresholds rather than systemic inflammation. Since dexamethasone does not appear to accelerate pleural fluid clearance or alter drainage characteristics, the duration of chest tube placement remains unaffected.

The dexamethasone group showed significantly shorter hospital stays, reduced fever duration, and lower CRP levels compared to controls. These findings are clinically meaningful, indicating faster recovery, decreased systemic inflammation, and potential reductions in healthcare resource utilization. However, no significant differences were observed in oxygen saturation or chest tube duration between groups. This may be explained by dexamethasone's anti-inflammatory effects mainly targeting systemic and febrile responses rather than local pleural healing or respiratory function parameters. Furthermore, the duration of chest tube placement is often determined by mechanical and procedural considerations rather than systemic inflammation.

Limited research has focused on the use of corticosteroids for empyema in children. Nevertheless, several studies have explored the effects of corticosteroids, such as dexamethasone, methylprednisolone, prednisolone, and hydrocortisone, as adjunctive treatments for pediatric patients suffering from acute viral infections, including parapneumonic pleural effusion and community-acquired pneumonia (CAP). For example, Vijayashekaran et al. demonstrated that dexamethasone can be a safe and effective adjunctive therapy for parapneumonic pleural effusion in children [15]. Similarly, Alfredo Tagarro et al. found that patients receiving dexamethasone had a shorter time to recovery compared to the placebo group in their study on parapneumonic pleural effusion [14]. Nematullo et al. concluded that steroid therapy is useful in reducing hospitalization in children with CAP [16]. Several studies have also investigated the effects of corticosteroids in adults with CAP. Meijvis et al. showed that dexamethasone reduced the length of hospital stay by one day in patients with CAP [17]. Blum et al. found that a 7-day course of prednisone shortened the time to clinical stability and reduced hospital discharge time in hospitalized patients with CAP [18].

A meta-analysis by Briel et al. concluded that adjunctive treatment with corticosteroids in hospitalized CAP patients reduces the time to clinical stability and length of hospitalization without significantly affecting mortality [19]. More recent meta-analyses have further supported the benefits of corticosteroids in CAP. Cheema et al. found that corticosteroids reduced the risk of all-cause mortality, with a greater reduction in younger patients [20]. They also showed that corticosteroids reduced the incidence of shock, the need for mechanical ventilation, and the length of hospital and ICU stay. XY See et al. reported that hydrocortisone was associated with a lower risk of death and reduced rates of mechanical ventilation, acute respiratory distress syndrome, shock, and ICU length of stay, while dexamethasone, methylprednisolone, or prednisolone did not show these associations. The antipyretic effect of dexamethasone may be one of the main reasons for its beneficial impact on outcomes. In the study by Meijvis et al., body temperature began to decrease from the day of admission in the dexamethasone group, while the decrease started one day later in the placebo group [17].

The findings of studies that have investigated the efficacy of corticosteroids in the treatment of respiratory infectious diseases suggest that the use of corticosteroids in combination with antibiotics can significantly improve survival rates and alleviate symptoms in patients with respiratory infections. These studies highlight the potential advantages of corticosteroid therapy in enhancing outcomes for children with respiratory infections.

Strengths and limitations

One of the key strengths of this study is its focus on children with empyema, unlike many previous studies that have examined corticosteroid effects in broader populations such as community-acquired pneumonia or parapneumonic effusion patients. This targeted approach provides specific insights into the potential benefits of administering dexamethasone directly through the chest tube as an additional treatment in empyema. However, the study's relatively small sample size limits its power to detect statistically significant differences in secondary outcomes, such as culture positivity and oxygen saturation. Larger, multi-center trials with greater sample sizes are necessary to further validate these findings and more definitively establish the efficacy of dexamethasone in this patient population.

Conclusion

These results highlight the potential benefits of dexamethasone in reducing the length of hospital stay, fever duration, and CRP levels in empyema patients. However, the lack of significant differences in other outcomes, such as PCR test results, cultures, oxygen saturation, and chest tube duration, suggests that dexamethasone may have a more limited impact on these specific parameters.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13052-025-02102-8.

Supplementary Material 1

Supplementary Material 2

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Author contributions

A.E. study conceptualization, performed treatment procedures, supervision, and manuscript preparation. N.H. study conceptualization, study design and manuscript preparation. A.M. manuscript preparation & statistical analysis. F.M. outcome assessor and manuscript preparation. Sh.A. data gathering, outcome assessor and manuscript preparation.

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Data availability

The data that support the findings of this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate

The Ethics Review Committee at Iran University approved our study (approval code: IR.IUMS.FMD.REC.1402.144). This study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from the parents or legal guardian of patients to participate in this study, which included permission for the publication of anonymized patient information in this article.

Consent for publication

Informed consent was obtained from the parents or legal guardian of patients to participate in this study, which included permission for the publication of anonymized patient information in this article.

Competing interests

The authors declare that they have no conflict of interest.

Author details

[1]Department of Pediatrics, School of Medicine, Aliasghar Children's Hospital, Iran University of Medical Sciences, Tehran, Iran
[2]Research Assistant, Pars Advanced and Minimally Invasive Medical Manners Research Center (PAMIM), Iran University of Medical Sciences, Tehran, Iran
[3]Research Assistant, School of Dentistry, Iran University of Medical Sciences, Tehran, Iran
[4]Department of Pediatrics, School of Medicine, Mahdieh Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[5]Department of Pediatrics, School of Medicine, Aliasghar hildren's Hospital, Iran University of Medical Sciences, Tehran, Iran

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References

1. Yang G, Wen Y, Chen T, Xu C, Yuan M, Li Y. Comparison of pediatric empyema secondary to tuberculosis or non-tuberculosis community-acquired pneumonia in those who underwent surgery in high TB burden areas. Pediatr Pulmonol. 2021;56(10):3321–31.
2. Kliegman R, Stanton B, St Geme J, Schor NF, Behrman R. Nelson Textbook of Pediatrics, Edition 21: Hunan ke xue ji shu chu ban she; 2020.
3. Muñoz-Almagro C, Selva L, Pallares R. Influence of Pneumococcal vaccine on the incidence of empyema. Curr Opin Pulm Med. 2010;16(4):394–8.
4. Amin M, Yousef pour S, Navidifar T. Detection of the major bacterial pathogens among children suffering from empyema in Ahvaz City. Iran J Clin Lab Anal. 2019;33(4):e22855.
5. Garvia V, Paul M. Empyema. StatPearls. Treasure Island (FL): StatPearls publishing copyright © 2022. StatPearls Publishing LLC.; 2022.
6. Liu X, Yang Y, Ma X, Wang X, Ma B, Li S. The Effect of CT-Guided Artificial Pneumothorax plus Thoracoscopy and Central Venous Catheterization on the Drainage Effect of Pediatric Empyema and Pulmonary Function. Contrast Media & Molecular Imaging. 2022;2022.
7. AlGhamdi ZM, Boumarah DN, Alshammary S, Elbawab H. Pleural empyema as a complication of pyogenic liver abscess: can the minimum achieve the optimal?? A comparison of 3 approaches. Am J Case Rep. 2021;22:e935169.
8. Santana-Rodríguez N, Aldebakey H, Albalkhi I, Hussein M, Alshammari A, Ahmed A et al. Surgical management of parapneumonic empyema. Shanghai Chest. 2022;6.
9. Higuchi M, Suzuki H. Current status and prospect of medical and surgical management for thoracic empyema. Curr Chall Thorac Surg. 2020;2:39.
10. McGee S, Hirschmann J. Use of corticosteroids in treating infectious diseases. Arch Intern Med. 2008;168(10):1034–46.
11. Yang EA, Kang HM, Rhim JW, Kang JH, Lee KY. Early corticosteroid therapy for Mycoplasma pneumoniae pneumonia irrespective of used antibiotics in children. J Clin Med. 2019;8(5).
12. Yang J-W, Yang L, Luo R-G, Xu J-F. Corticosteroid administration for viral pneumonia: COVID-19 and beyond. Clin Microbiol Infect. 2020;26(9):1171–7.
13. Pinzón MA, Ortiz S, Holguín H, Betancur JF, Cardona Arango D, Laniado H, et al. Dexamethasone vs Methylprednisolone high dose for Covid-19 pneumonia. PLoS ONE. 2021;16(5):e0252057.
14. Tagarro A, Otheo E, Baquero-Artigao F, Navarro M-L, Velasco R, Ruiz M, et al. Dexamethasone for parapneumonic pleural effusion: a randomized, double-blind, clinical trial. J Pediatr. 2017;185:117–23. e6.
15. Vijayashekaran D. Dexamethasone vs placebo in children having pneumonia with pleural effusion: pediatrician's viewpoint. Indian Pediatr. 2017;54(8):666.
16. Nematullo S, Yue XC, Bekzod O, Hong XZ, Hua ZZ. The effectiveness of using prednisolone in children with community-acquired pneumonia. Вестник Науки и образования. 2021 (4–1 (107)):57–65.
17. Meijvis SC, Hardeman H, Remmelts HH, Heijligenberg R, Rijkers GT, van Velzen-Blad H, et al. Dexamethasone and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-blind, placebo-controlled trial. Lancet. 2011;377(9782):2023–30.
18. Blum CA, Nigro N, Briel M, Schuetz P, Ullmer E, Suter-Widmer I, et al. Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet. 2015;385(9977):1511–8.
19. Briel M, Spoorenberg SMC, Snijders D, Torres A, Fernandez-Serrano S, Meduri GU, et al. Corticosteroids in patients hospitalized with Community-Acquired pneumonia: systematic review and individual patient data metaanalysis. Clin Infect Dis. 2018;66(3):346–54.
20. Cheema HA, Musheer A, Ejaz A, Paracha AA, Shahid A, Rehman MEU, et al. Efficacy and safety of corticosteroids for the treatment of community-acquired pneumonia: A systematic review and meta-analysis of randomized controlled trials. J Crit Care. 2024;80:154507.

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