

Clindamycin in Treatment of Lung Abscess in Children

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Abstract

Background and aims

Children with a lung abscess usually do well with antibiotics alone and surgical intervention is rarely needed. Standard practice is to use parenteral antibiotics until clinical symptoms abate and to follow with oral antibiotics for up to six weeks. The objective of this study was to observe and compare outcome, duration of antimicrobial treatment for lung abscess.

Methods

A prospective open, randomized clinical trial was conducted among 30 children aged 5 to 15 years with lung abscess and sequential antibiotic therapy either clindamycin (group 1; n=15) or ceftriaxone, flucloxacillin plus metronidazole (group 2; n =15) were administered until complete resolution of clinical and radiological abnormalities.

Results

Mean age was 11.5 years in group 1 and 11 years in group 2. Blood culture was negative in all cases but in sputum 33% cases staphylococcus aureus and 20% cases streptococcus pneumoniae was found and was sensitive to clindamycin, flucloxacillin and ceftriaxone. ESR exceeded 20 mm/hour in 94% and CRP exceeded 20 mg/L in 95% of the cases. ESR became normal in 21 days and CRP in 10 days and the cavity size on chest radiography was reduced after 14 days of treatment in first group but in second group CRP in 15 days, ESR in 28 days and reduced cavity size in 28 days. Mean duration of therapy was 21 days for first group and 39 days in second group. There were significant differences between the duration of treatment and outcome of the two groups ($P < 0.05$).

Conclusions

Clindamycin appears to be effective short course treatment option in lung abscess.

Keywords- Clindamycin, Lung, Abscess, Children.



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Introduction

Lung abscess is a necrotizing infection characterized by a pus filled cavitory lesion that often complicates necrotizing pneumonia. Primary lung abscesses occur in healthy children without lung parenchymal abnormalities; where as secondary abscesses occur in children with underlying lung disease, such as congenital cystic lung lesions, cystic fibrosis, primary immunodeficiency, or neurological conditions that predispose to aspiration. Abscesses may develop over a course of weeks with tachypnoea, cough, and fever being the common symptoms.¹ Common causative organisms include aerobic Gram positive bacteria (*Streptococcus pneumoniae*, *Staphylococcus aureus*, *Peptostreptococcus*, *Actinomyces*), aerobic Gram negative bacteria (*Klebsiella*, *Bacteroides*, *Fusobacterium*, *Proteus*, *Escherichia coli*), anaerobic Gram positive bacteria (*Bifidobacterium* spp, *Clostridium* spp), anaerobic Gram-negative bacteria (pigmented *Prevotella*, *Bacteroides* spp), and opportunistic organisms (*Candida*, *Legionella*, *Mycobacterium*). Abscesses often contain more than one organism²⁻⁴. However, microbiological information from sputum has limited value because of contamination with anaerobes from the oral cavity, and it is only helpful in abscesses caused by non-anaerobic organisms. Sputum should also be checked for acid and alcohol fast bacilli.

The treatment of lung abscess is not standardized and is based on experience. Most lung abscesses settle with conservative management, and four to six weeks of systemic broad spectrum Antibiotics are the mainstay of treatment. Conservative management with hospital admission and antibiotics for four to six weeks is the first line treatment. There are no clear guidelines about the duration of antibiotic treatment. Standard practice is to use parenteral antibiotics until clinical symptoms abate and to follow with oral antibiotics for up to six weeks. When information on antibiotic sensitivity is unavailable, empirical treatment must be comprehensive and cover common pathogens. The initial antibiotics of choice are penicillin or a third generation cephalosporin associated with clindamycin and metronidazole.⁴ Children with a lung abscess usually do well with antibiotics alone and surgical intervention is rarely needed. However, with the advent of interventional radiology, computed tomography guided drainage and pigtail catheter insertion are used in non-responders.⁵⁻⁷ If patients deteriorate despite antibiotics and drainage, thoracotomy with marsupialisation of the abscess cavity (cutting a slit into the cyst and suturing the edges of the slit to form a continuous surface from the exterior to the interior) is the next step.⁸

Objective

To compare the safety, efficacy of clindamycin versus ceftriaxone, flucloxacillin plus metronidazole among 30 children aged 5 to 15 years with lung abscess.

Materials and Methods

This was a prospective open, randomized clinical trial that included 30 known cases of lung abscess patient of both sexes aged 5-15 years presenting with fever, productive cough and a radiographic sign of cavitation with air fluid level who admitted in Pulmonology department but same aged children already on therapy, bronchiectasis, congenital heart diseases, cystic fibrosis and other chronic lung diseases with respiratory distress were excluded from the study.

All the eligible patients were randomly assigned. Sequential antibiotic therapy with either clindamycin (group 1; n=15) 30mg /kg per day in three divided doses or ceftriaxone, 75mg/kg per day in single dose, flucloxacillin, and 50 mg /kg per day in four divided doses, plus metronidazole, 22.5 mg/ kg per day in three divided doses (group 2; n =15) administered I/V until complete resolution of clinical and radiological abnormalities, with a predetermined series of erythrocyte sedimentation rate (ESR), C reactive protein (CRP), leukocyte count measurement, chest x-ray were performed. But clindamycin was administered parent rally for at least 10 days, and thereafter, when condition permitted, it was given orally in the same manner for at least 14 days depending on the patient clinical condition. A negative Montoux test excluded cavitating tuberculosis.

Study design

The study was conducted according to the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (CGP) and the clinical treatment protocol was approved by the ethical Committee of the University and departmental review board. A randomized prospective open hospital based comparative study was used to assess the effects of the two groups drugs on the above mentioned parameters. Randomization was performed using a random number sequence, a computer and STATA 8.0 software. Two resident doctors responsible for the study prepared the randomization series, the assignment was then performed.

Location and period of study

The study was carried out in the Pulmonology unit of Pediatric Department, Bangabandhu Sheikh Mujib Medical University (BSMMU), from September 2009 to August 2011.

Evaluation of efficacy

Evaluation of clinical response was performed at 7-14 days of onset of therapy and at the end of therapy. Resolution of radiographic abnormalities to a range that was considered normal for the individual patient and complete normalization of clinical signs and laboratory parameters of infection (i.e. ESR, C-reactive protein) were considered to represent a cure. Partial resolution of abnormalities in radiographic, clinical and laboratory findings

was classified as an improvement. In statistical evaluation, any ratings of cure or improvement were considered to constitute a response, and any signs of failure to constitute no response.

Data collection and evaluation

Parents or carers were given a detailed briefing about the purpose of the study. Informed consent forms were signed by the subject or the subjects legally authorized representative before his/ her participation in the study. Before and after giving treatment baseline clinical and laboratorial parameter RR, HR, SPO₂, and blood count, ESR, CRP, Blood culture, CXR were recorded and compared on a designed preformed. All the values were expressed as mean for pre and post treatment effects. Comparative analysis of baseline parameters of two groups and within the groups and improvement between these two groups before and after treatment were done.

Statistical analysis

Statistical analysis of the efficacies of both treatment options was based on clinical, laboratorial and radiological response and duration of treatment period were done using unpaired “t” test. All the statistical analysis was done by using SPSS package 16 version.

Results

Mean age was 11.5 years in group 1 and 11 years in group 2. Blood culture was negative in all the cases but in sputum culture 33% cases was staphylococcus, 20% cases streptococcus pneumonia were found and was sensitive to clindamycin, flucloxacillin and ceftriaxone. Anaerobic culture could not be done due to lack of facilities, a negative Montoux test excluded cavitating tuberculosis. ESR exceeded 20 mm/hour in 94% and CRP exceeded 20 mg/L in 95% of the cases. ESR normalized in 21 days and CRP in 10 days and reduced the cavity size on chest x-ray after 14 days of treatment in first group but in second group CRP 15 days, ESR 28 days and chest ray also 28 days. Mean duration of therapy was 21 days for first group and 39 days in second group shown in table 1. It was observed that most cases 90% radio graphical stabilization with a total course of 21 days of clindamycin. There were significant differences between the duration of treatment and outcome of the two groups ($P < 0.05$) There were no side effects observed from the administration of clindamycin.

Table 1. Clinical and laboritorical data of 15 patients treated with clindamycin and 15 patients treated with ceftriaxone, flucloxacillin and metronidazole

Treatment	Mean age years	Duration of fever before treatment days mean	Duration of fever after treatment days mean	ESR at admission >20mm	ESR normal after days mean	CRP at admission > 20mg/dl	CRP normal after days mean	Reduced cavity size days mean	Duration of treatment days mean
Group-1 Clindamycin	11.5	4	6	94 %	21	95 %	10	14	21
Group-2 Ceftriaxone+ Flucloxacillin+ Metronidazole	11	4.2	11.5	94 %	28	95 %	15	28	39

Remission of fever, ESR, CRP, Reduced cavity size and duration of treatment between these two groups were significant and p-value (<0.05).

Bacteriological findings

Valid microbiological samples were obtained from all 30 patients before therapy. Samples were derived from protected specimen sputum. A definite bacteriological diagnosis was achieved for 16 individuals. 33% cases was staphylococcus, 20% cases streptococcus pneumonia were found and was sensitive to clindamycin, flucloxacillin and ceftriaxone.

Discussion

The treatment of lung abscess is not standardized and is based on experience. Most lung abscesses settle with conservative management, and four to six weeks of systemic broad spectrum antibiotics are the mainstay of treatment. In non-responsive patients, some centres perform percutaneous ultrasound guided aspiration or catheter drainage, where as others favour open thoracotomy. Coverage of anaerobic bacteria is an important requirement in the antibacterial treatment of lung abscess. But anaerobic bacteria are rarely identifiable on culture because uncontaminated specimens are difficult to obtain and most laboratories do not culture anaerobes well or often, which is absolutely true for our laboratory also. Despite the limitation of cultured sputum for anaerobic diagnosis, these techniques were done in this study solely for the identification of aerobic microorganisms, with the proviso that a representative sample was obtained⁹⁻¹². Ampicillin plus the b-lactamase inhibitor sulbactam, compared to clindamycin with the optional addition of a second- or third-generation cephalosporin, was equally effective in terms of clinical response, with cure or improvement being achieved in more than two-

thirds (70.0%) of patients. There is evidence that aerobic pathogens play an active role in the disease rather than being commensals, supporting the approach taken in this study in testing for aerobic bacteria to help direct antimicrobial therapy¹². Since anaerobes are ubiquitous commensals of the oral cavity, sputum is of no value in the evaluation of anaerobic lung infections. The superior quality of specimens obtained by fiberoptic bronchoscopy, either bronchoalveolar lavage or protected specimen brush specimens, is generally accepted¹¹ which were not done in this study. Compared to previous studies, the overall response rate in this investigation appears to be relatively low. Success rates of up to 95% were published in early reports¹¹. In table 1 showed the erythrocyte sedimentation rate (ESR) was >20 mm/hour, C-reactive protein was also >20mg/dl in our study in both groups but CRP 10 days, ESR 21 days in group 1 and in group 2 CRP 15 days and ESR 28 days of treatment became normal which was also finding of the study done in Turkey¹³. In a more recent study, Gudiol *et al.*¹⁰ reported satisfactory clinical and radiological responses in 18 of 19 patients with anaerobic lung infection treated with clindamycin, whereas only ten of 18 patients treated with penicillin responded favorably to therapy, but our study showed 100% effective with clindamycin and clinical as well as laboratorial response occurred within 21days compared with 39 days in ceftriaxone, flucloxacillin and metronidazole group ($P < 0.05$) in table 1, though anaerobic culture was not possible in this study. Levinson *et al.*⁹ described similar results. Neither study reported underlying conditions, severity of disease, or mortality. Shah A *et al.*¹⁰ also mentioned clindamycin is considered effective alternative when penicillin and metronidazole did not respond even after 28 days of treatment. Barlet JG¹¹ recommended clindamycin is usual drug for lung abscess in children which was also the finding of this study. Recent reports described the development of diarrhea colitis after clindamycin therapy in adult¹⁴. The lack of occurrence of diarrhea and colitis among our patients confirm the report of rarity of these complications in pediatrics patients¹⁴⁻¹⁵.

Although antibiotic treatment is considered the primary therapeutic option for lung abscess, the value of surgical procedures for drainage of lung abscesses or resection of affected lung compartments has been discussed, either as an additional measure to antibacterial treatment or as an alternative if conservative therapy fails¹⁶⁻¹⁸. This study was intended to include follow-up of patients who did not reduced cavity size completely or sufficiently to antibacterial therapy. Never the less, of the 30 individuals from this study, none required additional or subsequent surgical procedures. Interestingly, the mean duration of study medication in this institution was significantly lower-39 days for ceftiaxone, flucloxacillin and metronidazole and 21 days for clindamycin-than the average duration of therapy in all institutions study¹² and clinical cure or improvement was achieved in 100 % of study subjects at the end of therapy. These findings support our view that, apart from severe and rare complications such as recurrent haemoptysis, persisting broncho-pleural

fistulas or empyema, antibiotic therapy especially clindamycin is the treatment of choice for lung abscess.

Conclusions

Clindamycin appears to be the effective short course treatment options against lung abscess but further studies may be done to evaluate its impact on clinical outcomes and duration.

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