Section: Respiratory Medicine

Original Research Article

COMPARISON OF EFFECTIVENESS OF INTRAPLEURAL INSTILLATION OF SODIUM 2 MERCAPTOETHANE SULFONATE (MESNA) WITH TUBE THORACOSTOMY VERSUS CONSERVATIVE MANAGEMENT WITH TUBE THORACOSTOMY ALONE IN LOCULATED PARAPNEUMONIC PLEURAL EFFUSION/EMPYEMA

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Abstract

Background: Pleural effusion is an abnormal fluid accumulation in the pleural space, often associated with bacterial lung infections. MESNA, a cost-effective mucolytic agent, has limited success in treating multiloculated effusions. Hence, the study aimed to evaluate the effectiveness of intrapleural instillation of MESNA in faster clearance of loculated parapneumonic effusions/Empyema and to compare its efficacy with conservative management. **Materials and Methods:** This hospital-based randomised open-label controlled trial was conducted at the Government Stanley Medical College, Chennai, for one year, from July 2018 to June 2019. One group received 240/m2 body surface area intrapleural instillation of sodium 2-mercaptoethanesulfonate (MESNA) for adhesiolysis of loculations and tube thoracostomy. The other groups managed conservatively with tube thoracostomy alone, which acts as a control. Patients were followed up for clinical and radiological improvement and increased pleural fluid drain. **Results:** In the MESNA group, fibrinolysis was successful in 20 out of 25 loculated effusions (80% success rate) and three out of ten loculated empyema patients (30% success rate). MESNA group had a significant increase in the volume of drain per day (138 ml/day vs 85 ml/day, p <0.001), reduced duration of the intercostal drainage tube (14.1 vs 21.1 days p value <0.001), reduced length of hospital stay (21.7 days vs 29.9 days, p < 0.001). The number of patients requiring thoracoscopy and surgical intervention was less in the MESNA group when compared to the control. No major adverse events were reported following intrapleural instillation of MESNA during the study period. **Conclusion:** MESNA is a safe and effective intrapleural fibrinolytic agent for breaking loculations and promoting faster fluid absorption in parapneumonic effusion and empyema, reducing surgical intervention needs.

INTRODUCTION

Pleural effusion is an abnormal accumulation of fluid in the pleural space. A parapneumonic pleural effusion is the accumulation of exudative pleural fluid associated with an ipsilateral lung infection, mainly pneumonia. Parapneumonic effusions are mainly associated with bacterial lung infections, abscesses, or bronchiectasis.[1,2] A parapneumonic effusion is called empyema thoracis when there is frank pus in the pleural space or evidence of bacterial infection of the pleural fluid. The bacterial infection of the pleural space is evidenced by either a positive Gram stain or a positive pleural fluid culture.[3,4]

In complicated parapneumonic effusion and empyema, loculation of effusion or empyema happens due to the formation of fibrin strands between visceral and parietal pleura, which is a part of the disease process to restrict the spread of sepsis to other areas. If the effusion is not treated early.[5] A loculated effusion poses a greater challenge in

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drainage with conventional tube thoracostomy, and patients with multiloculated effusion or empyema are more prone to complications of incompletely drained pleural fluid like organised effusion or empyema, trapped lung, bronchopleural fistula, persistent pleural sepsis.[6]

The various modalities of draining pleural fluid are therapeutic thoracentesis, pigtail catheter drainage, tube thoracostomy, intrapleural fibrinolytic therapy, medical thoracoscopy and surgical treatments like VATS decortication.[2] Since multiloculated effusions are difficult to drain with tube thoracostomy, additional modalities of treatment like intrapleural fibrinolytic therapy, medical thoracoscopy or VATS are more employed in multiloculated effusions to achieve a better and successful pleural fluid drainage.[7] In various studies, intrapleural fibrinolytic therapy showed good results in draining multiloculated parapneumonic effusions.

Many intrapleural fibrinolytic agents are available, like streptokinase, urokinase, tenectaplase, tPA, DNase, etc. These agents have their own merits and demerits. Recent studies showed that combining tPA with DNase as an intrapleural fibrinolytic therapy was superior to other fibrinolytic agents.[8] Unfortunately, this tPA/DNase combination intrapleural fibrinolytic therapy was not easily available at all centres, especially in developing countries, since both tPA and DNase are very costly when compared to other fibrinolytic agents.[9]

2-mercaptoethane-sulfonate-sodium (MESNA) is a mucolytic agent, and this agent has the property of breaking the disulphide bond in protein stands. This drug has been used as an intrapleural fibrinolytic therapy earlier with variable success. The advantage of using MESNA is that the drug is easily available and cost-effective compared to other agents. However, studies on MESNA as an intrapleural fibrinolytic agent were limited. Hence, the study aimed to evaluate the effectiveness of intrapleural instillation of MESNA in faster clearance of loculated parapneumonic effusions/Empyema and to compare its efficacy with conservative management.

MATERIALS AND METHODS

This hospital-based randomised open-label controlled trial was conducted at the Government Hospital of Thoracic Medicine, Tambaram sanatorium, and Department of Pulmonary Medicine, Government Stanley Medical College, Chennai, for one year, from July 2018 to June 2019. The participants were well-informed about the study; informed written consent was obtained, and the Institutional Ethical Committee approved the study.

Inclusion Criteria

All clinically stable inpatients with loculated parapneumonic effusion and empyema were included.

Exclusion Criteria

Critically ill patients, transudative pleural effusion, hemothorax, malignant effusion, free-flowing pleural effusion, pediatric patients, and patients unwilling to participate were excluded.

The data collection process involved using an evaluation form, which included the patient's name, age/sex, IP number, chief complaints, prior ATT, occupation, smoking history, biomass exposure, marital history, vital signs, pulse rate, respiratory rate, blood pressure, and SpO2, and blood investigations included CBC, RFT, and, BT/CT. The patient underwent chest radiographs, pleural fluid analysis, protein and glucose analysis, cytology, lymphocyte count, gram stain, LJ and MGIT culture, and a mode of intervention.

One group received 240/m2 body surface area intrapleural instillation of sodium 2-mercaptoethanesulfonate (MESNA) for adhesiolysis of loculations and tube thoracostomy. The other groups managed conservatively with tube thoracostomy alone, which acts as a control. Patients were followed up for clinical and radiological improvement and increased pleural fluid drain. Sonographic evidence of reduced loculations and pleural fluid volume is taken as successful adhesiolysis. No radiological evidence of a decrease in loculation or pleural fluid volume after three consecutive doses of MESNA is considered a failure of adhesiolysis. Patients were strictly monitored for any adverse drug reactions to MESNA.

Any adverse reactions noted were attended immediately and adequately treated to avoid undesired consequences. The ideal site for chest tube drain insertion is identified by chest sonography. The patient was positioned upright with a pillow, leaning forward over the table kept in front. Chest drain of appropriate size (self-retaining Malecot's catheter is commonly used) is inserted into the pleural cavity at a safe triangle or in the largest locule identified with chest sonography. The drain was kept in position with stay sutures and connected to a closed drainage system. The dressing was done, and the patient shifted toward after a few minutes of observation.

Patients were monitored in the ward that exclusively manages patients with tube thoracostomy. Chest tube drain chart was maintained, any complication was noted, and daily drain was noted in the chart. Patients developing pain due to tube thoracostomy were managed with analgesics. The study involved patients in the MESNA group who underwent chest sonography to assess the status of their loculations post-instillation. Radiologists studied the nature and number of loculations, and ideal sites for MESNA instillation were marked superficially over the skin. Patients were informed about the procedure, complications, and expected adverse reactions. After obtaining informed written consent and ascertaining the safety of MESNA with an intradermal test dose, patients were subjected to intrapleural instillation of MESNA therapy.

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The dose of MESNA used in previous studies was empirical, and in this study, the required dose was 240mg/m2 body surface area. The instillation was carried out in sterile aseptic precautions, and patients were subjected to daily chest sonography to assess their loculations status post-instillation. Any reduction in the number of loculations was monitored, and daily drainage was noted for those on ICD. Patients receiving percutaneous MESNA instillation were subjected to tube thoracostomy after successful adhesiolysis, which was ascertained by ultrasonography and monitored for daily pleural fluid drainage. If no improvement was observed, patients were subjected to medical thoracoscopy or referred for surgical intervention based on individual patient needs and benefits.

Patients in both groups were monitored in the ward with expertise in managing intercostal drainage tube patients. Monitoring methods included a serial chest ultrasound, daily confirmation of ICD functioning, recording of daily drain volume, daily inspection of ICD dressing and wound site for infections, presence of air leaks, improvement in symptoms, and any adverse events.

Statistical Analysis

The data were entered in an Excel sheet and analysed using SPSS software version 18.0. Quantitative parameters were presented as mean and standard deviation. Qualitative parameters were described as frequencies and proportions. Differences between MESNA and the control group in categorical variables were assessed using the chi-square test. The mean difference in length of stay and other quantitative variables were compared between the two groups by independent t-test. A "p-value" of less than 0.05 was considered statistically significant.

RESULTS

The majority are males, contributing to 81.5%; out of 70 patients, only 13 were females, contributing to 18.5%. Both sexes were almost equally distributed among the two groups. 70% of the total study population were in the age group of 31 to 50 years. 31 to 50 age group were the productive age group, and parapneumonic effusions affected more commonly in this age group of patients (Table 1). The mean age in the MESNA group was 41±10.4 years, and in the control group was 40.7±10.4 years.

Right-sided effusion was more prevalent than left. Only three among the population had bilateral parapneumonic effusion: one patient in the MESNA group and two in the control group. Of 35 patients, 25 had effusion, and 10 had pus in the pleural cavity. The distribution of effusion and empyema in the control group was the same as in the MESNA group. Among the MESNA group, 14 had thick septations, and 21 had thin septations. Among the control group, 18 patients had thick septations, and others had thin septations. Among the patients in the MESNA group, out of 35 patients, 13 had few septations in the chest sonogram, and 22 had multiple septations. Among the control group, 15 had few septations, and 20 had multiple septations. Among the MESNA group, 25.7% were positive for MTB, and among the control group, 45.7% were positive for MTB (Table 1).

Among both groups, diabetes remained the most commonly associated co-morbidity, with a prevalence of 20% in the MESNA group and 34.3% in the control group. 5.7% of patients in the MESNA group had both diabetes and hypertension. Only one patient in the MESNA group had rheumatoid arthritis with diabetes. Most patients in both groups (68.9% in the MESNA group vs. 65.7% in the control group) had no co-morbidities (Table 2).

On day 1, 15 patients had few loculations, and 20 had multiple loculations. On day 2, after two doses of MESNA, two patients showed no loculations, 28 had few loculations, and only 5 had multiple loculations. On day 3, after the final dose of MESNA, four patients had multiple loculations, 12 had few loculations, and 19 patients had complete disappearance of loculations (Table 3).

The mean pleural fluid volume in the MESNA group is 1360 ml, and in the control group is 1322.9 ml. In the MESNA group, the mean number of days on ICD drainage was 15.1±6.1 days; in the control group, the mean number of days on ICD drainage was 21.1±5.1 days. In comparison, patients in the MESNA group had a statistically significant shorter duration of ICD drainage therapy with a p-value of <0.001.

The patient in the MESNA group significantly increased in 24-hour pleural fluid drain volume following three doses of intrapleural MESNA. The mean 24-hour drain volume in the MESNA group is 138.6±64.2 ml, and in the control group is 85.4±21.6 ml. The mean 24-hour pleural fluid drain volume difference among both groups is statistically significant, with a p-value of < 0.001.

The mean length of hospital stay in the MESNA group was 21.7±8.3 days, and in patients in the control group, it was 29.9±7.5 days. Patients in the MESNA group had a shorter duration of hospital stay when compared with the control group. The difference in mean length of hospital stay between the two groups is statistically significant, as evidenced by a p-value of < 0.001 (Table 4).

Among the patients who received intrapleural MESNA, out of 35 patients, 23 had successful adhesiolysis with increased pleural fluid drain and shorter hospital stays. 20 out of 25 effusion patients and 3 out of 10 empyema patients had good therapeutic responses to MESNA, with a success rate of 80% and 30% in empyema patients. Hence, the efficacy of MESNA was better in effusion patients when compared to empyema.

Among the 35 patients in the MESNA group, 21 had thin septations, and 14 had thick septations. Successful adhesiolysis was achieved in 23 patients, 18 with thin septations and 5 in thick septation patients (Table 5).

Those patients who failed to respond to the adhesiolytic effect of intrapleural MESNA and those

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in the control group with poor pleural drainage were subjected to medical thoracoscopy. In the MESNA group, 8 out of 35 patients required medical thoracoscopy. In the control group, 17 out of 35 required thoracoscopy, and the thoracoscopic requirement was higher.

Those patients who developed complications due to failure of adhesiolysis were referred to a cardiothoracic surgeon for surgical intervention. Among the MESNA group, 13 patients needed surgical intervention, and in the control group, 20 patients required surgical intervention (Table 6).

Among the study population in the MESNA group, 83% reported no adverse effects. 2 patients reported an increase in cough, and three patients reported pain at the injection site following intrapleural instillation of MESNA. One patient had worsened breathlessness (Table 7).

Table 1: Gender and age between groups

		MESNA	ICD ONLY	Total	Percentage
Sex	Male	28	29	57	81.5
	Female	7	6	13	18.5
Age category	< 30	4	4	8	11.5
	31 to 40	9	13	22	31.5
	41 to 50	15	12	27	38.5
	51 to 60	5	4	9	12.8
	>60	2	2	4	5.7

Table 2: Patient characteristics in the study

Group		MESNA (n=35)		ICD only (n=35)	
Side of effusion	Bilateral	1	1 (2.8)	2	2 (5.7)
	Left	16	16 (45.7)	14	14 (40)
	Right	18	18 (51.4)	19	19 (54.3)
Nature of pleural fluid	Effusion	25	25 (71.4)	25	25 (71.4)
	Pus	10	10 (28.6)	10	10 (28.6)
Pattern of septation	Thick	14	14 (40)	18	18 (51.4)
	Thin	21	21 (60)	17	17 (48.6)
Number of septations	Few	13	13 (37.1)	15	15 (42.9)
	Multi	22	22 (62.9)	20	20 (57.1)
MTB positivity	Positive	9	9 (25.7)	16	16 (45.7)
	Negative	26	26 (74.3)	19	19 (54.3)
Co-morbidities	NIL	24	24 (68.9)	23	65.7
	DM	7	7 (20)	12	12 (34.3)
	HT	1	1 (2.9)	0	0
	DM/HT	2	2 (5.7)	0	0
	DM/RA	1	1 (2.9)	0	0

Table 3: Loculations in chest sonography

Septations	Day 1	Day 2	Day 3
Few	15 (42.9%)	28 (80%)	12 (34.3%)
Multiple	20 (57.1%)	5 (14.3%)	4 (11.9%)
None	0	2 (5.7%)	19 (54.3%)

Table 4: Pleural fluid volume, number of days of ICD, drain volume and length of hospital stay

	MESNA	ICD only
Pleural Fluid Volume	1360 ± 334.5	1322.9 ± 279.8
Number of days of ICD	15.1 ± 6.1	21.1 ± 5.1
Drain volume (ml)	138.6 ± 64.2	85.4 ± 21.6
Length of hospital stay in days	21.7 ± 8.3	29.9 ± 7.5

Table 5: The success rate of adhesiolysis and septations

Result	Total	Effusion (n=25)	Pus (n=10)
Success	23	20 (80)	3 (30)
Failure	12	5 (20)	7 (70)
Septations	**Number**	**Successful adhesiolysis**	**Percentage**
Thin	21	18	85.70%
Thick	14	5	35.70%

Table 6: Thoracoscopy and Surgical Intervention

		MESNA (n=35)	ICD only (n=35)
Thoracoscopy	Yes	8 (22.8)	17 (48.5)
	No	27 (77.1)	18 (51.4)
Surgical Intervention	Yes	13 (37.1)	20 (57.1)
	No	22 (62.9)	15 (42.9)

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Table 7: Adverse effects of MESNA

Adverse effects of MESNA	Number	Percentage
Increase in cough	2	5.70%
Pain at the injection site	3	8.50%
Worsening of dyspnoea	1	2.80%
Anaphylaxis major adverse events	0	0%
Major adverse events	0	0%
No adverse event	29	83%

DISCUSSION

The study involved 70 patients aged 31-50, with a mean age of 41±10.4 years in the MESNA group and 40.7±10.4 years in the control group, with a slightly higher prevalence of right-sided effusion. Wei Yang et al.[10] observed that pleural cavity infections were twice as high in males as in females. They also observed that long-term excessive drinking and diabetes are important risk factors for developing parapneumonic pleural effusion. Since alcohol intake and diabetes are more prevalent in Indian males when compared to Indian females, Indian males tend to have a higher incidence of parapneumonic effusion, as observed in our study. Aspiration pneumonia and its complications are more on the right lung when compared to the left, which accounts for slightly higher right-sided parapneumonic effusion in our study.

Abu Daff et al.[11] studied the risk factors for failure of intrapleural fibrinolytic therapy. They observed that pleural thickening > 2mm was an important risk factor for failure of fibrinolysis. Regarding this study, we divided the population into thick and thin septations with 2 mm as the cut-off value. The results showed that successful adhesiolysis was more noted in patients with thin septations and early-stage disease (85.7%) than with thick septations (35.7%). Diabetes is a common co-morbidity associated with parapneumonic effusion, increasing the risk of aspiration, pneumonia, and complications due to reduced immunity in the studied population.

In our study, tuberculosis prevalence in MESNA patients was 25.7%, with 45.7% in the control group. MESNA instillation reduced multiple septations, with 19 patients achieving complete resolution (54.3%) and 12 have only a few (34.3%), demonstrating successful adhesiolysis. Rajendra Kumar Chandel et al.[12] conducted a similar study in 2018. They compared the intrapleural fibrinolytic therapy between the multiloculated effusion and empyema groups. Our study also had similar results comparable with the above study. In our study, the mean number of days of an intercostal drainage tube requirement was 15.1±6.1 days in the MESNA group vs. 21.1±5.1 days in the control group. This observation is statistically significant, with a p-value < 0.001. Porcel JM et al.[13] compared the number of days on intercostal drainage tubes in patients treated with intrapleural fibrinolytic. They concluded that patients who received saline flushing with fibrinolytic had a shorter duration of the requirement of ICD. In our study, we also had similar results, which indicate that intrapleural fibrinolytic therapy with MESNA fastens the absorption and drainage of pleural fluid by reducing the septations in the pleural cavity.

In our study, following intrapleural instillation of MESNA, the average volume of drain in intercostal drainage per day has increased sufficiently, with a mean volume of drain per day of 138.6 ml vs. the control group, which had a mean value of 85.4 ml per day. The difference is statistically significant with a p-value < 0.001. This observation indicates faster drainage of loculated effusions following intrapleural instillation of MESNA. The length of hospital stay was lesser in the MESNA group than in the control group (21.7±8.3 days vs 29.9±7.5 days), and the difference is statistically significant with a p-value < 0.001. Faster absorption and drainage of pleural fluid secondary to adhesiolysis of loculations by intrapleural MESNA has reduced the length of hospital stay. These observations were similar to studies conducted by Porcel JM et al.[13] and Nie W et al.[14]

In our study, among the 23 patients in the MESNA group who had successful fibrinolysis, intra-group comparison between effusion and empyema showed that successful adhesiolysis was better achieved in effusion when compared to empyema (80% vs. 30%). Venkateswara Reddy Tummuru et al.[15] conducted a similar study in 2015 and observed that MESNA was 90% efficacious in effusions and 40% in empyema patients. Our observation correlates with this study. The low efficacy of MESNA in empyema is a late stage of parapneumonic effusion, characterised by thick septations rather than thin septations and associated pleural thickening. From this observation, it is inferred that early admission of intrapleural MESNA in loculated parapneumonic effusions will give better results.

In our study, the requirement for thoracoscopy was less in patients in the MESNA group compared to the control group (22.8% vs. 48.5%). The requirement for surgical intervention is higher in the control group compared to the MESNA group (57.1% vs. 37.1%). These observations indicate that early intrapleural fibrinolytic therapy with MESNA can reduce the need for medical thoracoscopy and surgical intervention in patients with multiloculated parapneumonic effusions or empyema. No anaphylaxis or any other major adverse effects were noted following intrapleural instillation of MESNA. A few patients had worsening cough and pain at the injection site, which were managed symptomatically, and these symptoms resolved well with treatment.

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Maskell et al.[16] reported serious and non-serious adverse events following intrapleural streptokinase instillation among 11% of the study population. Rahman et al.[8] reported similar adverse events among 17% of the study population for intrapleural tPA/DNase combination instillation. No serious adverse event was reported in our study, and the non-serious adverse effect was reported in a maximum of 8%. This observation indicates that MESNA has a good safety profile and is a safe drug for intrapleural fibrinolytic therapy.

CONCLUSION

2-mercapto ethane sulfonate sodium (MESNA) is an effective intrapleural fibrinolytic agent for breaking loculations and promoting faster fluid absorption in parapneumonic effusion and empyema. Its effectiveness is better in the parapneumonic effusion and can be instilled in the early stages for better results. MESNA is safe for intrapleural fibrinolytic therapy and is preferred due to its cost-effectiveness and safety.

Limitations

The study's small sample size limits generalizability to larger populations, and it's an open-label study, allowing observer bias. Radiologists subjectively interpreted ultrasonographic observations, and the dosing of MESNA is empirical.

Financial interest

Conflicts of interest

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REFERENCES

1. Villena Garrido V, Ferrer Sancho J, Blasco H, de Pablo Gafas A, Pérez Rodríguez E, Rodríguez Panadero F, et al. Diagnosis and treatment of pleural effusion. Arch Bronconeumol 2006;42:349–72. https://doi.org/10.1016/s1579-2129(06)60545-4.
2. Yu H. Management of pleural effusion, empyema, and lung abscess. Semin Intervent Radiol 2011;28:075–86. https://doi.org/10.1055/s-0031-1273942.
3. Light RW. Parapneumonic effusions and empyema. Proc Am Thorac Soc 2006;3:75–80. https://doi.org/10.1513/pats.200510-113jh.
4. Aquino SL, Webb WR, Gushiken BJ. Pleural exudates and transudates: diagnosis with contrast-enhanced CT. Radiology 1994;192:803–8. https://doi.org/10.1148/radiology.192.3.8058951.
5. Christie NA. Management of pleural space: effusions and empyema. Surgical Clinics. 2010;90:919-34.
6. Roberts HSA. BTS guidelines for the management of pleural infection * Authors' reply. Thorax 2004;59:178–178. https://doi.org/10.1136/thorax.2003.013094.
7. Brutsche MH, Tassi G-F, Györik S, Gökcimen M, Renard C, Marchetti GP, et al. Treatment of sonographically stratified multiloculated thoracic empyema by medical thoracoscopy. Chest 2005;128:3303–9. https://doi.org/10.1378/chest.128.5.3303.
8. Rahman NM, Maskell NA, West A, Teoh R, Arnold A, Mackinlay C, et al. Intrapleural use of tissue plasminogen activator and DNase in pleural infection. N Engl J Med 2011;365:518–26. https://doi.org/10.1056/nejmoa1012740.+
9. Ahmed AEH, Yacoub TE. Empyema thoracis. Clin Med Insights Circ Respir Pulm Med 2010;4:CCRPM.S5066. https://doi.org/10.4137/ccrpm.s5066.
10. Yang W, Zhang B, Zhang Z-M. Infectious pleural effusion status and treatment progress. J Thorac Dis 2017;9:4690–9. https://doi.org/10.21037/jtd.2017.10.96.
11. Abu-Daff S, Maziak DE, Alshehab D, Threader J, Ivanovic J, Deslaurier V, et al. Intrapleural fibrinolytic therapy (IPFT) in loculated pleural effusions—analysis of predictors for failure of therapy and bleeding: a cohort study. BMJ Open 2013;3:e001887. https://doi.org/10.1136/bmjopen-2012-001887.
12. Chandel RK, Bhandari C, Sharma S, Sharma A. Role of intrapleural instillation of mesna for adhesiolysis in multiloculated pleural effusion and empyema. J Dent Med Sci 2019; 18:36-44. https://doi.org/10.9790/0853-1804133644
13. Porcel JM, Valencia H, Bielsa S. Manual intrapleural saline flushing plus urokinase: A potentially useful therapy for complicated parapneumonic effusions and empyemas. Lung 2017;195:135–8. https://doi.org/10.1007/s00408-016-9964-2.
14. Nie W, Liu Y, Ye J, Shi L, Shao F, Ying K, et al. Efficacy of intrapleural instillation of fibrinolytics for treating pleural empyema and parapneumonic effusion: a meta- analysis of randomised control trials. Clin Respir J 2014;8:281–91. https://doi.org/10.1111/crj.12068.
15. Tummuru VR, Waghray P, Rao K, Veena V, Vaddepally CR, Bahadurbhai HR. Effectiveness of intrapleural instillation of MESNA for adhesiolysis in multi-loculated pleural effusions, parapneumonic effusions and empyema: our experience. Int J Therap App 2015; 23:5-9.
16. Maskell NA, Davies CWH, Nunn AJ, Hedley EL, Gleeson FV, Miller R, et al. U.K. controlled trial of intrapleural streptokinase for pleural infection. N Engl J Med 2005;352:865–74. https://doi.org/10.1056/nejmoa042473.

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