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Role of Intrapleural Instillation of Mesna for Adhesiolysis in Multiloculated Pleural Effusion and Empyema

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Abstract: *The management of Multiloculated pleural effusion and empyema with closed pleural aspiration and intercostal tube drainage fails most of the time due to the presence of thick viscous fluid and multiple septations . We extra plot that* ***MESNA (2-mercaptoethane sulfonate Na)*** *is an agent which is easily available, effective, safe and less expensive and due to its proved action as a mucolytic, chemical dissector and fibrinolytic along with our practical experience, we propose the hypothesis that MESNA can be an intrapleuralfibrinolytic agent which can overcome many limitation of presently available agents.*

Materials and Methods: *It was a Hospital based prospective type of interventional study.*

Results: *The present study was undertaken on 40 clinically and radio logically diagnosed patients of multiloculated pleural effusion (n= 20) and empyema (n=20). Septations were devided in to thin and thick septa as well as few and multiple septations. With instillation of MESNA, there was decrease in multiple septations on Day 1,2, and 3 in both groups and this change in number of septations was found to be statistically significant in both the groups (p<0.001). With instillation of MESNA there was decrease in thick septations on Day 1,2, and 3 in both groups and this change in thickness of septations was found to be statistically significant in both the groups (p<0.001). In Effusion group patient's, complete resolution was seen in 12 (60%), partial resolution seen in 2 (10%) and 6 (30%) patients still had no resolution. While in empyema patients only 6 (30%) patients had complete resolution, 10 (50%) had partial resolution and 4 (20%) of patients in empyema group had no resolution. This difference in resolution among the two groups was found to be statistically significant (p=0.021).*

Conclusion: *MESNA is a safe drug for intrapleural instillation. Fibrinolytics activity of MESNA is good and it is effective both in multiloculated pleural effusion and empyema. MESNA Can be used as primary intrapleural agent where facility of thoracoscopy and VATS are not available.*

Keywords: *Multiloculated effusion , Multiloculated empyema ,MESNA ,Septations*

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I. Introduction

Pleural effusion is an abnormal accumulation of fluid in the pleural space while pleural empyema is an accumulation of pus in the pleural space1. A pleural effusion is an excessive accumulation of fluid in the pleural space, indicates an imbalance between pleural fluid formation and removal. Accumulation of pleural fluid is not a specific disease, but rather a reflection of underlying pathology. Pleural effusions accompany a wide variety of disorders of the lung, pleura, and systemic disorders 2. It is the most common manifestation of pleural disease. Because the mesothelial boundaries are leaky, excess liquid can move across into this lower pressure, high capacitance space and accumulate as a pleural effusion 3. A pleural Empyema refers to a purulent collection in the pleural space 4. Empyema is typically associated with underlying pulmonary parenchymal infection, but may also be associated with blood-borne infection, thoracic surgery, trauma, abdominal infection, or neoplasm 5. Treatment of pleural effusion and pleural empyema depend on the type of effusion and symptom of the patients. Transudate pleural effusion need not to be drained most of the time. Exudative pleural effusions are mostly drained by closed pleural aspiration while pleural empyema commonly requires intercostal tube drainage. In multiloculated pleural effusion and empyema drainage by above methods are very difficult and many times results in incomplete drainage of fluid or pus 1.Difficulty in the drainage of fluid and pus in multiloculated pleural effusion and pleural empyema is due to the formation of many pockets in the pleural space by fibrin membrane due to adhesion of visceral and parietal pleura 1. It occurs due to an inflammatory response between the visceral and parietal surfaces which increases the procoagulant and depresses the fibrinolytic activity leading to deposition of fibrin sheets which impairs the free fluid drainage 6.With the time duration difficulty in fluid drainage increases, as forming of thick septation are increased and exudative and fibrino-purulent stage of empyema convert into organization 1.The management of these types of multiloculated effusion and empyema with closed pleural aspiration and intercostal tube drainage with drugs fails most of the

time due to the presence of thick viscous fluid and multiple septations.Various therapeutic options available for management of these types of multiloculated effusion and empyema include intrapleural instillation of fibrinolytic agents, breaking down of loculations or decortication either by video-assisted thoracoscopic surgery (VATS) or thoracotomy and open drainage procedures. Video-assisted thoracic surgery is a better option among above, but it is neither easily available nor affordable by the majority of patients in developing countries like India.Intrapleural instillation of fibrinolytic agents has been found to be a useful adjunctive therapy in various small, uncontrolled and randomized trials. The theory behind the use of intrapleuralfibrinolytics is that they destroy the fibrin membranes and facilitate drainage of the pleural fluid. The clearance of this fibrin by intrapleural administration of fibrinolytics prevents further intrapleural organization and loculization7.

Various fibrinolytics agents used commonly in practice are streptokinase, streptodornase, urokinase, Human recombinant deoxyribonuclease, tissue plasminogen activator. Above fibrinolytics have many side effects and are costly. Streptokinase and urokinase have been associated with febrile reactions, bleeding tendency and anaphylaxis in many studies [8,9]. tPA has also been associated with similar adverse effects[10]. Human recombinant DNase is not easily available in our country.The problem with all above-mentioned management modalities drive us to search for an intrapleural agent which can be easily available, safe and equally effective to present standard treatment.

MESNA (2-mercaptoethane sulfonate Na) is a drug which is used in various different therapeutic procedures. It is commonly used to prevent cyclophosphamide induced hemorrhagic cystitis. In recent past, its role as mucolytic and fibrinolytic is being extensively studied. It acts in a manner similar to cysteine, breaking the disulfide links on the macromolecules responsible for the viscosity of mucus secretions [1].
Mucolytic action of MESNA is well known and used by physicians as aerosol therapy in indoor patients and in ICU patients [11,12,13]. Intermittent aerosol therapy with MESNA has shown to decrease the incidence of recurrent infections in patients with Cystic fibrosis [14]. Intratracheal instillation of MESNA reduced the airway pressure in patients on mechanical ventilation [15].

After thorough literature search on MESNA we found that MESNA is used by surgeons for tissue dissection as a chemical dissector. They use MESNA in chemically assisted tissue dissection during surgery or invasive procedures, as it makes tissue dissection easy by separating surrounding tissues. MESNA is also used by ENT surgeons to remove debris in cholesteatoma surgery. MESNA is useful in surgery of atelectatic ears and adhesive otitis media as it makes the operation easy and safe by allowing elevation of the tympanic membrane by its mechanical and chemical actions. MESNA has good value in chemically assisted endoscopic mechanical submucosal dissection (CAEMSD) as MESNA significantly reduces tissue resistance to the initial balloon-catheter insertion into the submucosa. MESNA has a good utility as a local adjuvant in revision lumbar spine surgery in peridural fibrosis, as it contributes significantly to reduce the operative complications and confirms its ability as a chemical dissector. MESNA has been successfully used to ease abdominal myomectomies and excision of endometrial cysts[11,12,13,15,16,17,18,19,20.]

In vitro studies have shown that MESNA has an inhibitory effect on the formation of Escherichia coli biofilms[21]. In another study on rabbit models, MESNA was used to prevent capsule formation on the implant [22].

To our best knowledge till date, there is only one study on intrapleural instillation of MESNA in multiloculated pleural effusion and empyema. This study revealed that MESNA works as fibrinolytic with the significant p-value. A big limitation of this study was a small sample size [1]. We also used intrapleural MESNA in two patients of multiloculated empyema after taken consent at our institute and there was complete drainage of pleural fluid in both the patients and none of the patient reported any side effect. With the help of above data we can extraplot that MESNA is an agent which is easily available, effective, safe and less expensive and due to its proved action as a mucolytic, chemical dissector and fibrinolytic along with our practical experience, we propose the hypothesis that MESNA can be an intrapleuralfibrinolytic agent which can overcome many limitation of presently available agents. So with this view we planned the present study with permission of institutional Ethics Committee of Sawai Man Singh Medical College Jaipur Rajasthan INDIA.

II. Material And Methods

This hospital based prospective type of interventational study was carried out on patients of Department of Respiratory Medicine at Institute of Respiratory Diseases , SMS Medical College Jaipur , Rajastham INDIA from February 2017 to January 2018. A total 40 adult subjects (both male and females) of aged ≥ 18 years were included in this study.

Study Approval -: This study was approved by institutional ethical committee of SMS medical college Jaipur.

Place of Study-: This study was undertaken at Institute of Respiratory Disease SMS Medical College, Jaipur, Rajasthan.

Study Duration-: The planned duration was about 1 year (Feb. 2017 to Jan. 2018)

Study Type-: It was a Hospital based prospective type of interventional study.

Study Population-: Patients admitted with multiloculated pleural effusion and empyema, at Institute of Respiratory Disease SMS Medical College, Jaipur.

Sample Size -: 20 patients for each groups.Sample size was calculated at 80% study power and α error of 0.05 assuming effectiveness of MESNA as 90% and 40% respectively in multiloculated pleural effusion and empyema as per seed article. Following above assumption 14 patient in each group (multiloculated pleural effusion and multiloculated pleural empyema) are required as sample size for the study which evaluated and further rounded of 20 patients in each group expecting 20 % drop outs / loss to follow up.

Inclusion criteria -:
1. Patients willing to participate in the study and given an informed written consent.
2. Multiloculated pleural effusion and Multiloculated pleural empyema patients only.
3. Age group 18 – 60 year.

Exclusion Criteria-:
1. Haemodynamically unstable patients
2. Minimal effusion and empyema
3. Pregnant female
4. Hypersensitivity to MESNA
5. Transudative effusion

Procedure Method-:
This study was carried out at the Institute of Respiratory Diseases, SMS Medical College, Jaipur, during the period from February 2017 to January 2018. Patients with multiloculated pleural effusion and empyema diagnosed clinically and radiologically (X-ray and USG chest) were enrolled consecutively after applying inclusion and exclusion criteria. Radiologist used the term thin septation if thickness of septation was <1mm and thick septation if thickness of septation was >1mm. Radiologist also used the term few septation if septations were less in the pleural cavity and multiple septations if septations were more in the pleural cavity. Patient included in the study after consent and then subjected to the following:-
- Routine Lab investigations
- Prothrombin time
- Activated plasma thromboplastin time
- Pleural fluid investigations: biochemical, microbiological and cell count.

Transudative effusion patients (n=0) were excluded and exudative effusion were subjected to intradermal sensitivity test for MESNA. Those found insensitive to MESNA were instilled 1800 mg of MESNA intrapleurally (i.e.3 ampoules of "Mistabron" was injected into pleural cavity after dilution with 20 ml of normal saline) (Each ampoule have 3 ml solution which contains 600mg MESNA) under aseptic precaution under ultrasound guidance. The same procedure was repeated for three consecutive days in different pockets in those subjects in which complete adhesiolysis was not confirmed on day 1 or day 2. Patients were every day followed up with ultrasonography chest, to look for adhesiolysis or thickness of septations and number of septations. Once adhesiolysis was confirmed pleural fluid was drained by closed pleural aspiration and plural pus was drained by chest tube. If adhesiolysis was partial, process of instillation of MESNA was repeated for 3 sessions. After 3 days, pleural fluid was drained by closed pleural aspiration and plural pus was drained by chest tube. Resolution was confirmed by USG chest and chest x ray PA view. Primary Outcome was divided into complete, partial, and non-resolution of pleural effusion and empyema on basis of chest X– ray and USG chest.

Statistical analysis
Data was analyzed using Chi-square tests .The level $P < 0.05$ was considered as the cutoff value or significance.

III. Result

Table – 1: Septation characteristics among study subjects

Septation		Effusion		Empyema		P value
		N	%	N	%	
Number	Few	2	10	7	35	0.130
	Multiple	18	90	13	65	(NS)
Thickness	Thick	13	65	13	65	0.740
	Thin	7	35	7	35	(NS)

Table 1 shows that 90% of the subjects in effusion group and 65% of subjects in empyema group had multiple septations. However this difference was not found to be statistically significant (p=0.130). Most of the subjects in effusion group (65%) as well as in empyema group (65%) had thick septations. No significant difference was observed between the two groups in relation to thickness of septations (p=0.740).

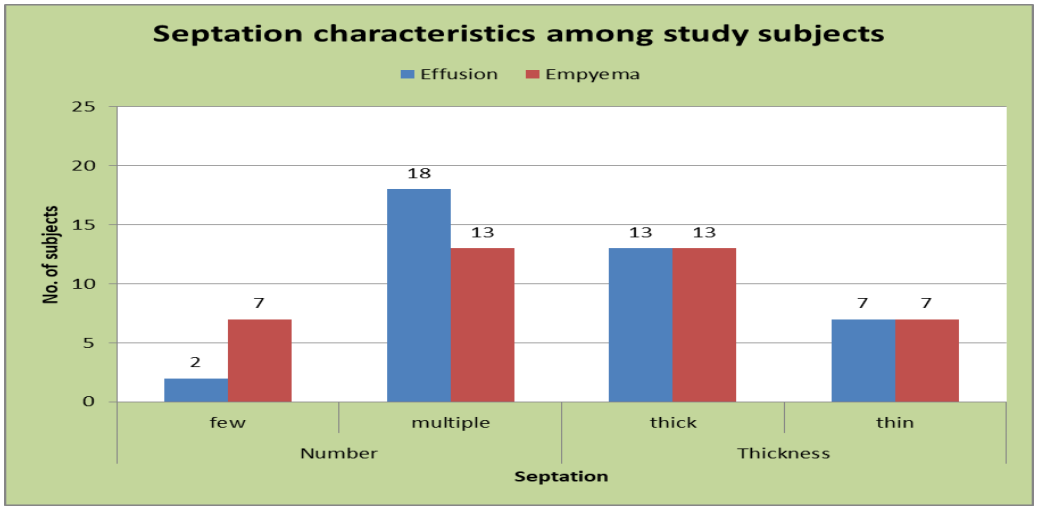


Table-2: Number of Septation detected by Follow up USG among study subjects

Follow up	Number of septa	Effusion		Empyema		P value
		N	%	N	%	
Day 0	Few	2	10	7	35	0.130
	Multiple	18	90	13	65	(NS)
Day 1	Few	5	25	8	40	0.500
	Multiple	15	75	12	60	(NS)
Day 2	No	2	10	1	5	0.086
	Few	7	35	14	70	(NS)
	Multiple	11	55	5	25	
Day 3	No	5	25	6	30	0.568
	Few	8	40	10	50	(NS)
	Multiple	7	35	4	20	
Intra group p value		<0.001 (S)		<0.001 (S)		

Table 2 shows that with instillation of MESNA, there was decrease in multiple septations on Day 1,2, and 3 in both groups and this change in number of septations was found to be statistically significant in both the groups (p<0.001). However on inter group comparison no significant difference was seen in between effusion and empyema groups. It could thus be inferred that MESNA is effective in both effusion and empyema and effect of MESNA instillation on number of septations could be considered similar in both effusion and empyema.

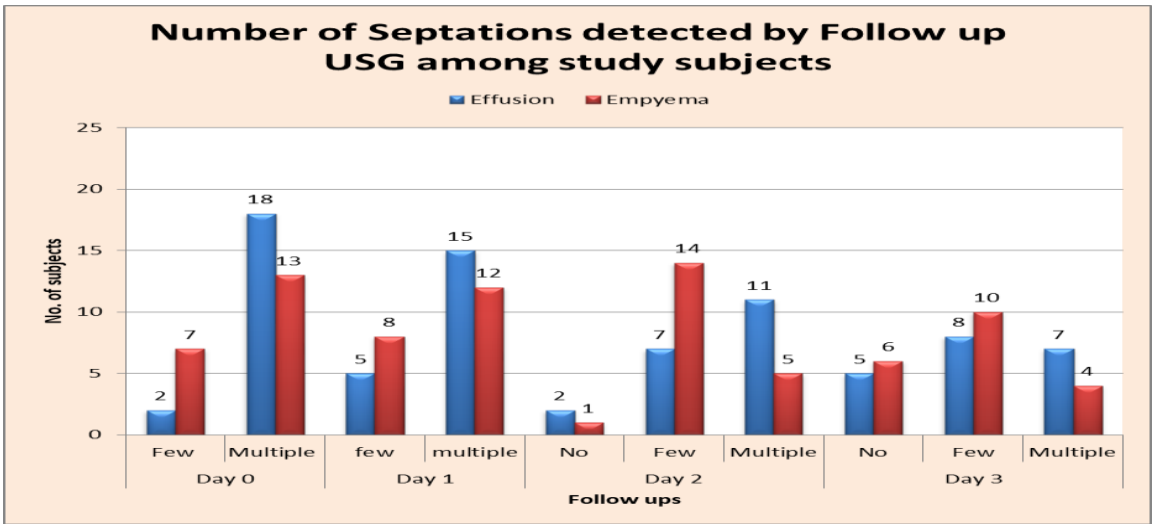


Table – 3: Septation thickness among study subjects

.Follow up	Thickness of septa	Effusion		Empyema		P value
		N	%	N	%	
Day 0	Thin	7	35	7	35	0.740 (NS)
	Thick	13	65	13	65	
Day 1	Thin	7	35	8	40	1.000 (NS)
	Thick	13	65	12	60	
Day 2	No	2	10	1	5	0.766 (NS)
	Thin	6	30	8	40	
	Thick	12	60	11	55	
Days 3	No	5	25	6	30	0.795 (NS)
	Thin	13	65	11	55	
	Thick	2	10	3	15	
Intra group p value		<0.001 (S)		<0.001 (S)		

Table 3 shows that with instillation of MESNA there was decrease in thick septations on Day 1,2, and 3 in both groups and this change in thickness of septa was found to be statistically significant in both the groups ($p<0.001$). However on inter group comparison no significant difference was seen between effusion and empyema groups on any day of follow up. It could thus be inferred that MESNA is effective in both effusion and empyema and effect of MESNA instillation on thickness of septations could be considered similar in both effusion and empyema.

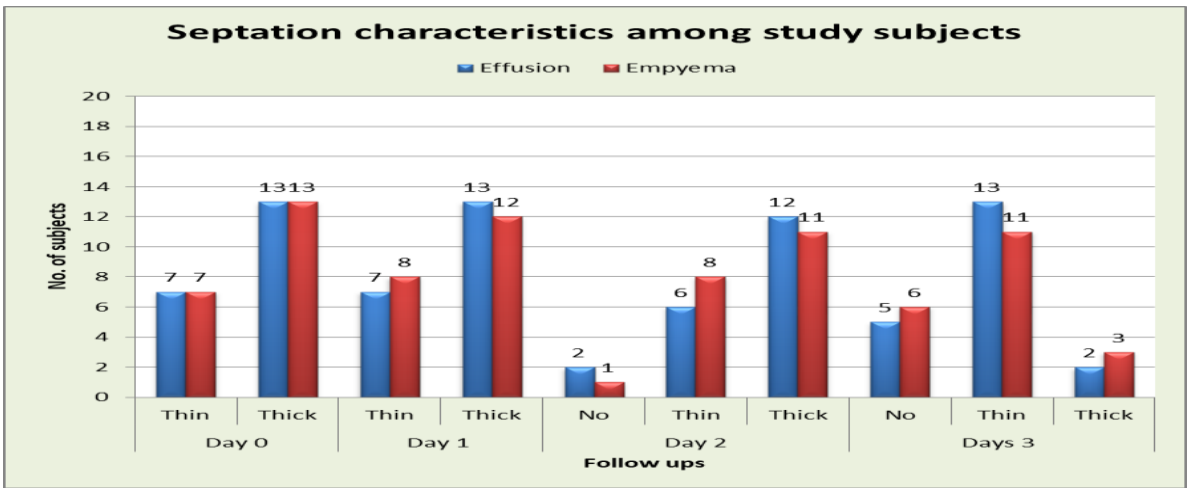
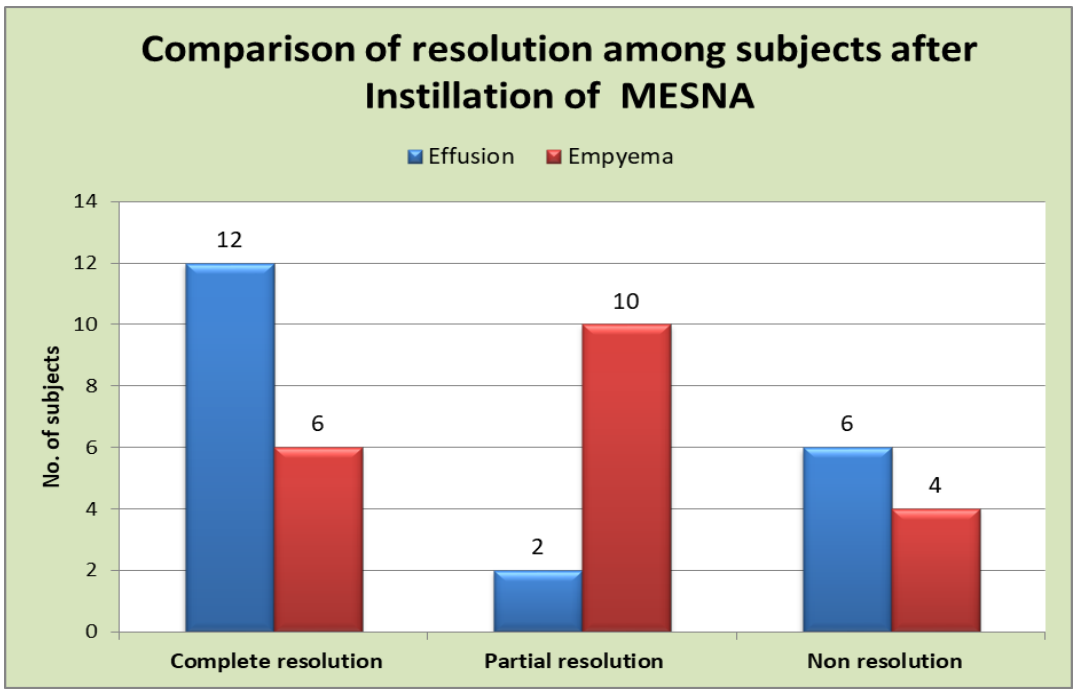


Table - 4: Resolution of fluid among subjects after instillation of MESNA

Resolution	Effusion		Empyema		Total	
	N	%	N	%	N	%
Complete resolution	12	60	6	30	18	45
Partial resolution	2	10	10	50	12	30
Non resolution	6	30	4	20	10	25
Total	20	100	20	100	40	100

Table 4 illustrates that in effusion group patients complete resolution was seen in 12 (60%) patients, partial resolution seen in 2 (10%) and 6 (30%) patients still had no resolution. While in empyema group patients only 6 (30%) patients had complete resolution, 10 (50%) had partial resolution and 4 (20%) of patients in empyema group had no resolution. This difference in resolution among the two groups was found to be statistically significant (p=0.021). i.e. complete resolution was more in effusion group patients as compared to empyema group patients.



IV. Discussion

The present study was undertaken on 40 clinically and radiologically diagnosed patients of multiloculated pleural effusion (n= 20) and multiloculated pleural empyema (n=20).

The age distribution of our subjects was fair among both groups. Patients in both effusion and empyema groups were mostly young (< 30 years and 30-39 years). The mean age of patients with effusion was 37.6 ± 18.69 years, while in patients with empyema was 34 ± 11.09 years. This difference seen in relation to age between the two groups was statistically not significant (p=0.856) and implies that development of multiloculated effusion and empyema is not affected by age. In present study most of patients in both the groups were male which accounted 80-85 % of total subjects. There was no baseline difference observe in gender of subjects, across our study groups (p=1.000)

The length of presenting symptoms between effusion group and empyema group in this study was found similar and not significant (p=0.459). Most of the subjects in both effusion group (50%) and empyema group (60%) had length of presenting symptoms between 1 to 2 months. The difference observed in length of presenting symptoms among study groups was statistically insignificant. Most of patients of both the groups have 1- 2 month of length of presenting symptoms, which is late and may be due to delayed referral to tertiary care center from district and peripheral areas. Only 3 cases came to the institute directly all were having presenting symptom of less than 15 days. All these cases were found to have thin and few septations only. All the cases were responded well to MESNA instillation. This fact is of importance as it suggests early referral should be done from peripheral center to a specialist center to prevent grave complications of pleural effusion and empyema. The main reasons for late referral to tertiary care centre (as our institute is tertiary care centre) in cases of multiloculated pleural effusion and empyema are late diagnosed in periphery, which may be due to unavailability of radiological diagnostic tools particularly USG . We observed that most of the patients in both

the group, who have more length of presentation of symptoms, have more multiple and thick septations and resolution by MESNA was less in that type of patients.

In Effusion group, before instillation of MESNA, (Day 0) few septations were present in 2 (10 %) patients while multiple septations were present in 18 (90 %) patients. After instillation of 1st dose of MESNA (Day 1), we observed the patients with few septations were 5 (25 %) and patients with multiple septations were in 15 (75%) patients. After instillation of MESNA on 2nd day (Day 2), no septation was seen in 2 (10%) patients, few septationsin 7 (35%) patients and multiple septations were still present in 11 (55%) patients. After 3rd day of intrapleural use of MESNA (Day 3) number of septations was obsereved as no septation seen in 5 (25%) patient, few septations in 8 (40%) patient and multiple septations in 7 (35%) patient. There was a change in number of septations observed after each instillation of MESNA and found that this difference was statistically significant as p value was<0.001 (Table -2).

In Empyema group, before instillation of MESNA (Day 0), few septations were present in 7(35%) and multiple septations were present in 13 (65%) patients. After instillation of 1st dose of MESNA (Day 1), there was a change in the number of septations as few septations were observed in 8 (40%) patients and multiple septations were seen in 12 (60%) patients. After instillation of MESNA on 2nd day (Day 2), no septation were seen in 1 (5%) patient, few septations in 14 (70%) and multiple septations were seen in 5(25%) patients. After instillation of MESNA on 3rd day (Day 3) noseptation seen in 6 (30%), few septations in 10 (50%) and multiple septations seen in 4 (20%) patients. There was a change in the number of septations observed after instillation of MESNA all the three days and we found this difference statistically significant as p value was< 0.001 (Table -2).

We observed that patients of both the effusion and empyema group have few and as well as multiple septations in pleural space before instillation of MESNA. There is decrease in numbers of septation were observed after instillation of MESNA into the pleural cavity in effusion group as well in empyema group. We found that septations were broken by MESNA in both group but the number was not significant (NS) statistically on all the three days when comparison was done between the two groups. P- Value on day 1st was 0.500 (NS), on day 2nd was 0.086 (NS) and on day 3 was 0.568.

It is clear that fibrinolysis by MESNA happened in both group of few septation and multiple septations, though complete adhesiolysis observed higher in few septation group compared to multiple septation. This phenomenon was observed similar in effusion group and empyema group. By above observation we can confidently conclude that fibrinolytic action of MESNA happens similar in effusion and empyema and presence of pus does not affect the mode of action of the investigatory drug.

After thorough search and best of our knowledge this is the first study which has observed and compared the fibrinolysis effect of MESNA on few and multiple septations.

In effusion group, before instillation (day 0) of MESNA thin septations were present in 7 (35%) patients, thick septations in 4 (20%) patients and thin and thick both present in 9 (45%) patients. For outcome analysis of fibrinolytic (MESNA) on thick septations, patients who have both thin and thick septations included in to thick septations. This is because breakage of thick sepatation is more important for resolution in the pleural fluid and pus after ICDT or aspiration. After merging the groups as above thin septations group was consist of 7 (35%) patients and thick septations group was consist of 13 (65%) patients (day 0). After instillation (day 1) of 1st dose of MESNA we observed that there was no changes in the number of thick and thin septations (Thin septations remain same as in 7 (35%) patients, thick septations in 13 (65%) patients). After 2nd day of MESNA instillation (Day 2) there was decrease in number of both thick and thin septation observed , no septations were seen in 2 patients (10%) , thin septations were decrease from 7 to 6 patients (30%) and thick septations decreased from 13 to 12 (60%) patients . After instillation of MESNA (Day 3) on 3rd day, no septation increased from 2 to 5 (25%) patients, thin septations increased from 6 to 13 (65%) patients, while thick septations markedly decrease from 12 to 2 (10%) patients. This increase in thin septation is due to conversion of thick sepation to thin septation is obvious as no of thick septation is markedly decrease. Most of the thin septations previously present resolved after MESNA instillation and thick septations converted into thin septations. Statistically this change is significant in effusion group patient as p value was <0.001 (Table -3).

In Empyema group, before instillation of MESNA (Day 0), thin septations were present in 7(35%) patients and thick septations were present in 1(5%) patient and thin and thick both were present together in 12(60%) patients. For outcome analysis of fibrinolytic (MESNA) on thick septations, patient who have both thin and thick septations included into thick septation.Finally thin septations present in 7(35%) patients and thick septations present in 13 (65%). After instillation (Day 1) of 1st dose of MESNA there was change in thickness of septations observed as thin septations seen in 8 (40%) patients and thick septations has seen in 12 (60%) patient. After instillation of MESNA on 2nd day (Day 2), thin septations present in 8 (40%) patients, thick septations has seen in 11 (55%) patients and 1 (5%) patient had no septations. After instillation of 3rd dose of MESNA (Day 3), no septa seen in 6 (30%), thin septations seen in 11 (55%) and thick septations seen in 3

(15%) patients. This study shows, changes in thickness of septations after instillation of MESNA in empyema group patients as p-value was <0.001 and it was statistically significant (Table -3).

In present study we enrolled patients with thin and thick septations and divided in effusion and empyema groups. After instillation of MESNA fibrinolytic action observed affecting both thin and thick septations, however the effect was more obviously seen on thick septations as most of them either completely broke down or converted into thin septations. The effect on thin septation is naturally should be more and they must have broken down in significant numbers but this factual observation is masked by increase in the number of thin septations due to conversion from thick septation into thin septation. When we analyse the thin septations group on day one we found that the patient with zero septations were rise from 0 to 5. This change establishes the fact that fibrinolytic effect of MESNA is more profound on thin septation. There was no obvious difference of fibrinolysis in septations observed on effusion group and empyema group on intergroup comparison. P-value was on day 1st is 0.931 (NS), on day 2nd is 0.482 (NS), on day 3rd is 0.795 (NS). By this data we can make a assumption that the action of MESNA in pus and fluid is same and not affected by the presence of pus. To our best knowledge till date this is the first study which observed the effect of fibrinolytics on both thin and thick septations.We can further say that more dosing of MESNA intrapleurally can be able to dissolve the septations but this was not in our protocol.

In present study after instillation of MESNA we observed that fibrinolytics used in both effusion group and in empyema group leading to decrease in number of fluid pockets. This effect on septations was associated with the increase in volume of fluid drained either by close aspiration or ICDT. In effusion group, effect of MESNA on septations and viscous fluid result in complete resolution, as seen in 12 (60%) patients, partial resolution in 2 (10%) patients, but 6 (30%) patients still had no resolution. On the other hand in empyema group, complete resolution was resulted in only 6 (30 %) patients, partial resolution in 10 (50%) patients and 4 patients (20%) had no resolution. This data is statistically significant (p = 0.021) and conclude that though amount of fibrinolysis is equal in both group but resolution is less in patient with empyema by instillation of MESNA. Reason for same could be presence of thick and multiple septations more in empyema group compared to effusion group. Also fibrinopurulent and organized stage of empyema is known for poor response (Table- 4).

Venkateswara Reddy Tummuru et al observed similar results in their study regarding fibrinolytic activity of MESNA. Authors found complete resolution in 90% of patients in effusion group and 40% in empyema group[1].

Fibrinolytics activity of MESNA has also been proved by many authors in past in different diseases and surgical procedures with success. Yilmaz M et al proved fibrinolytics activity of MESNA in atelectatic ears and adhesive otitis media[20], Luigi Benassi et al also proved fibrinolytics activity of MESNA in Chemically assisted dissection of tissues[16] , Vincenzo Denaro et al proved fibrinolytics activity of MESNA in their study on collagen fibres on Achilesh tendon[23], KazukiSumiyam et al observed same in chemically assisted endoscopic mechanical submucosal dissection[17], Chen S et al also find out fibrinolytics activity of MESNA on escherichia coli biofilms in vitro[21]. Our study establishes fibrinolytic activity of MESNA as a therapeutic tool for multiloculated pleural effusion and empyema as there was significant change in the number and thickness of septations.

Out of 40 patients 8 (40%) patients of effusion and 13 (65%) of empyema patients, failed on MESNA and required further intervention. Out of these, requirement of further procedure was more in patients of empyema group comparison to effusion group. 13 (65%)of empyema patients required medical thoracoscopy while only 8 (40%) of effusion patients required medical thoracoscopy. There was a large difference noted in number of patient (65 %,40%) for requiring further procedure but due to small sample size this difference was observed statistically not significant (p=0.068). The above difference in requirement of further procedure was due to presence of more multiple thick septations and organization of pus in empyema group patients compared to effusion group. We also observed that medical thoracoscopy of above patients compared to routine medical thoracoscopy was easier and safe as MESNA convert most of the thick septations into thin septation and remove fibrin layer from pleura surface .We felt that pleural biopsy by thoracoscopy become easier due to loss or decrease fibrin layer due to effect of MESNA.

V. Conclusion

This study concluded that -

MESNA is a safe drug for intrapleural instillation and is safer than other similar acting drugs.

Fibrinolytics activity of MESNA is good and it is effective both in multiloculated pleural effusion and empyema. MESNA can be used as primary intrapleural agent where facility of thoracoscopy is not available.

Fibrinolytic activity of MESNA can also be used prior to thoracoscopy to facilitate the procedure but controlled study is required to label it, as standards of care.

As MESNA is safe, further studies of intrapleural instillation in multiloculated pleural effusion and empyema with higher dose than used in present study can give us more beneficial results. Further studies are required for establishment of this conclusion.

References

[1]. Venkateswara Reddy Tummuru, PradyutWaghray, A.N. V. KoteswaraRao, V Veena, ChetanRaoVaddepally, HasnaniRikinBahadurbhai. Effectiveness of Intrapleural Instillation of Mesna for Adhesiolysis in Multi Loculated Pleural Effusions, Para Pneumonic Effusions and Empyema: Our Experience. International Journal of Therapeutic Applications.2015; 23: 5-9.

[2]. Karkhanis VS, Joshi JM. Pleural effusion: diagnosis, treatment, and management. Open Access Emerg Med. 2012;4:31-52.

[3]. V. Courtney Broaddus, Richard W. Light, Disorders Of The Pleura, 79 Pleural Effusion. Murray &Nadel's (Sixth edition) Textbook of Respiratory Medicine.

[4]. Bartlett JG, Gorbach SL, Thadepalli H, Finegold SM. Bacteriology of empyema. Lancet. 1974;1(7853):338-340.

[5]. Bartlett JG, Finegold SM. Anaerobic infections of the lung and pleural space. Am Rev Respir Dis. 1974;110(1):56-77.

[6]. Idell S, Girard W, Koenig KB, McLarty J, Fair DS. Abnormalities of pathways of fibrin turnover in the human pleural space. Am Rev Respir Dis. 1991;144(1):187-194.

[7]. Col (Dr) M.S. Barthwal. IntrapleuralFibrinolytic Therapy in Complicated,Parapneumonic Effusion and Empyema: Present Status. Indian Journal Chest Disease and Allied Science 2008; 50: 277-282.

[8]. Davies CW ShelokH, and Davies R J O. The systemic fibrinolytic activity of intrapleural streptokinase. Am J ResirCrit Care Med. 1998;157:328-330.

[9]. Cameron R. Intra-pleural fibrinolytic therapy vs. conservative management in the treatment of parapneumonic effusions and empyema. Cochrane Database Syst Rev. 2000;(3):CD002312.

[10]. Piccolo F, Pitman N, Bhatnagar R, Popowicz N, Smith NA, Brockway B, Nickels R, Burke AJ, Wong CA, McCartney R, Choo-Kang B, Blyth KG, Maskell NA, Lee YC. Intrapleural tissue plasminogen activator and deoxyribonuclease for pleural infection. An effective and safe alternative to surgery. Ann Am Thorac Soc.2014;11(9):1419-1425.

[11]. Tekeres M, Horváth A, Bárdosi L, Kenyeres P. Clinical studies on the mucolytic effect of mesna. ClinTher. 1981;4(1):56-60.

[12]. Risack LE, Vandevelde ME, Gobert JG. Effect of thiol derivatives on mixed mucus and blood clots in vitro. Resuscitation. 1978;6(1):9-20.

[13]. Goossens E. Aerosol therapy with Mesna in pneumology (Mistabronucb). ActaTubercPneumol Belg.1976;67(3-4):200-206.

[14]. Weller PH, Ingram D, Preece MA, Matthew DJ. Controlled trial of intermittent aerosol therapy with sodium 2-mercaptoethane sulphonate in cystic fibrosis.Thorax.1980;35:42.

[15]. Fernandez R, Solé J, Blanch L, Artigas A. The effect of short-term instillation of a mucolytic agent (mesna) on airway resistance in mechanically ventilated patients. Chest. 1995;107(4):1101-1106.

[16]. Luigi Benassi, GraziellaLopopolo, FlaviaPazzon, Luisa Ricci, Christine Kaihura, Fabio Piazza, Eugenio Vadora, Carlo Zini.Chemically assisted dissection of tissues: An interesting support in abdominal myomectomy.2000; 191:65–69.

[17]. KazukiSumiyama, Christopher J. Gostout, Elizabeth Rajan, Timothy A. Bakken, LPN, Mary A. Knipschield. Chemically assisted endoscopic mechanical submucosal dissection by using mesna .Gastrointestinal Endoscopy journal.2008;67:534.

[18]. Vincenzo Denaro, Alberto Di Martino, Umile Giuseppe Longo, Vincenzo Costa, Rocco Papalia, Francisco Forriol, Luca Denaro . Effectiveness of a mucolytic agent as a local adjuvant in revision lumbar spine surgery. European Spine Journal.2008;17:1752.

[19]. Weller PH, Ingram D, Preece MA, Matthew DJ. Controlled trial of intermittent aerosol therapy with sodium 2-mercaptoethane sulphonate in cystic fibrosis.Thorax.1980;35:42.

[20]. Yilmaz M, Goksu N, Bayramoglu I, BayazitYA.Practical use of MESNA inatelectatic ears and adhesive otitis media.ORL J OtorhinolaryngolRelat Spec.2006;68(4):195-198.

[21]. Chen S, He N, Yu J, Li L, Sun F, Hu Y, Deng R, Zhong S, Shen L. Inhibitory effect of 2-mercaptoethane sulfonate on the formation of Escherichia coli biofilms in vitro. Mol Med Rep. 2015;12(4):5223-30.

[22]. Ajmal, Nadeem, Riordan, Colin L., Cardwell, Nancy B.S., Nanney, Lillian B., Shack, R. Bruce. The Effectiveness of Sodium 2-Mercaptoethane Sulfonate (Mesna) in Reducing Capsular Formation around Implants in a Rabbit Model PlastReconstr Surg.2003;112:1455.

[23]. V. Denaro, F. ForriolA. Di Martino L. Denaro R. Papalia G. Caione. Effect of a mucolytic agent on collagen fibres: An optical and polarized light histologicalstudy. European Journal of Orthopaedic Surgery &Traumatology. December 2001;11 (4):209–212.

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