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ORIGINAL ARTICLE

Comparison of Post Pleurodesis Pain with and Without Lignocaine in Patients with Malignant Pleural Effusion

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ABSTRACT

Background: Chemical pleurodesis, using an intrapleuralsclerosing agent, is a good palliative measure to obliterate the pleural space, prevent fluid accumulation and improve breathing in patients with malignant pleural effusions. Lignocaine is usually administered intrapleurally just prior to pleurodesis for the relief of pain.

Objective: To compare the post pleurodesis pain with and without lignocaine in patients with malignant pleural effusions by using Visual Analog Pain Scale.

Methods: One hundred and eighty eight patients were randomized into two groups. Tetracycline was used as sclerosing agent for chemical pleurodesis. Group I comprised of patients in whom Lignocaine was not used along with sclerosant and Group II included those in whom injection Lignocaine 2% (200mg) was administered intrapleurally through intercostal tube 15 minutes prior to the administration of sclerosant. Pain was assessed twice by using Visual Analog Pain Scale **(VAS),** 15 minutes after pleurodesis **(VAS1)** and 2 hours after pleurodesis **(VAS2)**.

Results: Metastatic adenocarcinomawas the commonest malignancy (81 cases: 43.08%), followed by 49 (26.5%) cases of Mesothelioma. Mean age was 58.405$\pm$14.854 SD in Group I and 53.68$\pm$13.22SD in Group II. In Group I, VAS1 mean was 7.17cm$\pm$1.13, and VAS2 was 6.64$\pm$1.155. In Group II VAS1 mean was 4.85cm$\pm$0.792and VAS2 mean was 4.139$\pm$0.747($p < 0.001$)

Conclusion: Post-pleurodesispain was significantly reduced with the administration of lignocaine prior to pleurodesis.

KEY WORDS: Malignant Pleural effusion; Lignocaine; Pleurodesis; Visual Analog Pain Scale.

INTRODUCTION

Pleural effusion is common both in developed and developing countries. Common causes of exudative pleural effusions are malignancy and infections. The annual prevalence of malignant pleural effusion is 5% in hospitalized patients in Post Graduate Medical Institute (PGMI), Lady Reading Hospital (LRH) Peshawar, Pakistan[1]. Several palliative treatment options are available for the management of symptomaticmalignant pleural effusions[2,3]. Chemical pleurodesis, using an intrapleuralsclerosing agent, is a good palliative measure to obliterate the pleural space, prevent fluid accumulation and improve breathing[4,5,6]. Pleurodesis is achieved by adhesions of parietal and the visceral pleura for treatment of persistent pneumothorax or recurrent pleural effusion; it is done by instillation of a chemical sclerosing agent in the pleural space which produces a chemical inflammatory reaction causing eventual adhesion of the two surfaces. Different types of sclerosing agents are used[7]. Talc, Bleomycin and tetracycline are the commonest agents[8]. The advantages of tetracycline are its efficacy, excellent safety profile, ease of administration and low cost[9].

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Almost all patients experience pain after pleurodesis. Lignocaine (3 mg/kg; maximum 250 mg) is administered intrapleurally just prior to sclerosant administration. Analgesia and premedication should be considered to alleviate anxiety and pain associated with pleurodesis according to the recently published Guidelines of British Thoracic Society (BTS) for the management of pleural disease[10].

The intensity of pain can be best assessed by using **VAS**[11,.12].VAS is considered reliable and valid and has greater sensitivity compared to other scales like Simple Descriptive Pain Scale, Categorical Pain Scale, Numerical Rating Pain Scale and Faces Pain Scale[13]. It is easy to use,inexpensive to implement and is a standard tool in our practice for rating of pain-either by the patient or by the health care worker[14,25].

The use of lignocaine prior to the instillation of Tetracycline slurry for pleurodesis is not routine in Pakistan. We have carried out this study for the first time in Pakistan comparing the efficacy of Lignocaine in Tetracycline induced pleurodesis.

METHODS

This study was conducted in Post Graduate Medical Institute (PGMI), Lady Reading Hospital (LRH) Peshawar, Pakistan from March 2009 to October 2010. Sample size was 188, using 5% prevalence of malignant effusion in Khyber Pakhtunkhwa (KPK) Province of Pakistan, 5% level of significance and 90% power. The power calculation was done under WHO software for sample size determination. Patients were randomized into Group I (patients in whom lignocaine was not used) and Group II (patients, in whom lignocaine was used). Each group had 94 patients.

Patients were admitted in Pulmonology Department, PGMI and LRH from accident and emergency department(A & E) andoutpatient department (OPD). Patients were assessed clinically through history, examination & investigations.All patients with pleural effusion regardless of age and gender, who were proven malignant by cytology or biopsy, were included in the study. Patients suspected to have malignant pleural effusions but not proven by pleural fluid cytology or pleural biopsy, patients who are uncooperative or not willing for the pleurodesis and those in whom pleurodesis was performed previouslywere excluded from the study. Patients taking analgesics or sedatives were included in the study, 24 hours after stoppage of these medications. Informed written consent was taken from all the patients. Ethical approval was obtained from the ethical committee of Post Graduate Medical Institute (PGMI), Lady Reading Hospital (LRH) Peshawar.

Patency of chest tube was assessed and the proper location of Chest tube was also checked by doing repeat chest x-ray or ultrasound chest. Only one sclerosing agent, tetracycline was used in every patient included in this study because of its efficacy, excellent safety profile, ease of administration, availability and low cost. One gram of tetracycline was mixed with 40 ml of normal saline. This mixture was taken in 60 ml Disposable syringe and was injected intrapleurally through intercostal tube under aseptic conditions in Group I patients. The tube was

clamped for one hour after sclerosant administration. While in Group II patients, 10 ml of 2% (200mg) lignocaine 15 minutes prior to the administration of sclerosant tetracycline was injected intrapleurally through intercostal tube.

Pain experienced by the patient after administration of sclerosant was assessed in both Groups by using the**VAS**. Pleurodesis of patient and post pleurodesis assessment of pain was done on bedside. Pain was assessed by using **VAS** on a data collection form, which is 100 mm (10cm) horizontal line and the area of pain was marked. (see figure)

Pain assessment was done twice: 15 minutes (**VAS1)** and 2 hours (**VAS2)** after pleurodesis. All the other relevant data was entered in the data collection form.

Most patients in our set up are uneducated, for this purpose principle investigator had drawn the same visual analog scale which is 100 mm (10cm) horizontal line in numerical shape in the data collection form additionally to make it easier for the patients. Furthermore, it has reduced the chance of bias in this study. On the numerical type of Visual Analog pain Scale, principle investigator had asked the patient to identify how much pain he/she was having by choosing a number from 0 (no pain) to 100 (the worst pain imaginable) on horizontal line in the data collection form. The data was parametric and was entered in Statistical Package for Social Sciences (SPSS) Version 16 and is used for data analysis. In this study age and pain were Quantitative variables; sex and diagnosis were Qualitative variables. Mean $\pm$ standard deviation were calculated for quantitative variables like age and pain. Frequencies/percentages were calculated for Qualitative Variables like sex and diagnosis. Student **"t"** test was used to compare the intensity level of pain in both Groups of patients at the start of pain assessment task (15 minutes after pleurodesis) and at the end of pain assessment task (2 hours after injection of sclerosing agent). P-value $\leq$0.01 was considered significant. Results were presented in tables/charts.

RESULTS:

Patients were randomized into Group I and Group II with 94 cases in each group. Out of 188 patients, 104 (55.35%) were males;fifty (53.19%) in Group I, and 54 (57.45%) in group II.

Among these 188 patients, 81 (43.08%) were diagnosed as metastatic adenocarcinoma, 29 (30.85%) in Group I and42 (44.68%) in Group II. Other common diagnoses were mesothelioma 49(26.5%) followed by lymphoma 20 (10.65%) and bronchial carcinoma 15(7.97%). Less common ones included Breast carcinoma 9 (4.78%), hepatocellular carcinoma 4 (2.15%), carcinoma esophagus 3 (1.5%), renal cell carcinoma 3 (1.5%) and one case each of bladder carcinoma, carcinoma spinal cord, leukemia and ovarian carcinoma (2 % of all cases)

In Group I, patients' age range was from 16 to 90 years. While in Group II, the age range was from 20 to 75 years. Mean age was 58.405$\pm$14.854 SD in Group I and 53.68$\pm$13.22SD in Group II (Table III).

In Group I, VAS1 mean was 7.1797$\pm$1.13 cm(range between 9.20 and 4.00cm); VAS2 mean was 6.6406$\pm$1.155 cm(range between 8.80 and 3.20cm)

In Group II, VAS1 mean was 4.8522$\pm$0.7929 cm(range between 6.6 and 2.6); VAS2 mean was 4.1319$\pm$0.747 cm (range between 5.30 and 2.20cm)The p-value for both was <0.001 (Table II).

DISCUSSION:

Pleural effusion is defined as the abnormal collection of fluid in the pleural space resulting from excessive fluid production or decreased absorption[15]. The relative annual incidence of pleural effusion is estimated to be 320 per 100,000 people in industrialized countries[16].Malignant pleural effusion is a common cause of exudative pleural effusion in north western part of the country[17].It can be diagnosedby cytological examination and closed pleural biopsy[18].

Among the intrapleuralsclerosing agentstetracycline, talc and bleomycine are the commonest. Talc is effective but is associated with adverse effectsincluding infections, systemic embolization and Acute Respiratory Distress Syndrome (ARDS) leading to respiratory failure[19-21]. The advantages of tetracycline are its efficacy, excellent safety profile, ease of administration and low cost[9,22-24]. In our study we used only one agent i.e. tetracycline for uniformity of results. Fever has been observed in patients on the first day of pleurodesis with tetracycline. No other serious complications of tetracycline have been reported.

Although several studies are reported on pleurodesis, there is no consensus on which agent and what dose should be used. Some authors have used tetracycline derivates and reported about 50% success rates but severe pain after the procedure was observed in some patients.

Sherman, et al[10] have suggested that there is optimum anesthesia with intrapleural lignocaine during chemical pleurodesis with tetracycline. In our study there was significant reduction in pain with the use of lignocaine regardless of age and sex.An incidental finding documented was the number of failed pleurodesis (reaccumulation of pleural fluid) in twice as much cases in Group II with the use of lignocaineas compared to without (Table 3). Criteria for evaluating the success or failure of pleurodesis are not found in literature.

The association of occupational asbestos exposure with the development of mesothelioma is established and a potential test of its diagnosis is also described[26,27]. Approximately half of all patients with metastatic cancer develop a malignant pleural effusion which is likely to lead to a significant reduction in quality of life secondary to symptoms such as dyspnoea and cough[28].

The results of this study also showed that metastatic adenocarcinoma and mesothelioma were the most common causes of malignant pleural effusion in this region. All cases of mesothelioma in this study belonged to the Northern districts & agencies of the Province Khyber Pakhtunkhwa, a finding previously reported [29,30]. There is a strong possibility of asbestos in the environment of these areas and its association with the development of mesothelioma.

There are few limitations in this study. Pain was not assessed with the use of other sclerosing agents like bleomycin and talc. Patients with pneumothoraces have been excluded to reduce bias in the study results.This study was focused on pain assessment without regard to success or failure of pleurodesis with the use of lignocaine.Though we have noted statistically significant failure of pleurodesis with the use of lignocaine, but future studies should be carried out to properly evaluate thispossible effect.

CONCLUSION

We conclude that pain was significantly reduced with the administration of lignocaine intrapleurally just prior to pleurodesis. On the other hand it caused statistically significantfailure of pleurodesis. Further studies are needed to confirm this adverse effect.

TABLE I: Diagnosis In Both Groups (n=188)

Diagnosis	Groups		
	Lignocaine Not given (Group I)	Lignocaine given (Group II)	Total
Metastatic Adenocarcinoma	44(46.85%)	37(39.36%)	81 (43.08%)
Known Primaries other than Pleura	20(21.27%)	38(40.42%)	58 (30.85%)
Mesothelioma	30 (31.91%)	19 (20.21%)	49 (26.06%)
Total	**94 (100%)**	**94 (100%)**	**188 (100%)**

TABLE II: Comparison between The Groups For Pain After Pleurodesis - Visual Analog Pain Scale (N=188)

Pain Score	Group I (n=94) Mean±SD	Group II (n=94) Mean±SD	P-Value
VAS at 15 Minutes (VAS 1)	7.18±1.14	4.85±0.79	<0.001
VAS at 02 Hours (VAS 2)	6.64±1.20	4.13±0.74	<0.001

TABLE III: DEMOGRAHICS CHARACTEREISTICS OF PATIENTS IN BOTH GROUPS AND DELETERIOUS EFFECTS OF LIGNOCAINE USED ON FLUID REACCUMULATION IN THE PLEURAL SPACE (n=188)

	Group I		**Group II**		**P-value**
	Male	**Female**	**Male**	**Female**	
SEX	50 (53.19%)	44 (46.85%)	54 (57.45%)	40 (42.55%)	0.13
AGE	58.405±14.854 SD		53.68±13.22 SD		0.05
FLUID REACCUMULATION (NOTED)	8		19		0.001

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COMPARISON OF POST PLEURODESIS PAIN WITH LIGNOCAINE AND WITHOUT LIGNOCAINE IN PATIENTS WITH MALIGNANT PLEURAL EFFUSION

PROFORMA

Name: _____ **Age:** _____ **Sex:** _____
Address: _____ **Occupation:** _____
Date of admission: _____ **Admission No:** _____
DIAGNOSIS: _____

X-rays chest/Ultrasound Chest done: Yes / No

Lignocaine given: Yes(Group II) / No (Group I)

Rating of Pain During Pleurdesis by Visual Analog Pain Scale:

VAS Frame

The VAS Frame measures exactly 10cm. the distances from zero to the marking in cm are result indicators to be processed as continuous variable for statistical analysis.

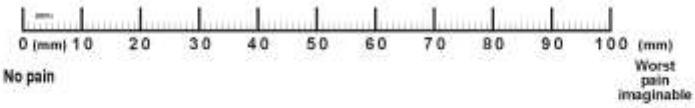
1. VAS1 is the level of pain at the start of Pain assessment task.(15 minutes after pleurodesis)
2. VAS2 is the level of pain at the end of Pain assessment task.(02 hours after pleurodesis)
3. The difference (VAS1) – (VAS2) is an indicator of the analgesic effect.
   VAS1_____, VAS 2_____, VAS1 -VAS2=_____.

VISUAL ANALOG PAIN SCALE"VAS 1" (15 Minutes after pleurodesis)

NO PAIN 0 (cm) _____ 10 (cm) WORST PAIN

Directions: Ask the patient to indicate on the line where the pain is in relation to the two extremes Qualification is only approximate; for example, a midpoint mark would indicate that the pain is approximately half of the worst possible pain.

VAS 1 in Numerical Shape



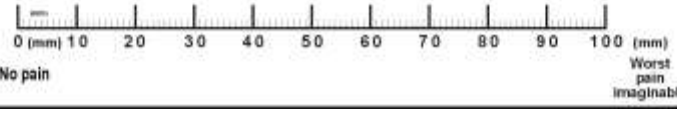
No pain — Worst pain imaginable

VISUAL ANALOG PAIN SCALE"VAS 2" (2 Hours after pleurodesis)

NO PAIN 0 (cm) _____ 10 (cm) WORST PAIN

Directions: Ask the patient to indicate on the line where the pain is in relation to the two extremes Qualification is only approximate; for example, a midpoint mark would indicate that the pain is approximately half of the worst possible pain.

VAS 2 in Numerical Shape



No pain — Worst pain imaginable

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