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Comparison of Efficacy of "Sedoanalgesia" To Conventional Topical Lignocaine Spray in Flexible Fibreoptic Bronchoscopy - A Prospective Randomized Study

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ABSTRACT: Flexible fibreoptic bronchoscopy (FOB) is a daycare procedure recommended for various diagnostic and therapeutic purposes in 'Pulmonary medicine. The use of supplemental sedation is not customary in many centers in India under the pretext that it might produce complications. The conventional technique of topical lignocaine spray is followed despite its limitations in terms of patient cooperation, intractable cough and even reduced level of comfort to the bronchoscopist.

Considering the mentioned facts, we have taken up the study to compare the efficacy of supplementing analgesia and sedation to the conventionaltechnique (Sedoanalgesia) to evaluate the relevance. The primary objective of the study is to look for**,** influence of pharmacological agents on hemodynamics**,** need for stay in High dependency unit, compare the tolerance of the procedure, patient's willingness to a repeat procedure if needed in future and comfort of the bronchoscopist.

Methods*:* One-hundred patients posted for FOB for evaluation of lung disease are randomly assigned to two groups. Fifty patients of Group L, received topical lignocaine and fifty patients of Group S were premedicated with Midazolam and Fentanyl in addition to lignocaine spray. Chi-square test, ANOVA test and student t-test are used for statistical analysis to compare the outcome between the two groups. The p-value of < 0.05 is considered significant and $p < 0.001$ as highly significant.

Results: Use of supplemental sedation and analgesia improved procedural tolerance compared to lignocaine spray alone. It was observed that there was a significant reduction in cough, distress, nausea and choking with a p value of <0.001in sedoanalgesia group. Mean duration of procedure is significantly low in sedoanalgesia group and acceptance of repeat FOB if indicated, is high (p value<0.001).

Conclusions*:* Supplementing Fentanyl and Midazolam to local lignocaine spray works convincingly better than lignocaine spray alone in FOB in terms of patient tolerance and ease of bronchoscopist.

KEY WORDS-Flexible Fibreoptic Bronchoscopy, Sedoanalgesia, lignocaine spray.

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I. INTRODUCTION

Flexible fibreoptic Bronchoscopy (FOB) has revolutionized the diagnosis and management of various lung diseases.

It is an indispensable tool for an anesthesiologist in anticipated difficult intubation. Unfortunately, patient may experience unpleasant symptoms such as cough, nausea, distress and choking during the procedure with the conventional topical lignocaine spray. Lignocaine is the most commonly used topical anaesthetic agent with a high safety margin. "Spray-as-you-go"techniquewith lignocaine is generally adopted for these procedures in India[1]. In spite of limitations with conventional technique in terms of patient cooperation, intractable cough choking nausea and distress and reduced level of comfort to the bronchoscopist, topical lignocaine spray is still commonly used in most of the centers in India[2].However, current recommendations in accordance with British guidelines [3] are to offer supplementary sedation which can improve tolerance, comfort and cooperation for

bronchoscopy. In the light of these observations, this comparative study of administering sedoanalgesia [4] (pharmacological sedation in combination with lignocaine spray) with topical lignocaine alone was undertaken.

The main objective of the study is to analyze the merits and demerits of sedoanalgesia in patients undergoing flexible bronchoscopy. There are reports in the literature that Midazolam and Fentanyl will improve tolerance by relieving anxiety while providing analgesic effect.[5]

In this prospective randomized study, additional factors like hemodynamic stability; suppression of cough andchoking; better control of physical movement and distress; patient's willingness to undergo a repeat procedureetc. were evaluated.The choice of benzodiazepines is generally Midazolam which is one of the most commonly used sedativesdue to its rapid-onset, anxiolytic and amnestic properties[6].Fentanyl is the primary choice of opioid for any day care procedures like bronchoscopies. An additional benefit to opioid use in a bronchoscopic procedure is its antitussive effect [7,8].

II. METHODS

The present study was undertaken in our institution by the department of Anesthesiology and pulmonary medicine with approval from the institutional ethical committee. A total number of100 patients in the age group of 20-70 years (M≅F) were scheduled for Flexible Bronchoscopy. Patients with severe comorbidities were excluded from the study. The procedure of Bronchoscopy was explained to the patients and written consent was obtained. The patients were educated about the use of Visual Analogue Scale [1].

Before commencing the procedure, the bronchoscopist and the unit staff went through a checklist (demographic data, informed consent, fasting period, lignocaine sensitivity test and availability of oxygen) to ensure that patients were adequately prepared.

Patients were shifted to thebronchoscopy suit and an intravenous access was obtained. Monitoring of respiratory and cardiovascular physiology was done by a multipara monitor. Baseline parameters like pulse rate, SpO2 and blood pressure were recorded. All patients were preloaded with 8 ml/kg, Ringer's Lactate, 15 minutes before the procedure and premedicated with 4 mg of intravenous Ondansetron. The oropharynx and larynx were sprayed with4% lignocaine until the swallowing reflex is blunted. Patients were randomly allocated into two groups. In Group L traditional spray-as-you-go technique with lignocaine was utilized and supplemental sedation was given in group S.

After allocation, Group L patientswere subjected tofiberoptic bronchoscopy(model BF-TE2E), 5.8 mm of Olympus)through trans-nasal route after pretreatment of the selected nostril with 2% lignocaine gel. As the bronchoscope is advanced, 4% lignocaine is administered in one or two aliquots (80-160 mg) onto the vocal cords under vision. Bronchoscopewas advanced further between the vocal cords and the tracheobronchial tree was anesthetized by 2ml aliquots of 2% lignocaine solution as and when required.The maximum safe dose of Lignocaine is considered to be 7mg/kg[9].

Group S received intravenous precalculated dose of Midazolam, 0.05mg/kg over 30 seconds followed by Fentanyl at the rate of 1 µg/kg over 30seconds. After waiting for5 minutes for attaining peak effect, bronchoscopy was performed as in the group L.

During the procedure,patients are appropriately monitored with the continuous measurement of pulse rate and oxygen saturation and intermittent assessment of blood pressure as there is a risk of bradycardia, hypotension and respiratory depression with the use of pharmacological sedatives. Monitoring was continued to the end of the procedure and until complete recovery of sedation. Only when the patient's vital signs are stable and are awake, alert and comfortable, they are considered for discharge.

A moderate level of sedation, referred to as conscious sedation, should be achieved, where the patient would be conscious and be able to respond to verbal commands. To anticipate and prevent any untoward effects, the depth of sedation was monitored throughout the procedure and documented using the "Modified Ramsay sedation score" (1 = Agitated, restless; 2 = Cooperative, tranquil; 3 = Responds to verbal commands while sleeping; 4 = Brisk response to glabellar tap or loud noise while sleeping; 5 = Sleeping patient with sluggish response to glabellar tap or loud noise, 6 = No response to glabellar tap or loud noise).A score of 3-4 is acceptable.

Pain was assessed using the "Visual Analogue Scale" advocated by Revill and Robinson in 1976. It is a linear scale, consisting of a 10 cm line ranging from 'No Pain-0' to Worst Possible Pain-10' [1].

Distressing effects like cough, nausea, choking and physical movement were objectively analysed and graded on a scale 1-5 (1- None, 2- Mild, 3- Moderate, 4 – Severe, 5- Worst).

Patient'swillingness to return for procedure were recorded and measured in a grading scale {1-Definitely not, 2-Probably not, 3- Unsure, 4- Probably would, 5- Definitely would return}.

Additionally, observer scoring wasrecorded, where the bronchoscopist marked the line to indicate the pain intensity on the VAS to assess intra procedural pain (0= no pain, 1=mild pain, 2= moderate pain,3= severe pain, 4= unbearable)**.**

Statistical analysis was done by applying Chi-square test, ANOVA test and student t-test and a "p" value was determined > 0.05 if not significant, p <0.05 if significant and p < 0.001 if highly significant.

III. RESULTS

Even though mean age was higher in Group L (51.54 ±13.72 years) compared to Group S (49.98 ± 14.32 years)it was statistically not significant, with a p value of > 0.5. Weight of the patients in group S**(**49.64+ 7.94)and that in group L(48.38+9.99) wascomparable (p value > 0.5).

The analysis of hemodynamic monitoring shows that initial part of the procedure (3 minutes) did not show any significant difference statistically. Heart rate is less in Group S at 6 mins, 9 mins,12 mins,15 mins and 18 mins than Group L with p values of 0.01, 0.018, 0.004, 0.001and 0.001 respectively (Graph 1).

Comparison of SpO2 in the two groups studied shows that SpO2 distribution is statistically not significant in Group Swith a p value of 0.5 during preoperative period and 0.051 at 3 minsafter administration of medication. SpO2 difference is significant with p values of 0.025, 0.005, 0.018, 0.011 at 6 mins, 9 mins, 12 mins, 15 mins, respectively, with patients in group S showing a higher drop in saturation than those in Group L. But patients of Group S did not need any supplemental oxygen except in one case. (Graph 2).

Although sedation level as assessed by Ramsay sedation scale is more in Group S as expected, it was maintained at acceptable level with the moderation in the doses of agents used.

Distribution of Visual analogue scale (VAS) in thetwo groups showed that Group S patients had better pain control compared to Group L, where incidence of pain felt is high and statistically significant; with p values of 0.048, 0.001, 0.001, and 0.001 at 12, 15, 18 and 21 mins respectively (Table 1).

Comparison of cough in both groups showed lesser episodes in Group S with a statistically significant p value of 0.001 (Graph 3).

Comparison of Physical movement in two groups showed decreased incidence in Group S with a statistically significant p value of 0.001 (Graph 4).

In addition, distress in Group Swas less compared to Group L, with a statistically significant difference.However, it was observed that incidence of nausea did not differ in the two groups. Willingness to return to the procedure was higher in patients in Group S(p<0.001) (Graph 5).

IV. DISCUSSION

Flexible fibreoptic bronchoscopy (FOB) is generally done on day care basis, by respiratory physicians under topical anaesthesia. FOB is the gold standard for directly visualising the airways, allowing numerous diagnostic and therapeutic interventions. Topical anaesthesia is imperative for this procedure as it is performed in awake patients. In our institution, fibreoptic bronchoscopy is performed under topical lignocaine by conventional 'spray-as-you-go' technique.

Lidocaine is the preferred topical anaesthetic for bronchoscopy, given its short half-life and wide margin of safety [9]. FOB is likely to provoke anxiety in patients as it is a relatively invasive procedure.The use of a combination of benzodiazepines and opiates is suggested because of their synergistic effects on patient tolerance during the procedure and the added antitussive properties of opioids [8]. The existing body of literature supports the safety and effectiveness of this approach when the proper agents are used in an appropriately selected patient population.

Of late, with the evolution of interventional bronchoscopy, more complex and longer procedures are being done, placing increasing importance on the use of sedation as a necessary adjunct to topical anaesthesia. Sedation is preferred to alleviate anxiety and reduce stress, impart amnesia, provide stable hemodynamic conditions, improve patient comfort and cooperation to facilitate the bronchoscopic procedure [6].

There is no standard practice for the use of sedation in bronchoscopy with a good deal of variation regarding the use of sedatives among various physicians.Various hypnotic agents such as propofol, ketamine; sympatholytics such as clonidine and labetalol, benzodiazepines such as diazepam, midazolam, lorazepam; cough suppressants such as dextromethorphan, codeine phosphate; bronchodilators like fenoterol and opioids such as alfentanil and fentanyl and different combination of these drugs were tried to improve tolerance to bronchoscopic procedure with variable success rates[10].Newer agents such as remimezolam, remifentanil, fospropofol, dexmedetomidine were also studied[10].

Properties of an ideal sedative, for use in outpatient bronchoscopy, include easy use, a rapid onset, short duration of action, easy titration, high clearance, and rapid recovery with promptreturn of cognition. Other properties like analgesia, amnesia, ability to suppress cough and reduction of chest discomfort are preferred. In addition, cardiovascular stability, and lack of respiratory depressant effects are also necessary. They should have a predictable pharmacokinetic and pharmacodynamic profile that is not altered by interactions with other drugs

and should be reversible with a predictable and specific antagonist. The agents which we selected have satisfied all the requisites of sedatives and analgesics.

Familiarity of the time course of drug effect is especially important to optimize sedation regimen. In particular, it is important to know the latency to peak effect after bolus injection to ensure that the previous doses have reached peak effect before additional doses are administered. Midazolam has a shorter onset time and half-life, but longer time to peak effectwhereas Fentanyl has a very short time to peak effect [11].

As per the consensus statement of ACCP (American College of Chest Physicians) and British thoracic guidelines, some form of sedation is almost always used during bronchoscopy to allay anxiety and improve comfort level of patients. Numerous studies demonstrate that sedation increases comfort and patient willingness to undergo future procedures [6]. Hence the present study was taken up to evaluate any additional advantages attained by supplementing sedation with Midazolam and Fentanyl thereby minimizing the requirement of Lignocaine, and improving the tolerance of the patient to the procedure[5].

Randomisedstudies comparing benzodiazepines alone to opioids alone, the former agents demonstrated better amnesia, less discomfort in nose and throat, and lower risk of respiratory depression, but more cough and more drowsiness. But studies using combination of benzodiazepines and opiates have reported better comfort and tolerance and improved cough control over benzodiazepines alone. The bronchoscopist were more comfortable with supplemental sedation and the duration of procedure was also short. The lack of major complications and better outcome suggested the use of sedation with midazolam as routine during FOB[11].In a prospective evaluation of patients undergoing FOB for immediate minor and major complications, proceduralist-administered sedation within their institution's guidelines were reported to be safe [12].

In the current study, all patients received intravenous precalculated dose of Midazolam, 0.05mg/kg followed by Fentanyl, 1 µg/kg over 30 seconds each. Bronchoscopist is asked to proceed with the FOB after 5 minutes. The control of coughing plays a leading role in the quality of bronchoscopy as this enables better field of vision, and ability to obtain adequate biopsy samples. In addition to Lignocaine spray, opiates play a paramount role in controlling cough during bronchoscopy [12]. This is due to the antitussive properties of Fentanyl as supported by many studies [8].

In our study, we used 'spray-as-you-go' technique for administration of Lignocaine to the airways. Recently, investigators from India suggested that 1% Lignocaine is as effective as 2% solutionand hence exposing the patient to lesser cumulative dose oflignocaine[13]. In our study, we have used 2% Lignocaine solution – nonetheless, the total dose of lignocaine used was within the standard prescribed limits. Sedation enabled further reduction in the dose of lignocaine used.

In a publishedstudy, it was stated that, use of a combination of benzodiazepines and opiates is preferable because of their synergistic effects on patient tolerance during the procedure and the added antitussive properties of opioids [8].

It was concluded in a double blind, placebo-controlled study, conscious sedation with Fentanyl and Midazolam combination can result in better patient and operator satisfaction when compared with Midazolam alone [14].

The haemodynamic parameters showed reduced cardiac frequency and better control of blood pressure in sedation group compared to Group L during 6-18minute observation period after initiating the procedure. There was a drop-in oxygen saturation during bronchoscopy, but needed no intervention as oxygen was supplemented throughout the procedure. Comparison of Ramsay Sedation Score in both the groups showed that it was higher in Group S, but the patients were sedated to the level where they responded to verbal commands.

Discomfort due to choking was significantly less in Group S patients. Cough suppression was very effective in sedation group. Physical movement and distress were also noticed to be less. Finally, willingness to return to the procedure was higher in patients who received pharmacological sedation.

There are many studies which support the fact that patient comfort is enhanced due to sedation, and the risks involved are small and manageable. During our study, a single event of significant oxygen desaturation occurred in Fentanyl-Midazolam group. This episode was managed without any serious consequences. This is in accordance with Japanese study [5].

The limitations in our study were; small sample size, we have not included placebo group in our study.Wedid not compare other available sedative and analgesic agents which were studied in conducting bronchoscopy.

V. CONCLUSIONS

Pharmacological sedatives and analgesics, Midazolam and Fentanyl improve procedural tolerance and patient satisfaction in diagnostic flexible bronchoscopy. There was an overall decrease in cough, distress, nausea and choking in sedoanalgesia group compared to topical Lignocaine group. Sedoanalgesia group were more willing to return to repeat procedure. The time taken for the procedure was also considerably less in

sedoanalgesia group, as the patients are more cooperative under conscious sedation enabling the bronchoscopist to work through.

With the doses of Midazolam and Fentanyl used in our study, side effects seldom occurred. Hence, with the help of supportive staff to monitor the patient, bronchoscopistcan conduct bronchoscopy under sedoanalgesia. Teaching institutes can take advantage of sedoanalgesia technique to train their postgraduates as the patients can tolerate the procedure for an extended period. Physicians with less experience can learn the procedure without causing discomfort to the patient and gain desirable expertise with pharmacological supplementation.

To conclude Fentanyl and Midazolam along with topical Lignocaine spray is superior compared to the Lignocaine spray alone for flexible bronchoscopy. It was suggested that, all physicians performing bronchoscopy should consider using sedoanalgesia, whenever feasible in selected patient population.

REFERENCES

[1]. Chandra A, Banavaliker JN, Agarwal MK. Fibreoptic bronchoscopy without sedation: Is transcricoid injection better than the "spray as you go" technique? Indian J Anaesth. 2011;55(5):483–487. doi:10.4103/0019-5049.89877Int J Tuberc Lung Dis. 2015 Mar;19(3):356-61. doi: 10.5588/ijtld.14.0632.

[2]. Madan K, Mohan A, Agarwal R, Hadda V, Khilnani GC, Guleria R. A survey of flexible bronchoscopy practices in India: The Indian bronchoscopy survey (2017). Lung India. 2018;35(2):98–107. doi:10.4103/ Lung india_417_17.

[3]. British Thoracic Society Guidelines on diagnostic flexible bronchoscopy. Thorax 2001; 56 (Suppl. 1): i1-2l.

[4]. González Aguirre JE[1], Chavarría Martínez U[1], Rodríguez Mier D[1], Acosta Moreno M[1], Mercado Longoria R[1]·Bronchoscope insertion route and patient comfort during flexible bronchoscopy.

[5]. Daisuke Minami et al,in 2016 in their prospective study in 37 patients to evaluate sedation with fentanyl and midazolam during bronchoscopy concluded that it should be recommended for use in Japan.

[6]. Rolo R etal. in 2012 in their prospective study in 100 patients undergoing FOB with Midazolam(0.05mg/kg) concluded that sedation with midazolam in FOB improved patients comfort and decreased complaints without significant hemodynamic changes. It should be offered to the patient on a routine basis.

[7]. Ricardo J Jose et al., in 2013 in their randomized single blind, prospective controlled study of 59 patients undergoing flexible bronchoscopy concluded that midazolam in combination with a short acting opioid (fentanyl or alfentanil) remain the pharmacological-administered sedation in bronchoscopy.

[8]. Wahidi MM et al., in 2011 study shows the use of a combination of benzodiazepines and opiates is suggested because of their synergistic effects on patient tolerance during the procedure and the added antitussive properties of opioids.

[9]. Momen M. Wahidi , MD, MBA, FCCP WahidiMM,JainP,Jantz M, et al.American College of Chest Physicians consensus statement on the use of topical anesthesia, analgesia, and sedation during flexible bronchoscopy in adult patients. Chest.2011;140:1342–50.

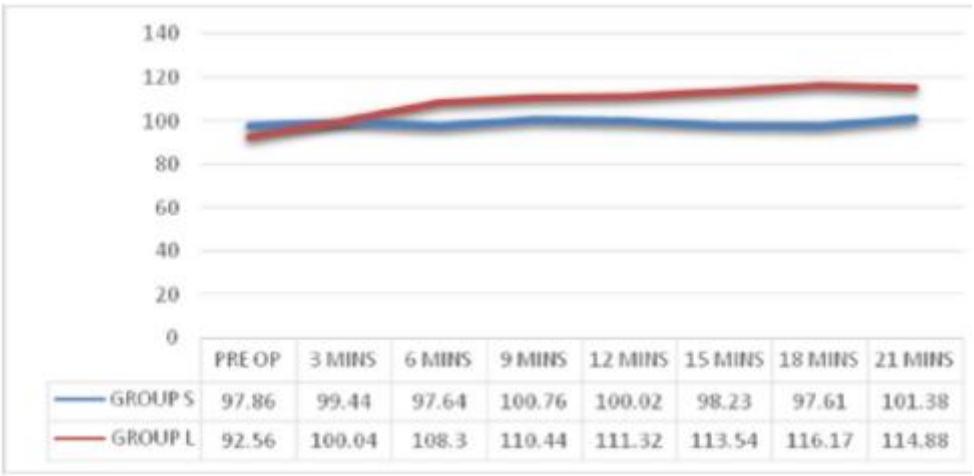
[10]. Sedation for flexible bronchoscopy: current and emerging evidence Ricardo J. José, Shahzad Shaefi, Neal Navani, European Respiratory Review 2013 22: 106-116; **DOI:** 10.1183/09059180.00006412.

[11]. Putinati S et al., cited in 'update on bronchoscopy in 2007', concluded that conscious sedation for bronchoscopy definitely had a beneficial effect on patient tolerance and rarely induced significant alterations in cardiorespiratory monitoring parameters.

[12]. Dang D et al., in 2012 in their prospective evaluation in patients undergoing FB for immediate minor and major complications, concluded that there were no complications from proceduralist-administered sedation. Flexible fibreoptic bronchoscopy and proceduralist-administered sedation within their institution's guidelines are safe.

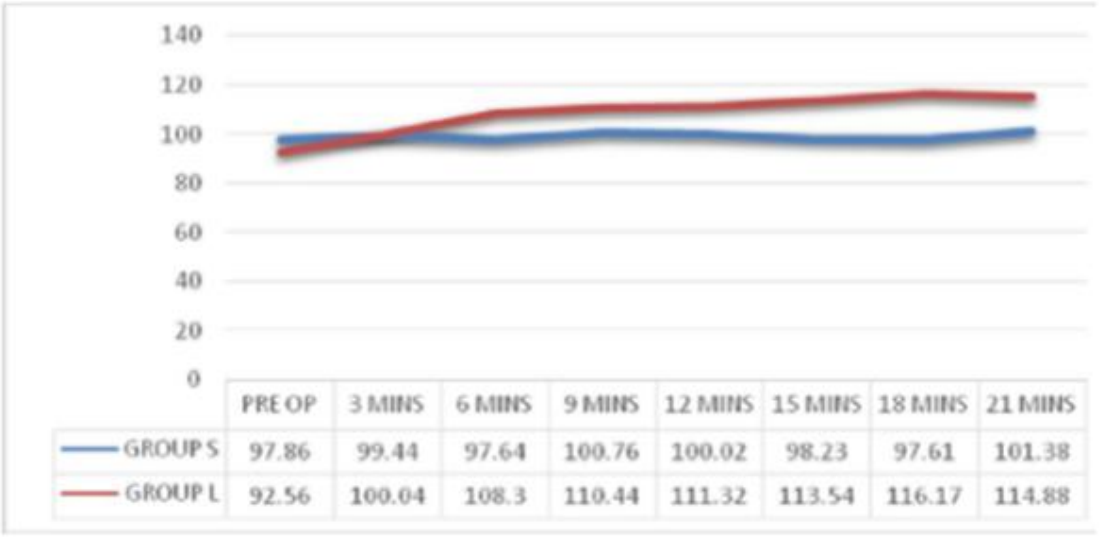
[13]. 1% versus 2% lignocaine for airway anesthesia in endobronchial ultrasound-guided transbronchial needle aspiration: A pilot, double-blind, randomized controlled trial
Biswal Shiba Kalyan, Mittal Saurabh, Hadda Vijay, Mohan Anant, Khilnani Gopi C, Pandey Ravindra M, GuleriaRandeep, Madan Karan,Year: 2018 | Volume: 35 | Issue Number: 6 | Page: 467-471.

[14]. Prabhudev AM et al., in 2017 in their double –blind, placebo controlled study of 144 patients undergoing flexible bronchoscopy received either midazolam or fentanyl-midazolam i.v . They concluded that conscious sedation with fentanyl and midazolam combination can result in better patient and operator satisfaction when compared with midazolam alone.



	PRE OP	3 MINS	6 MINS	9 MINS	12 MINS	15 MINS	18 MINS	21 MINS
GROUP S	97.86	99.44	97.64	100.76	100.02	98.23	97.61	101.38
GROUP L	92.56	100.04	108.3	110.44	111.32	113.54	116.17	114.88

Graph 1- Comparison of heart rate between sedation group (Group S) and lignocaine spray group (Group L)



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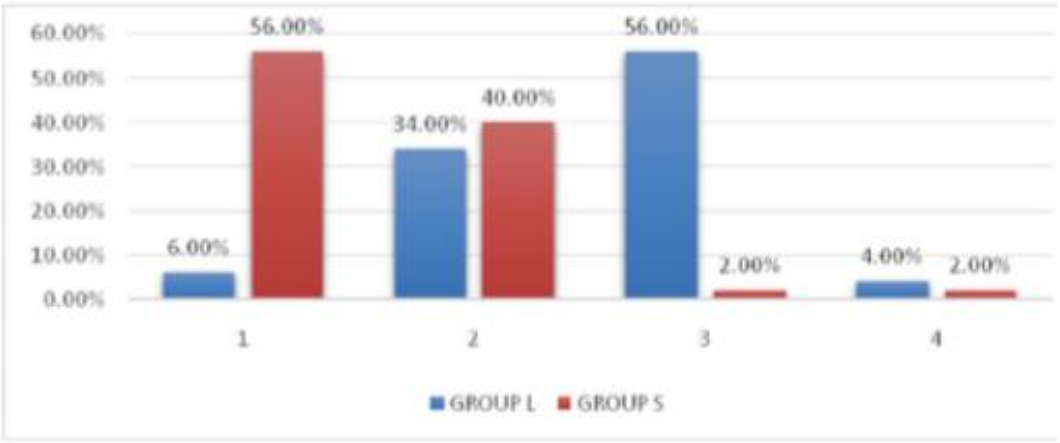
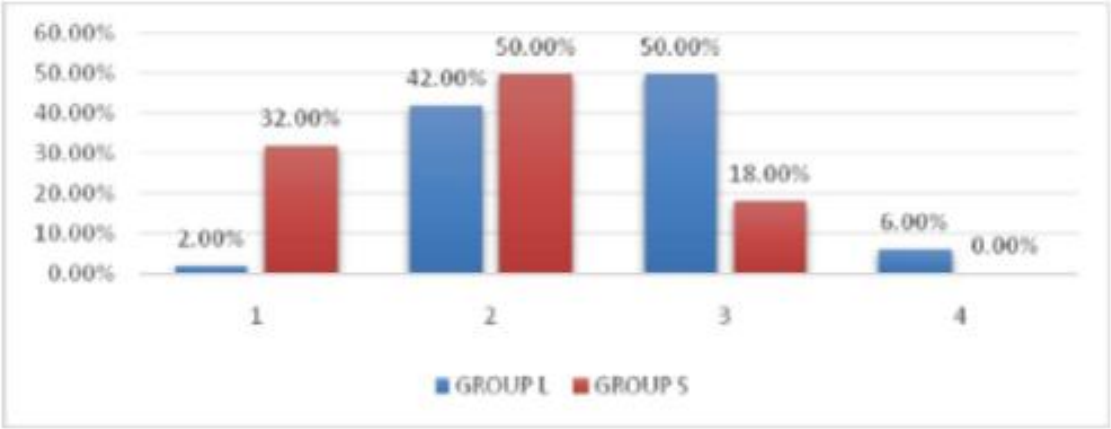
GROUP L	92.56	100.04	108.3	110.44	111.32	113.54	116.17	114.88

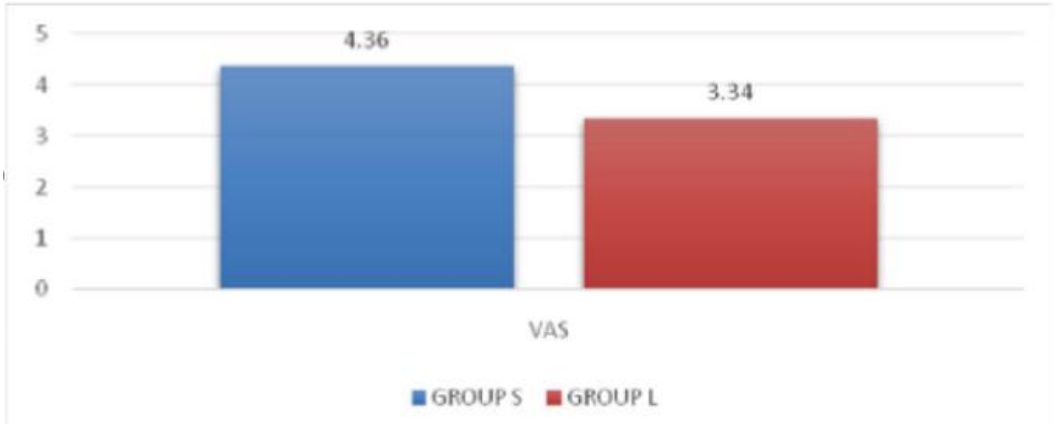
Graph 2: Comparison of Spo2 between sedation group (Group S) and lignocaine spray group(Group L).



Graph 3- Comparison of episodes of cough between sedation group (Group S) and lignocaine spray group (Group L).



Graph 4: - Comparison of physical movements between sedation group (group S) and lignocaine spray group (group L).



Graph 5: Comparison of willingness for repeat procedure

TIME	GROUP S MEAN + SD	GROUP L MEAN + SD	T TEST	P VALUE
3 MINS	1.60 + 0.60	1.40 + 0.49	1.807	0.07 (NS)
6 MINS	2.00 + 0.63	1.72 + 0.53	2.374	0.02 (S)
9 MINS	2.48 + 0.81	2.34 + 0.89	0.818	0.415 (NS)
12 MINS	2.92 + 0.63	3.24 + 0.93	1.999	0.048 (S)
15 MINS	2.97 + 0.78	3.57 + 0.81	3.615	0.001 (S)
18 MINS	2.87 + 0.73	3.67 + 0.82	4.562	0.001 (S)
21 MINS	2.90 + 0.75	3.76 + 0.95	3.432	0.001 (S)

Table 1: Distribution of vas in thetwo groups. Group S had better pain control compared group L

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