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Original Article

Comparative evaluation of effects of intrapleural block with adjuvants on analgesia and pulmonary function after intercostal drainage: A pilot study

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ABSTRACT

Background: Inter-costal chest drain (ICD) used for varied thoracic pathologies causes continuous pain and irritation of the pleura, which limits respiratory efforts and impairs ventilatory function. Intrapleural block deposits local anaesthetic between the layers of pleura and may improve ventilatory function especially in non surgical patients.

Methods: Twenty eight ASA I-III patients treated with ICD, who could perform incentive spirometry, were included for study. They were randomized to 'Group C' (control group); 'Group B' (Bupivacaine); 'Group M' (Bupivacaine + Morphine) and 'Group D' (Bupivacaine + Dexmedetomidine). The drugs were administered via the ICD itself and clamped thereafter for 15 min. The success of the block was assessed by time for first analgesic demand, maximum inspiratory volume generated and Numerical Rating Scale score for pain; by patients.

Results: Effective analgesia was observed in Group B, M and D. Addition of an adjuvant significantly prolonged time for rescue analgesic demand. Patients who received local anaesthetic alone or with an adjuvant had significantly improved maximal inspiratory volume and required lesser rescue analgesics. No significant complications were observed in any group. Pain relief in post-surgical patients using intrapleural block is masked by systemic analgesics. However its application in patients with ICD for non surgical indications was explored in this study and was found to improve patient comfort and ventilation.

Conclusion: Intra-pleural blockade is safe and effective in relieving the constant pleural irritation and pain of ICD, thus enabling the patient to improve ventilatory effort and faster recovery of respiratory function.

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Introduction

Placement of an inter-costal drain (ICD) is indicated in several situations where fluid or air collects in the pleural space. The presence of ICD tube renders each breath painful thus leading the patient to breathe at a shallow and rapid rate. The pain is further aggravated by movement and becomes pronounced when patients are transferred between facilities. For the armed forces this is especially relevant when patients are evacuated by road to higher echelons sometimes taking hours or even days. Usual method employed to reduce this pain is the use of a systemic analgesic such as NSAIDs. Intra-pleural block¹ is a novel analgesic technique of introducing local anaesthetic (LA) into the pleural space to produce ipsilateral somatic block of multiple thoracic dermatomes. Studies suggest that pain relief is due to bilateral spread of LA which blocks both the sympathetic chains and the splanchnic nerves.² Intra-pleural block has been effectively employed in the past for post-surgical pain originating unilaterally from the chest or upper abdomen,^{3–5} which can be administered as single shot or intermittent boluses, or continuous infusions via an indwelling catheter in the pleural space.^{6,7} Use of an adjuvant along with the LA has the potential to prolong the analgesia.

In this study the hypothesis was that intra-pleural block may help relieve pain and irritation in non-surgical patients with indwelling ICD and thus improve ventilatory function. Few studies using intra-pleural analgesia and only one study using an adjuvant (fentanyl) along with LA⁸ for the block have been found in literature. In the current study the effect of intra-pleural block using LA alone or with adjuvants was compared with a control group in which analgesia was given strictly as per the institutional protocol. An additional issue is the quantification of pain relief following instillation of LA. We hypothesized that other than subjective reporting by the patient, assessment of improvement in pulmonary function can be a good surrogate of evaluating analgesia. Spirometry and forced expiratory manoeuvres are contraindicated in most pathologies where an ICD is indicated (pneumothorax, haemothorax etc.),⁹ hence in the study protocol pulmonary functions was assessed by volumetric incentive spirometry, which is a common prescription among respiratory patients.

Materials and methods

The study was approved by the institutional ethical committee, registered with CTRI (Registration No 2016/04/011150AU) and carried out in a tertiary care cardio-thoracic hospital over one year – in consultation with a respiratory physician. The study design was a single blinded pilot randomized controlled trial involving 28 patients. The inclusion criteria consisted of patients aged 18–60 years in ASA physical status I–III with an ICD in situ (introduced within 48 h prior to the study), who consented to perform incentive spirometry as per the study protocol. Patients with cardiovascular co-morbidities, disturbances in the coagulation profile, having a history of allergy to the local anaesthetic (LA) agents or those unable or unwilling to perform the desired incentive spirometry were excluded

from the study. The project was a pilot study with no references available for calculation of the sample size. Hence the sample size was arbitrarily taken as the number of patients who participated in the study over a period of one year, which were 28. The procedure was explained, written and informed consent was obtained from the patients.

Block randomization was used to allocate patients into one of the four groups (Group B, Group M, Group D and Group C) using computer generated random allocation sequence (<https://www.sealedenvelope.com/simple-randomiser/v1/lists>). Sequentially numbered, opaque sealed envelopes were used for allocation concealment. The patients in all the groups received the drug solution via the ICD itself. Group B received 2 mg/kg of 0.25% Bupivacaine only, Group M received 2 mg/kg of 0.25% Bupivacaine with 50 µg/kg Morphine and Group D received 2 mg/kg of 0.25% Bupivacaine with 0.5 µg/kg Dexmedetomidine. Group C which served as the control group received 0.8 ml/kg of Normal Saline for the purpose of blinding. The total volume of the drug/combination in all the groups was 40–50 ml. The patients were made to sit upright and the drug solution was introduced into the pleural space via the ICD in several aliquots of 8–10 ml each. After each aliquot the patient was asked to take a deep inspiration till the entire aliquot of the drug in the ICD was drawn into the pleural space, (thereafter the ICD was clamped immediately). Throughout the procedure attempt was made to maintain an airtight seal with no leakage of air into the pleural space. The ICD was then clamped for 15 min after the complete drug administration. The patient was asked to lie supine immediately to allow spread of the drug. The observer was blinded to the drug(s) being administered.

The primary outcome recorded was the time for first analgesic demand which was defined as the time from the administration of the block to the first request for pain relief by the patient. Inj. PCM 1000 mg IV was administered on demand as the rescue analgesic in accordance with the institutional protocol. V_{miv} and the NRS were the secondary outcomes measured at 30 min, 1 h, 3 h, 6 h and 9 h, 12 h, 15 h and 18 h after the block. A volumetric incentive spirometer manufactured by Hudson RCI, graduated from 0 to 2500 ml was used in the study and the maximal inspired volume generated (V_{miv}) was recorded. The process was demonstrated and patients were instructed in the use of the incentive spirometer prior to performance of the block. The patients were allowed to practice the manoeuvre till he/she was comfortable with it. 15 min after performing the block the test was carried out with the patient sitting erect at 90° to the horizontal position with head in neutral position. The patient was asked to put the mouthpiece in his/her mouth with lips tightly closed around it. The patient was instructed first to exhale normally and then inhale slowly and deeply through the mouthpiece to try to raise the indicator up as high as possible without pain or discomfort and thereafter hold the breath for at least three seconds and then exhale slowly and passively while avoiding any forceful expiration. The maximum volume achieved was noted. The patient was asked to perform the test three times and the best of the three readings was taken. Pain was assessed using the numeric rating scale (NRS) from 1 to 10, with 1 being no pain and 10 as the worst pain imaginable at the same time intervals as for recording of the V_{miv} .

Statistical analysis

All the data were analyzed using SPSS v 21.0. The V_{miv} and time to first analgesic request was calculated as mean $\pm$ standard deviation. Repeated measures ANOVA was done after testing for normality to detect whether there was a significant difference in the V_{miv} values over time in the different groups. Normality was tested using the Shapiro-Wilk test of normality and the sphericity assumption for the variances to be equal or homogeneity was tested using Mauchly's test of sphericity using SPSS Statistics. However due to small sample size the

assumptions were not met. The time to first analgesic request was assessed using Kruskal-Wallis test. The NRS was expressed in the form of median with range and analyzed using Friedman's test (data being non continuous in nature). A p value of less than 0.05 was considered to be statistically significant.

Results

Twenty eight patients were studied in four groups as depicted in the consort flow diagram in Fig. 1. All the four groups were

Fig. 1 – Consort diagram.

Table 1 – Demography of study population.

Demography study population			
Demographic parameter→ Study groups↓	Age (yrs) Mean ± SD	Weight (kgs) Mean ± SD	Sex distribution
Group C	50.43 ± 9.99	54.86 ± 3.35	5M/2F
Group B	48.29 ± 16.97	55.29 ± 3.35	4M/3F
Group M	43.14 ± 14.69	53.42 ± 7.29	6M/1F
Group D	49.14 ± 10.76	55.14 ± 5.01	3M/4F
p Value	0.88704 ^a	0.75321 ^a	0.562 ^b

^a Kruskal-Wallis test.
^b Freeman-Halton extension of the Fisher exact probability test.

Table 2 – First analgesic demand.

Groups	Descriptive				
	n	Mean	Std Dev	95% confidence intervals for mean	
				Lower bound	Upper bound
Group C	7	1.43	0.535	0.93	1.92
Group B	7	6.14	1.345	4.90	7.39
Group M	7	15.57	4.504	11.41	19.74
Group D	7	17.43	4.077	13.66	21.20
Total	28	10.14	7.342	7.30	12.99

comparable with respect to the demographic parameters as well as the pre-procedure recording of V_{miv} and NRS as depicted in Table 1.

To detect whether there was a significant difference between the times to first analgesic among the groups Kruskal–Wallis test was applied (as heterogeneity assumption was not met). The data for first analgesic demand has been represented in Table 2 and depicted as a box and whisker plot in Fig. 2. The analysis showed that there was a significant difference in the time to first analgesic requirement across the groups with $p = 0.001$.

The inter-group post hoc analysis (Table 3) revealed that the Groups (C vs. M) with $p = 0.001$, (C vs. D) with $p < 0.001$ and (B vs. D) with $p = 0.045$ were significantly different. Clinically

Group D had maximum time to analgesic requirement with mean time of 17.43 h followed by Group M with mean time of 15.57 h, Group B with mean time of 6.14 h, whereas Group C had a mean time of only 1.43 h.

NRS record at the selected time intervals is shown in Table 4 as median (range) and depicted in Fig. 3. The NRS scores for the D Group were the lowest at 1 (no pain) for the longest duration. Highly significant difference (Table 2) was noted in measurements (except between Group M vs. D) at all times after the block till block regression (15–18 h).

The maximal inspiratory volume (V_{miv}) recorded has also been shown as mean ± SD in Table 4 and depicted in Fig. 4. The pre-procedure V_{miv} among all the groups showed no significant difference. Repeated measures ANOVA showed a significant difference ($p = 0.001$) w.r.t. V_{miv} among the groups of interventions over time. The inter group analysis (Table 2) showed that Group C was significantly different from Groups M and D. Though there was no statistically significant difference between Group C and B, clinically the difference among the V_{miv} values was evident for up to 6 h as seen in Table 4 (V_{miv} increased by 80–120% during this period). However there was no clinical or statistically significant difference among Groups B, M and D.

Discussion

Analgesia for indwelling ICD has been largely neglected especially in non-surgical patients. In surgical patients on the other hand, pain of the ICD is usually masked by analgesics for the surgical site. The use of multiple intercostal nerve blocks for these cases may result in over dosage and is prone to technical lapses. The requirement of analgesia is even higher for patients requiring transportation over long distances, and often any compromised ventilatory function due to pain goes unnoticed.

The focus of this study was on analgesia for indwelling ICD in non-surgical patients instead of post-operative analgesia studied previously.^{3–5} The working hypothesis was that the use of an adjuvant along with LA for intra-pleural block in such patients would provide superior and prolonged analgesia. This hypothesis was verified by the study and patients who received Dexmedetomidine or Morphine along with LA had the lowest pain scores for the longest duration (12–15 h), which also reduced the total dose of rescue analgesic demanded significantly. Literature has not revealed any study using Dexmedetomidine for this block. However a study comparing

Fig. 2 – First analgesic demand (h).

Table 3 – Inter-group comparisons of outcomes (^bsignificant if $p < 0.05$).

Inter-group comparison	p value of 1st analgesic demand ^a	p value of V_{miv} ^b	p value of NRS ^c
Group C vs. Group B	0.662	0.198	0.001
Group C vs. Group M	0.001	0.015	<0.001
Group C vs. Group D	<0.001	0.013	<0.001
Group B vs. Group M	0.205	1.000	0.018
Group B vs. Group D	0.045	0.177	<0.001
Group M vs. Group D	1.000	1.000	0.177

^a Kruskal Wallis test.^b Repeated measures ANOVA.^c Freidman's test.**Table 4 – Numerical rating scores (NRS) and maximum inspiratory volume (V_{miv}) data.**

Numerical Rating Scale scores (NRS)				
Groups→	Group C	Group B	Group M	Group D
NRS median (range)↓				
Pre-block	9 (8–10)	9 (7–9)	9 (8–10)	10 (6–10)
At 30 min after block	7 (6–9)	2 (2–3)	1 (1–2)	1 (1)
At 1 h after block	8 (7–9)	2 (2–3)	1 (1–2)	1 (1)
At 3 h after block	9 (8–9)	3 (2–3)	2 (1–3)	1 (1)
At 6 h after block	8 (8–9)	5 (3–6)	2 (1–3)	1 (1)
At 9 h after block	8 (8–9)	6 (5–7)	2 (2–3)	1 (1)
At 12 h after block	8 (8–9)	8 (8–9)	2 (2–6)	1 (1–5)
At 15 h after block	8 (8–9)	8 (8–9)	5 (2–8)	1 (1–5)
At 18 h after block	8 (8–9)	8 (8–9)	8 (2–9)	3 (1–8)
Maximum inspiratory volume generated (V_{miv})				
Mean V_{miv} values (ml)	Group C	Group B	Group M	Group D
Pre-block	442.9 ± 67.3	400.0 ± 70.7	421.4 ± 63.6	385.7 ± 55.6
At 30 min after block	464.3 ± 80.2	871.4 ± 321.3	900.0 ± 173.2	864.3 ± 55.6
At 1 h after block	442.9 ± 45.0	900.0 ± 262.9	876.6 ± 168.0	950.0 ± 165.8
At 3 h after block	442.9 ± 45.0	885.7 ± 307.8	921.4 ± 207.9	957.1 ± 151.2
At 6 h after block	442.9 ± 45.0	742.9 ± 316.8	900.0 ± 208.2	921.4 ± 172.8
At 9 h after block	428.6 ± 56.7	571.4 ± 215.7	900.0 ± 208.2	914.3 ± 186.4
At 12 h after block	428.6 ± 56.7	407.1 ± 67.30	771.4 ± 294.2	842.9 ± 270.0
At 15 h after block	435.7 ± 55.6	400.0 ± 70.70	685.7 ± 309.2	792.9 ± 289.3
At 18 h after block	428.6 ± 56.7	392.9 ± 60.70	535.7 ± 226.8	650.0 ± 321.4

Fig. 3 – Inter-group comparisons of NRS. **Fig. 4 – Inter-group comparisons of V_{miv} .**

Morphine vs. Bupivacaine for intra-pleural analgesia in post-thoracotomy patients concluded a better result using Bupivacaine rather than Morphine; however a combination of the two drugs was not used in this study.¹⁰ A combination of LA with fentanyl in post-CABG patients was found to improve pain relief.⁸ We also found our results at variance with the article by Ho et al.⁴ who termed temporary clamping of the ICD as an “imperfect solution”. In our study using LA + adjuvant, the temporary clamping resulted in effective analgesia for 15–18 h.

In this study instead of concentrating on the volume and concentration of the drug (as in previous studies),¹¹ the emphasis was on keeping the total LA dose within the toxic limits. However since the block itself appears to be a volume dependant block,¹² an adjuvant was added to offset the compromise on the concentration. The flow of LA from the pleural surface to the intercostal nerves is restricted by absorption of drug by the visceral pleura. Also since the speed and amount of LA absorption is unpredictable after pleural injury, disease or inflammation, caution needs to be exercised during dose calculation.¹ The perceived danger of such a technique is the possibility of Local Anaesthetic Systemic Toxicity (despite studies to the contrary)¹³ which has precluded intra-pleural block as a favoured technique.

Literature has described two techniques 'Negative Pressure' technique and 'Loss of Resistance' technique^{14,15} for intra-pleural block though both carry a risk of lung parenchymal injection.⁴ This study however used the indwelling ICD itself for instillation of the drug solution or Normal Saline which was a readily available access to the pleural space. Adequate care during the process of introduction of the drug (as mentioned in the methodology) ensured that ingress of air was avoided and pneumothorax if any is likely to be small and inconsequential.⁴

A volumetric incentive spirometer was used in this study for assessment of respiratory function. Incentive spirometry, also referred to as sustained maximal inspiration (SMI)^{16,17} is a manoeuvre prescribed to improve lung expansion in patients. The volumetric incentive spirometer provides a visual feedback of the inspiratory effort and dual-sided calibrations identify volume achieved up to 4000 ml. Literature review has not revealed this technique as a means of pulmonary function assessment in any study so far. Post intra-pleural block recordings show a significant improvement in maximal inspired volume (V_{miv}) from the control group ranging from 80 to 120% during maximal block effectiveness (1–6 h). However the improvement was significantly prolonged (12–15 h) if an adjuvant was used along with the LA.

Although the precise mechanism of action of intra-pleural analgesia is not clear, it has been suggested that LA solution diffuses out of the pleural cavity, blocking multiple intercostal nerves, the sympathetic chain of the upper extremity, brachial plexus, splanchnic nerves, phrenic nerves, coeliac plexus and ganglia producing effective analgesia both above and below the diaphragm.¹⁸ Stomata (2–12 μ m diameter) present between the mesothelial cells of the parietal pleura¹⁹ are the most likely channel of fluid transport. Cadaveric studies demonstrated spread of India ink through the parietal pleura into the sub-pleural space and then backwards to multiple intercostal nerves.^{19–21} Computerized tomographic studies using contrast media in the intra-pleural injectate demonstrated fluid spread

in a gravity-dependent manner.²² Most of the fluid collected in the most dependant part of the pleural cavity but no drug collected in the epidural or paravertebral spaces. They concluded that spread of the drug varies with body position. In the supine position it was from the T₃ to L₁ in a cranio-caudal direction and T₅ to L₁ in lateral position. This formed the basis of inclusion of positioning in the methodology of our study.

This study has a limitation of small sample size and reliance on volumetric observation. Further studies using larger sample size with a digital spirometer measurement could give a more accurate analysis.

Conclusion

Intra-pleural block is a safe and effective technique for analgesia and improves maximal generated tidal volume by 80–120% in patients with ICD. Though the block is effective with LA alone addition of an adjuvant such as Morphine or Dexmedetomidine further enhances the quality of pain relief and prolongs the duration of analgesia.

Conflicts of interest

The authors have none to declare.

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