Original Article

Can saline injection protect phrenic nerve? – A randomised controlled study

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ABSTRACT

Background and Aims: Various methods were attempted to reduce the incidence of phrenic nerve palsy during interscalene brachial plexus nerve block. Mechanism of phrenic palsy was presumed to be due to the spread of local anaesthetic anterior to the anterior scalene muscle. We hypothesised that by injecting saline in this anatomical location prior to performing an interscalene block might reduce the incidence of phrenic palsy. **Methods:** This was a double-blinded randomised controlled study performed in a single-centre, university-teaching hospital. A total of 36 patients were randomised to either group C (conventional group) or group S (saline group). Ultrasound-guided interscalene block was administered with 20 ml of 0.25% levo-bupivacaine in both groups. Ten ml of normal saline was injected anterior to anterior scalene muscle in group S prior to performing interscalene block. A blinded radiologist performed diaphragmatic ultrasound pre- and post-operatively to document phrenic palsy. Bedside spirometry was used to perform baseline and post-operative pulmonary function test. The primary outcome was to look at the incidence of phrenic palsy as measured by diaphragmatic palsy on ultrasound performed by radiologist. Statistical Package for the Social Sciences (SPSS) version 25 was used for statistical analysis. **Results:** Significantly less patients in the saline group developed diaphragmatic paresis when compared to conventional group (44% vs. 94%, Chi-squared = 10.01, $P = 0.002$). There was no difference in post-operative pain, subjective sensation of dyspnoea or patient satisfaction between the groups. **Conclusion:** Injecting saline anterior to anterior scalene muscle reduces the incidence of diaphragmatic palsy when performing interscalene block.

Key words: Diaphragmatic palsy, interscalene block, regional anaesthesia

INTRODUCTION

Hemi-diaphragmatic palsy is one of the most common undesirable effects of interscalene block. Incidence as high as 100% has been reported.[1,2] The effect on pulmonary mechanics, although tolerated by most of the healthy individuals, can lead to significant morbidity in patients with compromised respiratory function.[3,4]

Various methods have been proposed to reduce the incidence of phrenic nerve palsy from reduction in dose to extra fascicular injection.[5,6] These techniques either delay the onset of block, limit the duration of analgesia or provide insufficient surgical analgesia.

Mechanism of phrenic palsy is presumed to be due to the spread of local anaesthetic anterior to the anterior scalene muscle as opposed to a more central spread.[7] We hypothesised that by injecting saline in this anatomical location prior to performing an interscalene block might reduce the incidence of phrenic palsy.

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METHODS

Ethical approval for the study was provided by the Research Ethics Committee of the hospital on 21 December 2016. The study was registered with Clinicaltrials.gov registry (NCT02893228). The study was conducted between January 2017 and December 2017.

The study was conducted in a university-teaching hospital. American Society of Anesthesiologists (ASA) I–III patients between 18 and 80 years of age undergoing surgery in shoulder, humerus or clavicle were eligible for inclusion in the study. Exclusion criteria included patient refusal, allergy to local anaesthetic, severe coagulopathy, contralateral phrenic palsy, local infection, ASA grade IV and above and moderate-to-severe pulmonary dysfunction (GOLD stages II, III or IV).

Patients were randomised to either group S (saline group) or group C (conventional group) by computer-generated random numbers and allocation enclosed in a sealed envelope. Randomisation was done prior to recruiting the first patient. Anaesthesiologist performing and/or supervising the block were the only personnel who were aware of the randomisation. Patients were blinded to the study group. Intraoperative management of the case was done by an anaesthesiologist blinded to the study group. Outcome measurements were recorded by study observers blinded to the group allocation. All patients underwent nurse-led preoperative assessment in clinic and routine preoperative instructions including fasting were provided.

Following written informed consent, the patient had routine monitors attached which included electrocardiography, pulse oximeter and non-invasive blood pressure. Intravenous access was secured, and patients were placed in 45° head-up position for the block with head turned to the non-operative side. Intravenous sedation with midazolam (2 mg) and fentanyl (50–100 μg) and supplemental oxygen was administered to all patients prior to the block. The ultrasound machine was positioned on the side opposite to the block. Skin was prepped with 2% chlorhexidine (Chloraprep) following which the block was performed under strict aseptic precautions with the anaesthetist wearing a mask and sterile gloves. The high-frequency linear probe (sonosite) was aligned transversely across the neck at the interscalene level to identify C5 and C6 nerve roots. 2% lidocaine was used for skin infiltration and 'stop before block' performed prior to insertion of block needle. In-plane posterior approach was used with a 50-mm short bevel block needle (Braun) advanced through middle scalene muscle. Following this, the technique differed between the two groups.

In group C, the needle tip was positioned between C5 and C6 nerve roots. At this location, 20 ml of 0.25% levobupivacaine was injected in 5 ml increments with intermittent aspiration. The needle tip was not repositioned unless the patient complained of paraesthesia.

In group S, at the same level chosen for interscalene block, needle tip was positioned anterior to anterior scalene muscle. At this location, 10 ml 0.9% saline was injected. This was then followed by repositioning of needle between roots of C5 and C6 where 20 ml of 0.25% levobupivacaine was injected in 5 ml increments with intermittent aspiration. The needle tip was not repositioned unless the patient complained of paraesthesia.

Following performance of the block, all patients received general anaesthesia. Anaesthesia was induced with 2–3 mg/kg of propofol, followed by rocuronium 0.6 mg/kg for muscle relaxation. Anaesthesia was maintained with inhaled sevoflurane (MAC 1 end-tidal concentration) along with air and oxygen mixture to deliver an inspired oxygen concentration of 40%. Antibiotics were given as per hospital protocol prior to incision. In the absence of contraindications, all patients received intravenous paracetamol 1 g and parecoxib 40 mg as a part of multimodal analgesia regimen. All patients also received intravenous dexamethasone 8 mg and ondansetron 4 mg for post-operative nausea and vomiting prophylaxis. Further doses of fentanyl in 25 μg increments were administered by the anaesthesiologist if the heart rate increased by more than 15% of baseline values obtained prior to induction. Patients were reversed by sugammadex. If at least two twitches were present during train of four (TOF) measurement, 2 mg/kg dose was administered. If less than two twitches were present, 4 mg/kg dose was administered.

Following transfer to recovery unit, if patient-reported pain score by numerical rating score was >3, morphine 2 mg increments were given intravenously by the recovery staff. This was repeated every 5 min till the pain score was <4. In patients needing more than 10 mg of morphine in the recovery, anaesthesiologist

was requested to review the patient. Post-operatively, in the absence of contraindications, all patients were prescribed regular paracetamol 1 g, 6 hourly and celecoxib 200 mg, 12 hourly. For breakthrough pain, oxycodone 10 mg as needed once every 4 h was prescribed. Anti-emetics (ondansetron 4 mg, 8 hourly and cyclizine 50 mg, 8 hourly) were prescribed for all patients to be administered as required. Patients were also asked about the presence or absence of subjective feeling of dyspnoea and report satisfaction of overall anaesthetic management (numerical rating scale 0–10) prior to discharge from recovery.

Diaphragm assessment and bedside spirometry were done at two time points. First measurement (time point 1) was done at the baseline as soon as the patient arrived in the induction room. This was done prior to administration of any sedative agents or regional block. Second assessment (time point 2) was done post-operatively once the patient was deemed to be ready for discharge from recovery back to the ward.

A radiologist was recruited to perform dedicated diaphragmatic ultrasound before and after the interscalene block was administered. The radiologist was blinded to the control and research groups. The ultrasound was performed in the supine position at 45°; both the right and left diaphragms were imaged. The ultrasound was performed on a sonosite machine. The curvilinear probe was placed along the mid-axillary line. Motion of the diaphragm was documented during resting respiration and upon deep inhalation using B-mode sonography. M-mode sonography was then adopted to document the sniff test. The patient was instructed to take a short, sharp inspiration through the nose. The sound beam was placed at a 30° angle of the cranial-caudal midline and the sinusoidal curve was recorded [Figure 1].

Each patient had a normal sinusoidal curve peak of 2 cm symmetrically prior to administration of the interscalene block. Post-operatively patients who had no diaphragmatic paralysis had a persistent 2-cm curve peak with M-mode imaging. In some cases of diaphragmatic paralysis, the patients had a paroxysmal depression of the sinusoidal curve [Figure 2]; in other cases, there was no documented sinusoidal curve with M-mode ultrasound.

Bedsides spirometry assessments were done with patients sitting up. They were requested to make

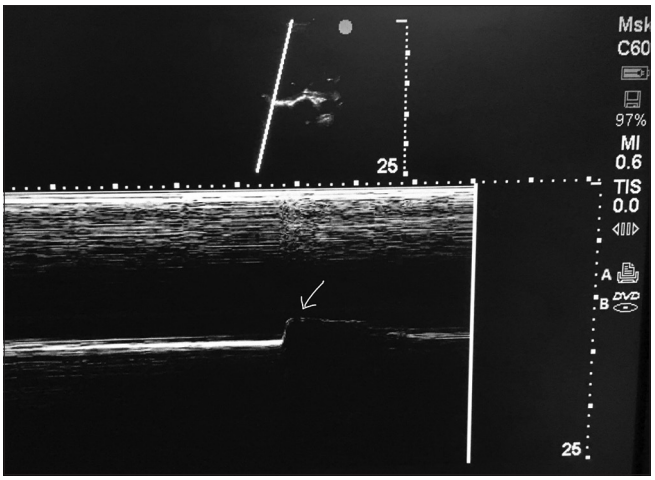

Figure 1: Ultrasound view of diaphragm with M-mode. The arrow points towards the sinusoidal wave pattern during sniff test. This image corresponds to normal diaphragmatic activity

maximum inspiratory effort and blow as hard and fast into the device. Best reading from three repeated measurements was recorded.

Primary outcome was the rate of diaphragmatic paresis as recorded in the post-operative period (time point 2). Secondary outcomes included (a) respiratory function assessments (time point 2) – forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), peak expiratory flow rate (PEFR) and subjective feeling of dyspnoea; and (b) pain control outcomes – intraoperative fentanyl consumption, morphine consumption in recovery, total morphine equivalents consumed in first 24 h, pain scores (numerical rating score 0–10) on arrival to recovery and pain scores (numerical rating score 0–10) at 24 h. Patient satisfaction scores (obtained by numerical rating score 0–10) obtained prior to discharge from recovery were also compared between the two groups.

Based on previous studies, the incidence of diaphragmatic paresis following interscalene block using 20 ml of local anaesthetic is reported to be 90%.[5] We hypothesised a 50% reduction in the incidence of diaphragmatic paresis with the intervention. For alpha error of 0.05 and power of 80%, 16 patients per group were needed for the study to be adequately powered. We planned to recruit 36 patients (18 per group) to allow for 10% dropout. Statistical Package for the Social Sciences(SPSS) version 25 was used for statistical analysis. Data distribution was tested for normality using Q–Q plot and Shapiro–Wilk test. Chi-square test was used for categorical variables. Linear regression was used to identify difference in pulmonary function accounting for preoperative baseline variability. *T*-test was used

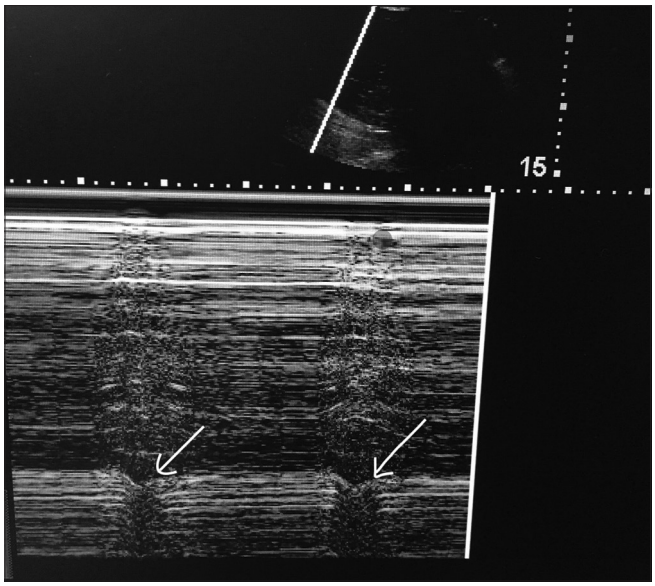

Figure 2: Ultrasound view of diaphragm with M-mode. The arrow points towards the inverse sinusoidal wave pattern during sniff test. This image corresponds to diaphragmatic palsy

to compare parametric variables. Nonparametric data were analysed by Mann–Whitney *U* test.

RESULTS

A total of 36 patients were recruited in the study [Figure 3]. The baseline patient characteristics were similar between the two groups [Table 1]. One patient in the conventional group was lost to post-operative follow-up due to the unavailability of clinician to assess patient in the post-operative recovery room. All analyses were done by original assigned groups.

There was a significant difference in the proportion of patients who developed diaphragmatic paresis between treatment groups [Table 2]. Eight (44%) patients in the saline group developed diaphragmatic paresis post-operatively, as compared to 16 (94%) patients in the conventional group.

There was no significant difference in the proportion of patients who reported feeling dyspnoeic post-operatively. Coefficients' modelling accounting for pre-operative values showed no significant difference in postoperative PEFR ($P = 0.65$) and FEV1 ($P = 0.38$). Linear regression through origin was used to calculate the difference between the groups.

Pain scores were recorded on a scale of 1–10, with 10 being the most painful. No significant differences in distribution were found between the groups ($P = 0.078$). Opioid consumption was also recorded intra-operatively, in recovery and in the 24 h post-operation. There was no significant difference in opioid consumption between the groups in any of these time periods. Similarly, 24-h pain scores showed no significant difference between the groups ($U = 140.00$, $P = 0.868$).

Patient satisfaction scores were also recorded on a scale of 0–10. Satisfaction scores in the conventional group ranged from 5 to 10 with 10 (59%) reporting a score of 10. Scores in the saline group ranged from 7 to 10 with four patients reporting a score of 7 (22%) and the remainder evenly divided between scores of 8 and 10. A Mann–Whitney *U* test was performed. No significant differences in distribution were found between the groups ($U = 127.5$, $P = 0.367$).

Table 1: Baseline parameters

Parameters	Conventional *n*=17	Saline *n*=18	*P*
Gender, male	9 (52.9)	11 (61.1)	0.74
Age (years)	57.41 (12.53)	53.56 (14.72)	0.75
Pre-op diaphragm US, normal	17 (100)	18 (100)	0.33
Baseline HR (beats/min)	65.65 (8.84)	68.44 (11.04)	0.58
Pre-op PEFR (l/s)	6.15 (3.47)	4.71 (2.07)	0.42
Pre-op FEV1 (l)	2.43 (1.14)	2.60 (1.04)	0.37
Pre-op FVC (l)	3.16 (1.39)	3.52 (1.34)	0.41

US: Ultrasound, HR-Heart rate; PEFR-Peak expiratory flow rate;FEV1-Forced expiratory volume in one second;FVC-Forced vital capacity

Table 2: Cross-tabulation of treatment group and post-operative status of diaphragmatic patients

Group	Post-op ultrasound		Total (*n*)	Chi-square
	Normal (*n*)	Palsy (*n*)		
Conventional	1	16	17	Chi-squared=10.01, *P*=0.002
Saline	10	8	18	
Total	11	24	35	

Post-op=Postoperative

DISCUSSION

Injection of 10 ml of normal saline anterior to anterior scalene muscle prior to interscalene block was found to reduce the incidence of hemi-diaphragmatic palsy. However, there was no significant difference in subjective feelings of dyspnoea or objective pulmonary function tests between the two groups.

There are few possible mechanisms to explain the phrenic nerve sparing. It is possible that the dilution of local anaesthetic by normal saline around phrenic nerve, thereby reducing or eliminating the local anaesthetic from reaching the phrenic nerve, may have played a significant role in preventing phrenic

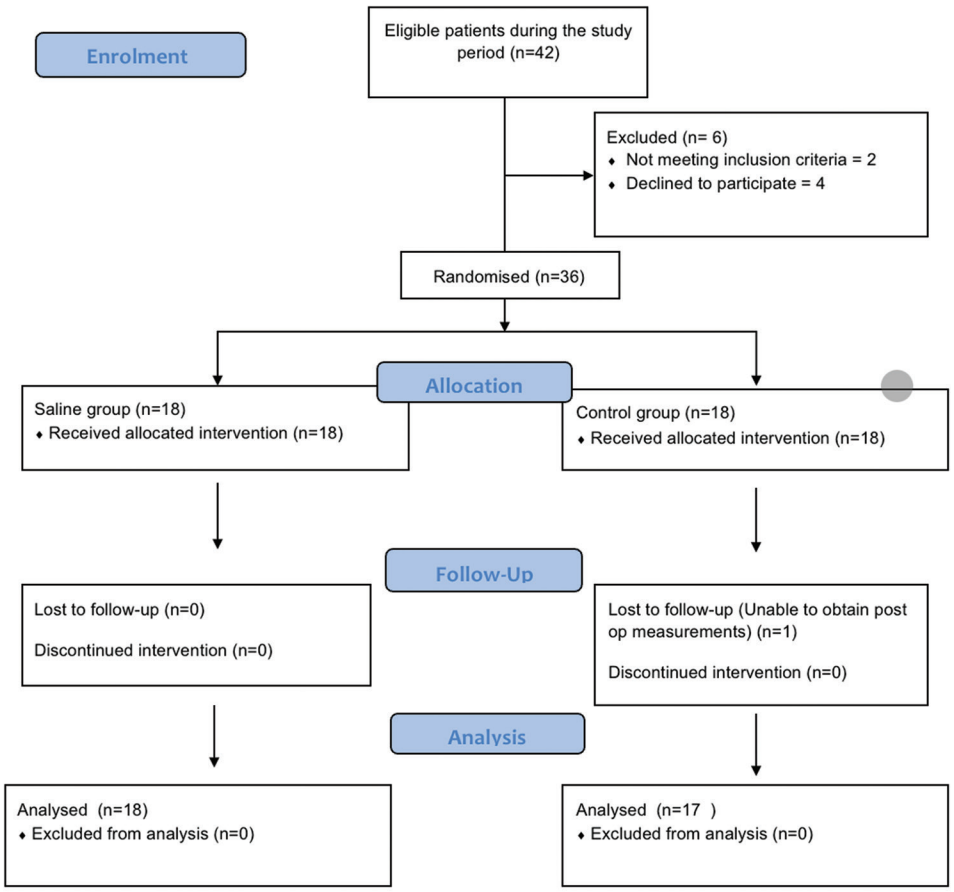

Figure 3: CONSORT flow chart

nerve palsy. Other possible reasons could include alteration of local pH and increase in sodium load in the environment.[8]

We noted no difference in the analgesia between the two groups. The reason for preservation of interscalene analgesia might be due to the difference in impulse traffic frequency between different peripheral nerves.[9] Phrenic nerve has high impulse traffic frequency, thereby causing rapid onset and recovery from local anaesthetic compared to interscalene brachial plexus which has slow impulse traffic. Hence, we speculate that the dilution of local anaesthetic allowed phrenic nerve to recover quicker than interscalene plexus. Earlier studies aiming to reverse analgesic effects of brachial plexus block with saline were not successful, which reinforces the above concept.[10]

The injection of saline to wash away or dilute local anaesthetic is not a novel concept. It has been tried in the past with neuraxial blocks.[11,12] Case reports of saline injection via interscalene catheter to reverse phrenic palsy have also been reported.[8,13,14] In a recent study by Gerber *et al.*,[15] 10 ml of saline was injected post-operatively via interscalene catheter to aid reversal of diaphragmatic palsy. They demonstrated partial reversal of phrenic palsy but none had total reversal. Our study differs from the above in couple of ways. First, the current study is a prospective randomised study where the intervention was applied prior to phrenic nerve palsy, that is the saline injection was done prior to local anaesthetic injection. To the authors' knowledge, this is the first study of its kind. Second, this was done for a single shot interscalene injection which is a lot more commonly performed than interscalene catheters.

In the previous studies, the authors recommended higher volumes (20–30 ml) of saline to reverse phrenic palsy.[16] Our study shows that 10 ml of normal saline will be sufficient in reducing phrenic palsy by 50% if injected prior to administration of local anaesthetic.

This reduction of incidence of hemi-diaphragmatic paresis, along with no significant reduction in quality of analgesia or patient satisfaction, indicates that our novel technique could be used in place of the conventional technique. Our method may be

of particular benefit in patients with pre-existing respiratory insufficiency. We noted that some patients in saline group still had phrenic palsy. This could be due to a couple of reasons. First, the saline injection is aimed at protecting the phrenic nerve. Accessory phrenic nerve is present in up to 36% of population.[17] This may not be blocked by saline injections. Second, epidural spread of local anaesthetic has been reported following interscalene block.[7] The above two reasons might explain the presence of phrenic palsy in the saline group. Combination of low-volume interscalene block with saline injection anterior to anterior scalene can further reduce the incidence of phrenic palsy.

The advantages of saline injection are as follows: first, it requires the same amount of needle insertions as the conventional method; second, it does not take a significantly longer time to perform with no additional complications. Strengths of our study included that it was double blinded and expert input from radiologists was obtained to perform ultrasound scanning.

The limitations of the study are that it is a single-centre study in a small patient population. But this was a hypothesis-generating study and was appropriately powered. We believe that the results can be replicated in a bigger study.

Future studies with low-volume interscalene block combined with saline injection around the phrenic nerve can potentially reduce the incidence of phrenic palsy even further. This is a novel concept and has the potential to be applied to different clinical scenarios where one would wish to protect a target nerve during nerve block.

CONCLUSION

In conclusion, the saline technique demonstrated a non-inferior analgesia as the conventional interscalene block technique while showing a significant reduction in the incidence of hemi-diaphragmatic palsy.

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Conflicts of interest

There are no conflicts of interest.

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