Effect of Bilateral Ultrasound-Guided intermediate cervical plexus Block combined with general anesthesia on THE stress response in patients undergoing anterior cervical spine surgery. A randomized controlled study

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INTRODUCTION

Introduction:

Stress response is the name given to the hormonal and metabolic changes which follow injury or trauma. It may lead to changes in the nervous, endocrine and immune systems, and alterations in metabolic processes and functions(1). *The stress response can shift from an adaptive and protective role to a pathogenic occurrence, especially when it is strong and chronic.*

Stress hormones, the most prevalent of which is cortisol, have a circadian pattern in which they gradually climb after night sleep to reach a peak at early morning wake-up time, then gradually decline as the day progresses (2).
This pattern, however, can be disrupted by any stressful situation, such as severe pain from surgery, which has been linked to a progressive rise in cortisol levels both intraoperatively and in the early postoperative period.

Cytokines are group of low molecular weight proteins that modulate the systemic inflammatory response elicited by surgical intervention. Increased levels of proinflammatory cytokines, including interleukin-6 (IL-6) which is the main cytokine responsible for inducing the systemic changes, is an early features of acute injury. Interleukin-6 could be a good marker for research purposes that reflects and compares postoperative stress levels.

Spine surgeries are increasingly being performed as short-stay surgical procedures, and anterior cervical decompression and fusion is one such procedure (3).*Postoperative incisional pain has been described as moderate in intensity, requiring opioid analgesics in most cases. Nonetheless, opioid-related side effects such as nausea, vomiting, and respiratory depression are undesirable in these patients who are at risk for airway problems due to surgical retraction or wound hematoma*(4).

Regional anesthesia inhibits the stress response to surgery and can also influence postoperative outcomes. . The endocrinal stress response to the surgical operation is reduced as a result of inhibiting afferent impulses from the surgical site. Furthermore, a reduction in this type of stress response is seen as a key indicator of a successful regional block.

Intermediate cervical plexus block (CPB) is a safe and simple technique that has been shown to provide good pain relief through blocking all four cutaneous branches of the

cervical plexus, as well as sensory and motor branches (5).*Not only Intermediate (CPB) is superior to superficial CPB in terms of effectiveness, but also is safer than deep (CPB)* (6).

There is a paucity of evidence for the effect of bilateral cervical plexus block for anterior cervical spine surgeries. Prior research had employed recovery questionnaire score, 24-h opioid usage and length of hospital stay in assessment of cervical plexus block effectiveness (7)*, however estimating the effect of Intermediate (CPB) on stress biomarkers as serum cortisol and interlukien-6 has not been discussed yet.*

Aim of the work

The aim of the present study is to investigate the effect of Bilateral Ultrasound-Guided intermediate cervical plexus Block combined with general anesthesia on the stress and inflammatory response in patients undergoing anterior cervical spine surgery (ACSS).

Objectives:

- *To compare between serum level of cortisol and interlukien-6 pre-operative and 24 hours post-operative in both groups.*
- *To identify Hemodynamics variables (mean arterial blood pressure and heart rate) peri-operatively.*
- *To assess the pain score during 1st 24 hours postoperative according to numeric pain rating scale (NPRS).*
- *To measure the incidence of complications within both groups.*

Hypothesis:

We hypothesize that intermediate cervical plexus block will offer a significant suppression of stress response and adequate post-operative analgesia in patients undergoing anterior cervical spine surgeries.

Ethical Considerations:

Our study will be conducted in Kasr El Aini Hospital, Cairo University after approval of the Research Ethics Committee. Full written informed consent will be obtained from the patients before inclusion in this study.

Methodology

Methodology

I. Study design:

A randomized controlled study.

II. Study setting and location:

The study will be conducted in the Neurosurgery operating rooms at Cairo University hospital.

III. Study population:

(66) Patients, aged from 18 to 65 years old, ASA physical status I-II, scheduled for anterior cervical spine surgery will be included in the study. Patients will be randomly allocated using concealed closed envelope method into one of two groups:

- *Group A (n=33): will include the patients who will undergo bilateral ultrasound guided intermediate cervical plexus block after general anesthesia.*
- *Group B (control group) (n=33): will include the patients who will undergo general anesthesia with conventional analgesia.*

IV. Eligibility Criteria

1. Inclusion criteria:

1. ASA I & ASA II patients.

2. Age group: from 18 to 65 years old.

3. Patients undergoing anterior cervical discectomy or fixation.

4. Genders eligible for study: both sexes.

2. Exclusion criteria:

- *Patient refusal.*
- *Patient Undergoing posterior fixation in addition to anterior.*
- *An allergy to local anaesthetics.*
- *Infection at block puncture site.*
- *Bleeding disorders (Coagulopathy: PTT > 40seconds, INR > 1.2, platelet count < 120 x 103 / L.).*
- *Emergency surgeries & patients in sepsis.*

V. Study Procedures

1. Randomization:

Patients will be randomly allocated by a computer-generated table into one of the study groups; the randomization sequence will be concealed in sealed opaque envelopes

2. Study Protocol:

Patients will be subjected to systematic preoperative assessment including history taking, physical examination and review of the results of routine investigations. NPRS (numeric pain rating scale) will be explained to all candidates where zero corresponds to no pain, and 10 is indicative of the worst unbearable pain. Upon arrival to the preparation room: An18-gauge intravenous (IV) cannula will be inserted into a peripheral vein. Patients will be premedicated by intravenous 0.01 mg/kg midazolam and 10mg metoclopramide. Patients will be then transferred to the operating room where basic monitoring, Electrocardiography (ECG), Non-invasive Blood Pressure (NIBP) monitor and pulse oximetry will be attached.

General anesthesia will be induced in a standardized way with intravenous propofol 2.5mg/kg, fentanyl 1 µ/kg and atracurium 0.5mg/kg. Anesthesia will be maintained by inhalational isoflurane and intravenous atracurium 0.1mg/kg/20min.

Group A: The patient will be placed in a supine or semi-sitting position, with the head turned slightly away from the side to be blocked to facilitate operator access. The skin is disinfected and a linear-array ultrasound probe (Siemens ACUSON X300 Ultrasound System) is placed on the lateral neck, overlying the sternocleidomastoid muscle at the level of its midpoint (approximately the level

of the cricoid cartilage), Once the SCM has been identified, the transducer is moved posteriorly until the tapering posterior edge is positioned in the middle of the screen. At this point, an attempt should be made to identify the brachial plexus and/or the interscalene groove between the anterior and middle scalene muscles. The cervical plexus is visible as a small collection of hypoechoic nodules (honeycomb appearance) immediately superficial to the prevertebral fascia that overlies the interscalene groove.

Once the plexus has been identified, the needle is passed through the skin, platysma, and investing layer of the deep cervical fascia, and the tip is placed adjacent to the plexus. . Following negative aspiration, 1–2 mL of normal saline is injected to confirm the proper injection site. Then after confirmation of safe needle position and absence of vascular spread, bupivicaine 0.25% (5–15 mL) is administered to envelop the plexus, and the block is repeated with the same technique on the opposite side.

(Figure 1).

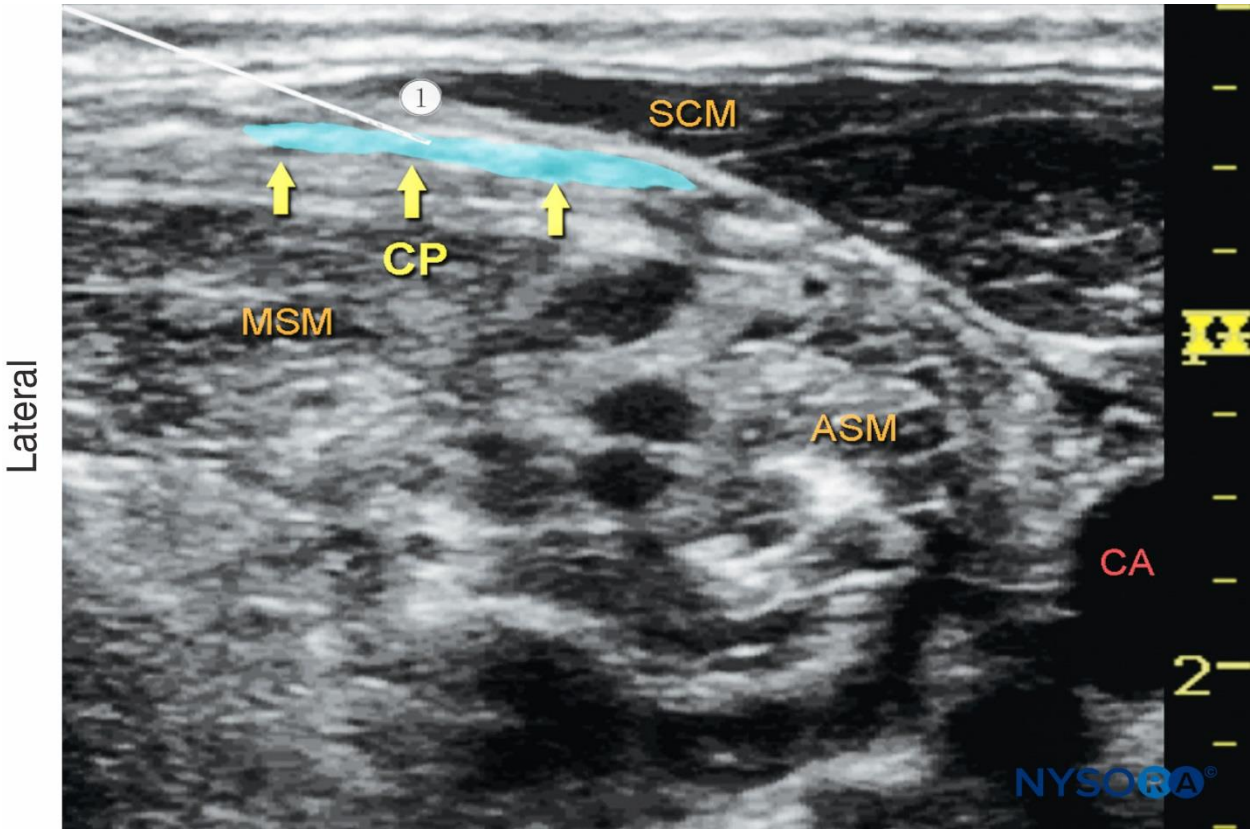

Figure 1. *Cervical plexus (transverse view): desired distribution of local anesthetic (blue-shaded area) to nerve block the cervical plexus. Needle path: 1. ASM, anterior scalene muscle; CA, carotid artery; CP, cervical plexus; MSM, middle scalene muscle; SCM, sternocleidomastoid muscle.*

Group B: *Induction of general anesthesia as Group A, without performing intermediate cervical plexus block, intravenous morphine will be given in a dose of 0.1-0.2mg/kg to maintain intraoperative analgesia.*

All operations will be performed in the morning, taking into consideration circadian rhythm of hormone release. In both groups, venous blood samples to measure serum cortisol and interlukien-6 level will be collected before surgery as a baseline, then 24 hours post-operative.interlukien-6 is normally low and may be undetectable within 30-60 min after start of surgery while reaching maximum level at 24 hours post-operative.

During the intraoperative period; heart rate and mean arterial blood pressure will be recorded every 15 minutes throughout the surgery. Intravenous fentanyl bolus doses (0.5 µg/kg) will be adjusted to keep the HR and mean arterial blood pressure within 20% of the pre-induction values.

At the end of surgery, atracurium will be stopped and neuromuscular blockade will be reversed with intravenous neostigmine 0.04 mg/kg and 0.01 mg/kg atropine and endotracheal tube will be removed.

After operation, patients will be transferred to post anesthesia care unit (PACU) for complete recovery and monitoring. A standard postoperative analgesia regimen will be prescribed as intravenous paracetamol 1gm every 8 hours. Intravenous morphine 0.05 mg/kg will be given as a rescue analgesic dose if numeric analogue score was ≥ 3. Metoclopramide 0.15 mg/kg IV will be prescribed for patients complaining of nausea or vomiting.

The maximum dose of morphine that will be given is 20 mg/24 hrs.

The block will be considered a failed block if the patient required more than two doses of rescue analgesia in the first hour postoperatively.

Measurement tools

- *Demographic data: age, sex, body mass index (BMI).*
- *Serum cortisol and interlukien-6 pre-operative and 24 hours post-operative.*
- *Hemodynamics {heart rate, arterial blood pressure (systolic, diastolic and mean blood pressure)}will be recorded at the following intervals: baseline reading , Intraoperative 15 minutes post-intubation (pre-block), 15 minutes after the block/administration of morphine and then every 15 minutes throughout the surgery, and postoperative at 1 ,6,12 , 24 hours..*
- *NPRS score at 15, 30, and 60 min, 6, 12, 24 hours post-operatively.*
- *Number of patients in each group who need intraoperative additional analgesic doses of fentanyl and total fentanyl dose for each patient.*
- *Total postoperative analgesic requirements.*
- *Failure rate of the block (the block will be considered a failed block if the patient required more than two doses of rescue analgesia in the first hour postoperatively.*

VI. Study outcomes

1. Primary outcomes:

- *The serum cortisol level 24 hours postoperatively.*

2. Secondary outcomes:

- *The serum interlukien-6 24 hours postoperatively.*
- *Intraoperative hemodynamics {heart rate, arterial blood pressure (systolic, diastolic and mean blood pressure)*
- *Intraoperative additional fentanyl requirements.*
- *NPRS score postoperative during 1st 24 hours. 15, 30, and 60 min, 6, 12, and 24 hours after surgery.*
- *Time to first postoperative analgesic request (duration of analgesia).*
- *Block failure rate.*
- *Incidence of complications. (Nerve injury, Hematoma formation, LA toxicity, intravascular injection.*
- *Block failure: The block will be considered a failed block if the patient required more than two doses of rescue analgesia in the first hour postoperatively.*

Statistical Analysis

Statistical Analysis

I. Sample size

Our primary outcome is the serum cortisol level 24 hours postoperatively. In a previous study, the serum cortisol level after 24 hours was 21.8 ± 4.7 micrograms per deciliter (mcg (ref) after lumbar fixation surgeries. We calculated a sample size that could detect a mean difference of 20% between both study groups. MedCalc Software version 14 (MedCalc Software bvba, Ostend, Belgium) was used to calculate the sample size 60 patients (30 Patient per group) at least were estimated to have a study power of 95% and an alpha error of 0.05. This number will be increased to 66 patients (33 patients per group) to compensate for possible dropouts.

Sample size calculation was performed guided by power of 95%, confidence level of 95 %.(8)

II. Statistical analysis

For data analysis, the Statistical Package for Social Science (SPSS) software, version 26 for Microsoft Windows (SPSS Inc., Chicago, IL, USA) will be used. The Chi squared test will be used to examine categorical data, which will be given as frequency (percent). The Shapiro-Wilk test will be used to verify for normality in continuous data, and the results will be provided as mean (standard deviation) or median (interquartile range) as appropriate. Depending on the data's normality, the unpaired t test or the Mann Whitney test will be used to assess it. Repeated measures will be examined using analysis of variance (ANOVA), with post-hoc pairwise comparisons using the Boneferroni tests. A P value less than 0.05 will be considered statistically significant.

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