Ultra-sound guided supraclavicular brachial plexus block: The value of adjuvants: Review article

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Abstract

Background: Upper limb surgeries are frequently performed using peripheral nerve blocks, like ultra-sound guided supraclavicular brachial plexus block, which provides safe and effective anaesthesia. Search for safe and effective adjuvants to regional nerve blocks continues, with medication that increases the duration of analgesia although it has fewer side effects. Using of drugs as dexmedetomidine, opioids, ketamine, clonidine, midazolam, epinephrine, neostigmine, magnesium sulphate and dexamethasone along with local anaesthetics for this aim with different degrees of success.

Objectives: This review research investigated safety and efficacy of various additives, namely dexmedetomidine, ketamine, fentanyl, and dexamethasone, when added to bupivacaine in ultrasound guided supraclavicular brachial plexus block in order to evaluate onset and duration of sensory and motor block, estimate sedation score, pain scale and total analgesic consumption and to investigate side effects when added to bupivacaine.

Conclusion: This research implies that there is still to research about the of effect of different adjuvants added to bupivacaine in ultra-sound guided supraclavicular brachial plexus block.

Keywords: Supraclavicular block; Dexmedetomidine; Adjuvants; Ketamine; Brachial plexus.

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1. Introduction

Adjuvants have been used to prolong supraclavicular block, shorten block onset times, and extend duration of post-operative analgesia. To enhance duration of block and postoperative analgesia, various adjuvants such as dexmedetomidine, ketamine, fentanyl, midazolam, magnesium sulphate, dexamethasone, and neostigmine have been added to local anaesthetics **(Yadav et al,.2008)**.

2. Brachial plexus (Bp)

Brachial plexus innervates upper extremity, including the scapular region, with somatic motor and sensory innervation. Brachial plexus comprises multiple named regions as it travels through posterior triangle of neck into axilla, arm, forearm, and hand, depending on how plexus is created.**(Leung et al,.2015)**

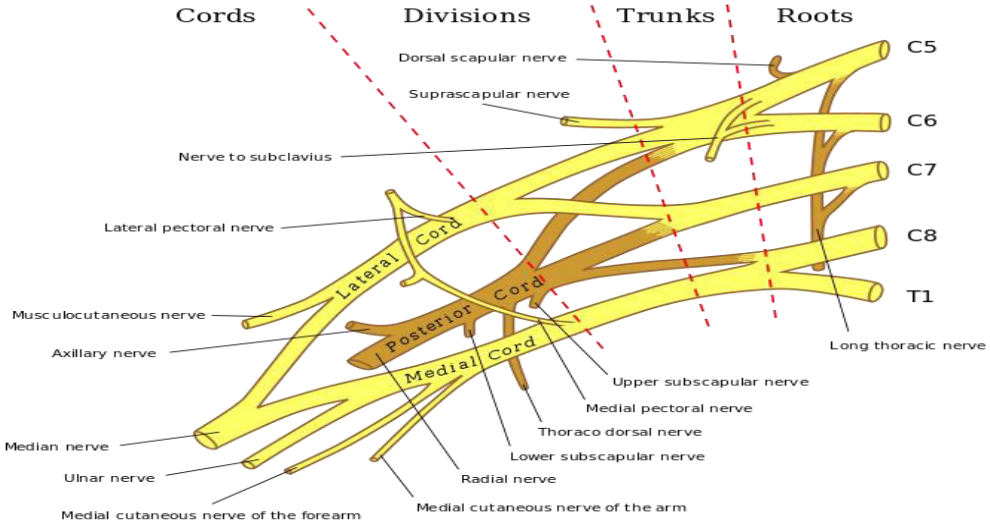

Fig.1.Anatomy of brachial plexus (Leung et al,.2015)

2.1. Embryology

Motor nerve fibers, such as those present in brachial plexus, emerge from cells within developing spinal cord's basal plate and travel to ventral nerve root. Neural crest cells give rise to sensory nerve fibers discovered in dorsal nerve root. Dorsal nerve root will eventually join ventral nerve root to establish spinal nerve.**(Johnson et al,.2010)**

2.2. Blood Supply and Lymphatics

Blood supply to brachial plexus is provided by subclavian artery (SCA) and its branches. Subclavian, axillary, and subscapular arteries deliver blood to cords **(Zhonget al,.2017)**

2.3. Branches of brachial plexus

Dorsal scapular nerve and long thoracic nerve both originate entirely from roots of brachial plexus. Most of brachial plexus branches emerge from cords. Cords continue like five terminal branches, releasing seven other nerves with varying functions **(Fig.1), (Benes et al,.2021)**.

The lateral cord gives rise to single non-terminal branch, lateral pectoral nerve, which innervates pectoralis major muscle and includes spinal levels C5 to C7 **(Noland et al,.2022)**.

Three non-terminal branches emerge from medial cord: medial pectoral, medial brachial cutaneous and medial antebrachial cutaneous nerves. Pectoralis major and minor muscles are both innervated by medial pectoral nerve. Medial brachial cutaneous nerve innervates arm's medial side, whereas medial antebrachial cutaneous nerve innervates forearm's medial side. Upper, middle and lower subscapular nerves are three non-terminal branches of posterior cord. Latissimus dorsi muscle is innervated by middle subscapular nerve, which moves with thoracodorsal artery. Musculocutaneous, median, ulnar, axillary, and radial nerves are brachial plexus's five terminal branches. **(Johnson et al,.2010).**

The lateral cord completely forms musculocutaneous nerve, which gives motor innervation to muscles of anterior compartment of arm. Medial and lateral cords contribute to formation of median nerve. It innervates most of musculature in anterior forearm and thenar compartment in palmar hand. Nerve innervates lateral three and half fingers of palmar hand **(Hunter et al,.2020)**.

Medial cord completely forms (C8-T1) ulnar nerve. In hand, it divides into superficial branch and deep branch. Deep branch of ulnar nerve innervates hypothenar and adductor-interosseous compartments of hand's muscles **(Agarwal et al,.2019)**.

3. Ultra-sound guided supraclavicular brachial plexus block

3.1. Steps of ultrasound- guided supraclavicular brachial plexus block.

3.1.1. Step 1: studied case position

Studied case should be asked to lie in semiFowler's position, i.e. supine with trunk elevated between fifteen & forty-five degrees. Hold probe perpendicular to skin..(**Kimetal,.2014)**

3.1.2.Step 2 preparation for supraclavicular block

Whereas studied case is supine, sterile sheet should be draped over thoracic area, leaving only supraclavicular fossa revealed.

Twenty G one hundred mm echogenic needle is suggested for this approach should be used to inject anaesthetic solution. Throughout procedure, aseptic methods should be followed. (**Kimetal,.2014)**

3.1.3. Step 3: palpate and mark important landmarks

Clavicle should be palpated and marked at midpoint with index and middle fingers of non-dominant hand. This relates to sternocleidomastoid muscle's borders, particularly clavicular head of sternocleidomastoid muscle and interscalene groove interscalene groove and tissue space is located at level of cricoid cartilage between anterior & middle scalene muscles. BP is posterior to mid-clavicle and deep to supraclavicular fossa.**(Kimetal,.2014)**

3.1.4. Step 4: probe placement

Linear probe is placed in supraclavicular fossa, superior and parallel to midpoint of clavicle, proximity to posterior border

of sternocleidomastoid muscle, after palpating clavicle. clavicular head of sternocleidomastoid muscle. Probe is positioned in parasagittal and coronal oblique plane to achieve optimum short-axis view of SCA, first rib, pleura, lungs and BP trunks/divisions. Probe is initially pointed inferiorly toward chest and mediastinum. On ultrasound screen, SCA should appear like round, pulsating hypoechoic structure. Color Doppler imaging can indicated existence of SCA. BP, which is found posterolateral to SCA, has grape-like appearance, with many hypoechoic bundles embedded in hyperechoic supporting connective tissue surrounded by epineurium.(**Demondionet al,.2003)**

3.1.5. Step 5: landmarks visualized on ultrasound image

Hyperechoic structure at bottom of screen identifies first rib. Because of its reflective characteristics, rib appears like white horizontal/oblique line Middle scalene muscle is found postero-laterally, and anterior scalene is found anteromedially. If needle is advanced below this point, it is very likely that it will penetrate parietal pleura, resulting in pneumothorax, hypoechoic ring, dark, round; pulsating circle superficial to rib can be used to identify SCA. Pulsating artery is affirmed using ultrasound machine's colour doppler function, that will show up in red. Cephalad to subclavian artery SCA is brachial plexus BP. Middle scalene muscle is found postero-laterally, anterior scalene is found anteromedially. If needle is advanced below this point, it is very likely that it will penetrate parietal pleura, resulting in pneumothorax **(Fig.2), (Christie et al,.2015)**

3.1.6. Step 6: needle insertion and course

Needle should be implanted at probe's lateral border using in-plane method. Once skin has been pierced, needle should be progressed in same plane as ultrasound beam, from lateral to medial, towards BP located posterolateral to SCA.Needle is advanced in same plane as ultrasound probe so that entire length of needle & needle tip are visible as it is directed towards BP. Needle should pierce axillary sheath that provides some resistance characteristic 'pop' sensation. Despite being dependent on site of surgery intended extent of block coverage, ideal location is at junction of BP , posterolateral border of SCA and superior to first rib.(**Christie et al,.2015**)

3.1.7. Step 7: injecting local anesthetic solution

Once needle's tip has been affirmed, local anaesthetic can be injected near BP (Figure 10). Using 'hydro Pectoralis minor reflected to expose course of BP in anterior neck & clavicular region, anaesthetic can be infused between divisions of plexus. Structures' relationship to lung is obvious.

Studied case is supine, with head of bed lifted up and turned to contralateral side of block. Placing local anaesthetic within axillary sheath— fascia that extends from cervical prevertebral layer & surrounds BP components will result in quicker onset and more extensive coverage.

Suggested volume will continue to stay same in both cases (twenty ml). Even so, anesthetic agent dilution will differ.

Twenty mL of 0.5percent bupivacaine is suggested for surgical procedures, while twenty mL of 0.25percent & 0.125 percent bupivacaine is suggested for analgesic blocks.

Because of their inherent vasoconstrictive characteristics, ropivacaine & levobupivacaine may prolong duration of action & slow systemic absorption. To avoid injecting air, needle must be flushed with local anaesthetic (**Hanumanthaiahet al,.2015**)

3.1.8. Step 8: spread of local anesthetic solution(Figure 2)

When axillary sheath is penetrated, there is slight reduce in resistance, as well as 'click' or 'pop.' anaesthetic solution in syringe can now be slowly injected into axillary sheath. Nerve bundle will differentiate after anaesthetic solution is injected into axillary sheath. Positioning needle tip then injecting local anaesthetic outside axillary sheath will necessitate larger volume of local anaesthetic to ensure adequate anaesthesia (**Demondionet al,.2003**).

On ultrasound image, local anaesthetic solution appears as hypoechoic fluid that is black. Precise volume can then be determined; injection can be stopped once all of nerve constructions have been bathed in local anaesthetic solution at level of BP trunks/divisions.

Supraclavicular BP has been noted to have success rate of eighty five percent higher.(**Kimet al,.2015**)

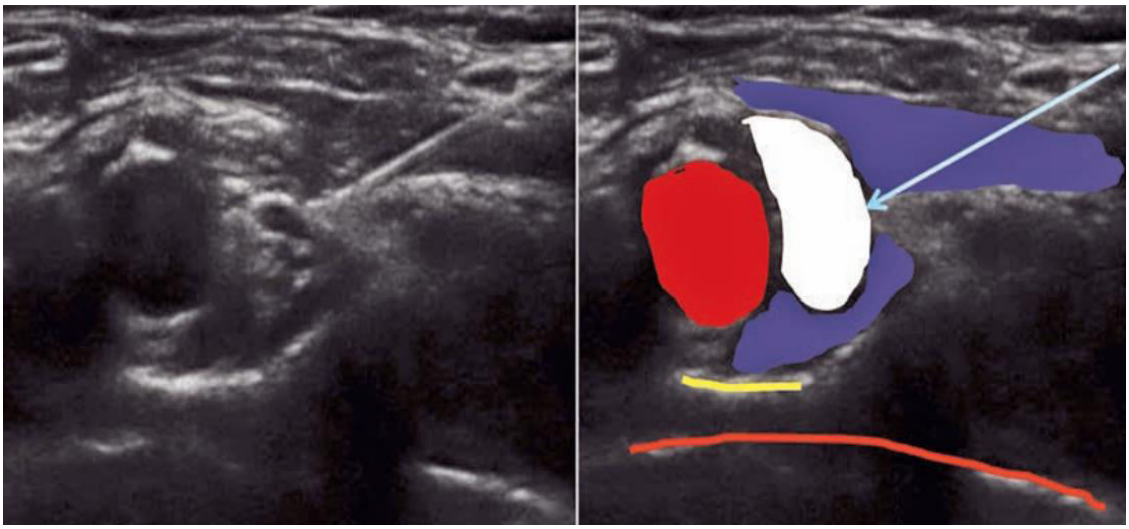

Fig.2 .Spread of local anaesthetic superficial to the plexus.

Red color : subclavian artery, white color: brachial plexus, yellow line: periosteum of first rib, red line: pleura, blue arrow: needle, navy area: local anaesthetic(**Feigl et al,.2020**)

3.2 Indication of supraclavicular approach to brachial plexus

Supraclavicular approach to brachial plexus provides consistent anaesthesia of entire arm, however only on rare occasions of territory of intercostobrachial nerve. It is used for orthopedic procedures below mid-humerus level, such as elbow, forearm,

hand surgery, as well as arterio-venous fistulas from mid-arm to mid-forearm level. Bilateral blocks should not be conducted in studied cases with lung disease due to risk of respiratory compromise caused by pneumothorax. Phrenic nerve block that can happen in thirty six percent to sixty seven percent of studied cases. **(Demondion et al,.2003)**

Supraclavicular approach to brachial plexus frequently does not block intercostobrachial nerve. It provides small strip of skin along upper arm's medial aspect. It can be directly blocked by infiltrating approximately ten millilitres of local anaesthetic subcutaneously from upper biceps to lower triceps at anterior axillary line. It can be obstructed directly using ultrasound guidance, which may decrease tourniquet pain throughout awake surgery under supraclavicular block, yet this has yet to be proven because tourniquet pain is likely mediated by tissue ischemia as well as local sensation.(**Christieet al,.2015**)

3.3. Complications of supraclavicular blocks

Supraclavicular blocks have the same difficulties as peripheral nerve blocks, such as risk of infection, bleeding, neuropathy. With advent of ultrasonography, risk of pneumothorax can be reduced by maintaining constant visualisation of needle tip, first rib and pleura. Hoarseness from ipsilateral laryngeal nerve block, Horner syndrome from stellate ganglion block, hemi diaphragmatic paresis from phrenic nerve block are all common, self-limiting side effects of other proximal brachial plexus blockade.Systemic toxicity from local anaesthetics is possible. Because transverse cervical and dorsal scapular arteries are anatomically close to brachial plexus, colour Doppler is suggested (**Patil et al,.2017).**

Other problems that may happen involve recurrent laryngeal nerve injury, which causes hoarseness, phrenic nerve injury, which causes hemi-diaphragmatic paresis (thirty three percent), and vascular puncture**(Gausset al,.2014)**

Horner's syndrome, which outcomes from paralysis of ipsilateral sympathetic cervical chain due to drugs, surgery, local compression, has also been defined. Horner's syndrome is distinguished by three symptoms: miosis, excessive pupil constriction; ptosis, drooping of upper eyelid; anhidrosis, lack of perspiration and failure of sweat glands. If what performed under ultrasound guidance not, good way, regular practise, solid understanding of human anatomy are essential. **(Helayel et al,.2007)**

4. Dexmedetomidine

Dexmedetomidine is potent and selective two-adrenoceptor agonist with anxiolytic, sedative and analgesic characteristics. (**Belleville et al,.1992).** It has been registered in United States since 1999. It was authorized for intravenous sedation of mechanically ventilated adult studied cases in intensive care unit for up to twenty four hours. Dexdorand Precedex vials comprise dexmedetomidine hydrochloride concentrate equivalent to one hundred g/mL dexmedetomidine**.(Takrouri et al,.2002)**

4.1. Pharmacokinetics

Because of first pass metabolism, dexmedetomidine has low bioavailability. It is ninety four percent protein bound and does not displace majority of protein-bound drugs commonly used in anaesthesia and intensive care.

Dexmedetomidine is completely biotransformed to inactive metabolites via glucoronidation and aliphatic hydroxylation mediated by cytochrome P 450. These metabolites are excreted in urine (ninety five percent of time) and faces (four percent of time). Because of slower metabolic rates in studied cases with hepatic failure, dose must be adjusted. (**Dewolf et al,.2001)**

Table 1 :-Routes of Administration

Route	**Dose**	
Intravenous	Loading dose:-1 mcg/kg over 10-20 minutes. Maintenance infusion:- 0.2 0.7mcg/kg/hr.	**(Anttillaet al,.2003)**
Intramuscular	(2.5 mcg/kg)	**(Anttilla et al,.2003**
Intra-thecalblock	0.1-0.2 mcg/kg	**(Memis et al,.2004)**
Epidural block	1-2mcg/kg	**(Memis et al,.2004)**
Peripheral nerve block	1mcg/kg	**(Obayah et al,.2010)**
Buccal	1-2 mcg/kg	**(Cimenet al,.2013)**
Intranasal	**1**-2mcg/kg	**(Yuenet al,.2008)**

4.2. Pharmacodynamics

Two adrenergic agonist, dexmedetomidine, works by binding to G protein coupled two adrenergic receptors found in central, peripheral and autonomic nervous systems, as well as various vital organs and blood vessels throughout body. **(Afsani et al,.2010)**

These receptors are divided into 3 subtypes: 2A, 2B, and 2C, each with its own set of functions and activities. **(Fairbanks et al,.2009)**

Locus ceruleus is site of action for dexmedetomidine's sedative effects, which are mediated by hyperpolarization of noradrenergic neurons, inhibiting noradrenaline discharge and activity in reducing medullo -spinal noradrenergic routes. **(Carolloet a,.2008)**

Analgesic impacts are primarily mediated by 2C and 2A receptors found on neurons in superficial dorsal horn of lamina II, which inhibit release of pronociceptive transmitters such as substance P and glutamate and cause spinal interneurons to hyperpolarize. **(Ishii et al,.2008)**

Activation of post synaptic α two receptors causes sympatholysis,

hypotension and bradycardia, which aids in attenuating stress response.

Dexmedetomidine also reduces salivation, increases glomerular filtration, decreases intraocular pressure, decreases shivering threshold, decreases bowel motility and decreases pancreatic insulin release. **(Philippetal,.2002)**

4.3. Role of dexmedetomidine as adjuvant

4.3.1Adjuvant in general anesthesia

Because of its sympatholytic impacts, dexmedetomidine dampens hyperdynamic response to laryngoscopy and surgery and maintains stable hemodynamic profile. **(Talke et al,.2000)**

It has been discovered to enhance impacts of all anaesthetic agents and to have opioid sparing impacts, resulting in lower doses needed. **(Talke et al,.2000).** It can help to reduce body's oxygen demand and inhibit intraoperative myocardial ischemia. **(Memisetal,.2004)**

Dexmedetomidine has lately been used to aid in awake fiberoptic intubation in studied cases with compromised airways because of anatomical distortions and upper airway infections. **(Kanaziet al,.2005)**

It offers good sedation and analgesia with little and no respiratory depression and no impact on airway reflexes, allowing studied case to stay calm and reducing risk of aspiration. **(Bekkeret al,.2006)**

It has been used as the sole sedative agent in an awake fiberoptic intubation without topical anaesthesia of upper airway in studied case with documented allergy to local anesthetics. Dexmedetomidine has sympatholytic and anesthetic sparing impacts, making it ideal for inducing and maintaining controlled hypotension in several surgeries, minimizing blood loss and providing optimal conditions for surgery like spinal fusion surgery, endoscopic nasal and sinus surgery and maxillofacial surgery. **(Scheret al,.2003)**

4.3.2. Adjuvant in Regional Anesthesia

When used neuro axially, dexmedetomidine is highly lipophilic and thus quickly dispersed in neural tissues, producing antinociceptive impacts by binding to α two receptors in spinal dorsal horn. Use of epidural dexmedetomidine as adjuvant with local anaesthetics extends duration of sensory and motor blockade, resulting in more intense motor blockade and good postoperative analgesia. **(Salgado et al,.2008)**

When used in conjunction with general anaesthesia, use of epidural dexmedetomidine like adjuvant to local anaesthetics has been found to reduce intraoperative anaesthetic demands, improve oxygenation and prolong postoperative analgesia. **(Bajwa et al,.2011)**

Intrathecal dexmedetomidine introduced to local anaesthetics enhances sensory block, generates more intense motor blockade and prolong postoperative analgesia, allowing dose of local anaesthetics used to be reduced. (**Al-mustafaet al,.2009).**

Numerous intrathecal doses have been tried with favorable results of sensory/motor block prolongation with maintained hemodynamics; even so, prolonged motor block may not be ideal for ambulatory surgeries. When used in conjunction with local anaesthetic, regional nerve blocks in peripheral nerve block dexmedetomidine has shown efficacy in prolonging duration of sensory block

and also post-operative analgesia. (**Al-Ghanemet al,.2009)**

4.3.3. Uses of dexmedetomidine postoperative period

Characteristics of dexmedetomidine favor its use in recovery room. Continuous sedation and sympathetic blockade may be advantageous in lowering high rate of early postoperative ischemic events in high-risk studied cases undergoing noncardiac surgery. (**Talke et al,.2000)**

5. Ketamine

Ketamine is hydrosoluble arylcycloalkylamine with pKa of 7.5 and molecular mass of 238 g/mol. Ketamine is often combined with benzethonium chloride and chlorobutanol like preservative when used as chlorhydrate in slightly acidic aqueous solution. (**Noppers et al,.2011)**

5.1 Pharmacokinetics of ketamine:

Ketamine metabolism is distinguished by low affinity for plasma proteins. Ketamine has wide distribution due to its five-fold higher lipid solubility than thiopental. Volume of central compartment is approximately seventy land distribution volume at steady state is approximately two hundred land 2.3 l/kg. **(Noppers et al,.2011)**

Ketamine is primarily metabolized in norketamine (eighty percent) by microsomal enzyme system, active metabolite that is primarily hydroxylized in 6hydroxynorketamine (fifteen percent) before being excreted in bile and urine after glucuronoconjugation. 3 other minor metabolites are produced. **(Noppers et al,.2011)**

Another method converts ketamine directly into hydroxyketamine (five percent). This metabolism does not just entail liver, especially in animals: substantial metabolism occurs in kidneys, intestine and lungs. (**Edwardset al,.2001).**

Ketamine removal clearance is great, equal to and then dependent on, liver blood flow. Ketamine has removal half life of two-three hours. Three compartment model can be used to define its pharmacokinetics. Its approval in women may be twenty percent greater than in men. **(Sigtermans et al,.2009)**

5.2 Pharmacodynamics of ketamine

5.2.1. ***Respiratory system***

Airway is normally well preserved throughout ketamine anaesthesia, with some conserving of pharyngeal and laryngeal reflexes. Ketamine has history of increasing laryngeal spasm rates. Several of these findings could be because of ketamine-induced partial airway obstruction, which is very common and usually reacts to simple airway clearance.

Ketamine acts like bronchodilator likely through 2 ways: central impact inducing catecholamine release, thereby stimulating β2 adrenergic receptors, resulting in bronchodilation and anticholinergic impact acting directly on bronchial smooth muscle via inhibition of vagal routes. **(Green et al,.2000)**

5.2.2. Cardiovascular system

Ketamine elevates blood pressure, stroke volume and heart rate while maintaining systemic vascular resistance. These impacts typically peak around two minutes after injection and fade over fifteen–twenty minutes. Individual responses vary widely and there is occasionally significant increase in blood pressure that is unrelated to pre-operative history of hypertension.

Because of these characteristics, ketamine is excellent agent for shocked studied case but is less suitable for studied cases with severe ischemic heart disease. **(Lau et al,.2001)**

5.2.3. Central nervous system

Dissociative anaesthesia is produced by ketamine. Throughout anaesthesia and surgery, studied case's eyes are frequently open and reflex motions are made. It takes longer than other intravenous anaesthetics to take effect after intravenous bolus (one-five minutes). Duration of action is determined by route of administration. It may be necessary to switch to different type of anaesthesia on occasion.(**Green et al,.2000)**

Ketamine tolerance can develop after repeated sedation and anaesthesia with drug, as seen in burn studied cases, with progressively large doses needed. This tolerance usually lasts three days.

Studied case may become agitated during healing as result of hallucinations caused by ketamine anaesthesia. Reported frequency of these hallucinations ranges between five and thirty percent. Children have lowest rate of hallucinations. Female sex, high ketamine doses and rapid intravenous boluses are associated with higher incidence. Hallucinations can be limited by premedication with benzodiazepines and, alternatively, promethazine, that has additional benefit of anti-emetic impact other benzodiazepines that have been used effectively involve midazolam and lorazepam. Benzodiazepines can be provided as last resort.

Ketamine is powerful analgesic that can be used as sole analgesic agent during surgery. Balanced anaesthesia, which includes intra-operative administration of opiates and tramadol, decreases amount of ketamine needed for anaesthesia repairs. This decrease recovery time and occurrence of some ketamine side effects, but it raises chances of intra-operative respiratory depression. (**Greenet al,.2000)**

Ketamine is progressively being used in both acute and chronic pain settings in both developed and developing worlds, in furthermore its intraoperative analgesic impacts. Use of intra-operative ketamine has been found in researches to decrease morphine consumption postoperatively in adults, even when ketamine is not continued into postoperative period.

Method for this is thought to be related to antagonistic impacts of ketamine at NMDA receptor, which is involved in 'wind-up.' Wind-up is condition in which nerves that carry pain signals from spinal cord's dorsal horn become sensitized.(**Zhanet al,.2001)**

Ketamine has traditionally been considered dangerous in studied cases with head injuries. Even so, there is mounting evidence that this may not be case. Ketamine rises cerebral blood flow in spontaneously breathing volunteers, though not in brain-injured studied cases during controlled ventilation and sedation. Increase in arterial pco2 has been recognized as primary factor responsible for increase in intracranial pressure with ketamine in spontaneously breathing studied cases. There is now some laboratory evidence that ketamine may play role in neuroprotection. Ketamine has been shown in animal researches to reduce ischemia-induced injury. According to proposed

model, blocking NMDA receptor prevents signal transduction to destructive intracellular mechanisms. (**Zhanet al,.2001**)

5.2.4. Gastro-intestinal tract

Ketamine causes increased salivation, which can cause airway issues such as laryngeal spasm or obstruction. Atropine is usually given like premedication to decrease salivation. Alternatively, glycopyrrolate may be used. ketamine is more likely than thiopental and propofol to cause nausea and vomiting; even so, because of its opioid-sparing impacts in peri-operative period, overall incidence of postoperative nausea and vomiting is decreased(**Kolbel et al,.2000**).

5.4 Adverse effects of ketamine

Table 2.Adverse effects of ketamine(Dadiomov et al,.2019)

Central nervous system	Drowsiness, dysphoria, confusion and seizures
Cardiovascular system	Arrhythmias, frequently high blood pressure, low heart rate, hypotension, left ventricular dysfunction in heart failure, respiratory and cardiac arrest
GIT	Anorexia, nausea and vomiting
Allergic reactions	Anaphylaxis, breathnessless, eadema of face, lips, throat and tongue
Muscular	Stiffness and spasms/tonic-clonic movements resembling seizures, increase skeletal muscle tone
Respiratory system	Apnea, increase laryngeal, tracheal secretions, laryngospasm, infant airway obstruction, and respiratory depression
Ophthalmologic	Diplopia, elevated intraocular pressureand nystagmus
Psychiatric	Amnesia, anxiety, confusion, depression, disorientation, dysphoria, dissociative state ,emergence phenomenon, delirium, hallucinations, extreme fear, excitement and irrational behavior
Skin	Local pain at injection site, redness and skin rash

5.5. Contraindications

Ketamine is not recommended for studied cases who have underlying conditions that would raise risk of problems, like aortic dissection, uncontrolled hypertension, myocardial infarction and aneurysms.

It is not recommended for people who have previously demonstrated hypersensitivity to drug.

It is not advised to use this medication throughout obstetrics, pregnancy

and breastfeeding because it is unknown whether it goes into breast milk.

Because of additive sedation, studied cases who are intoxicated with ethanol must be treated with caution. (**Brincket al,.2018)**

6. Fentanyl

6.1. Fentanyl Pharmacology

Fentanyl's pharmacological impacts are mediated by activation of mu opioid receptor, which has low affinity for delta and kappa opioid receptors. Unlike morphine, that is alkaloid extracted from opium poppy, fentanyl is synthetic, lipophilic phenylpiperidine opioid agonist. Fentanyl is highly effective MOR agonist, with binding affinity of 1.35 nM at recombinant human MORs, which is comparable to that revealed using guinea pig membranes. **(Azzam et al,.2019)**.

There has been wide range of observed fentanyl binding affinities for MOR, which most likely reflects distinctions in radio ligand, species, assay and tissue used. This affinity resembles morphine binding at MOR. **(Azzam et al,.2019)**.

Furthermore, elimination/clearance half-life of fentanyl and morphine is comparable, with t1/2 of two-four hours for fentanyl and two hours for morphine. When compared to morphine, fentanyl has faster onset, much shorter duration of analgesic action and greater analgesic potency.

Human and preclinical researches show that fentanyl is fifty times more potent than morphine, however most physicians recognize that fentanyl is approximately one hundred times more potent than morphine. Furthermore, fentanyl crosses blood-brain barrier quickly, leading to greater analgesic potency, as evidenced by half-life of five min for equilibrium between plasma and cerebrospinal fluid **(Rickli et al,.2018)**.

Binding affinity and half-life do not clarify fentanyl's higher analgesic potency and faster onset when compared to morphine. **(Barbani et al,.2018)**.

Fentanyl is poorly absorbed from GI tract and yet is completely metabolized, with renal excretion accounting for less than ten percent of dose. Predominant degradative route in humans, accounting for ninety nine percent of fentanyl metabolism, is piperidine N-dealkylation to norfentanyl, inactive metabolite. Numerous adverse drug conversations are caused by CYP3A-dependent metabolism, such as HIV protease inhibitor ritonavir **(Garnock et al,.2016)**.

Opioids' ability to produce distinct impacts on nociception, respiratory depression and constipation is most likely due to combination of their chemistry, which influences their distribution within central nervous system, metabolism, receptor selectivity and receptor signaling **(Quirion et al,.2020)**.

6.2Indications

Fentanyl is powerful synthetic opioid that is equivalent to morphine however produces more analgesia. This powerful pharmacologic agent is typically fifty to one hundred times stronger. Single dose of one hundred micrograms can provide analgesia similar to about ten mg of morphine. Fentanyl, on other hand, has very different characteristics and pharmacokinetics. **(Ramoset al,.2021)**.

Because of its versatility in titration scenarios, it is commonly administered

like sedative via drip. When used as sedative

In studied cases who require mechanical ventilation, it may necessitate large doses. Fentanyl is option for perioperative pre-medication for processes that are likely to cause discomfort. Finally, fentanyl use can be used to cure epilepsy. **(Armenian et al,.2018)**.

6.3Adverse effects of fentanyl

Fentanyl's side effects are similar to those of heroin, causing euphoria, confusion, respiratory depression, drowsiness, nausea, visual disturbances, dyskinesia, hallucinations, delirium, subset of latter known as "narcotic delirium," analgesia, constipation, narcotic ileus, muscle rigidity, constipation, Alcohol and other drugs can exacerbate fentanyl's side effects, generating multi-layered clinical scenarios that can be difficult to manage. When these substances are combined, they cause undesirable conditions that complicate studied case's prognosis.**(Armenian et al,.2018)**.

7. Dexamethasone

Dexamethasone has wide range of medical applications. Dexamethasone is effective glucocorticoid with little to no mineralocorticoid activity. (**Williams et al,.2018).**

7.1. Dexamethasone pharmacology

The body responds to dexamethasone in number of ways. It works by inhibiting neutrophil migration and reducing lymphocyte colony proliferation. Capillary membrane also becomes less permeable. Lysosomal membranes have become more stable. Prostaglandins and some cytokines are inhibited. Dexamethasone has been shown to enhance surfactant levels and improve pulmonary circulation. Dexamethasone is primarily excreted in urine after being metabolized by liver. Dexamethasone has half-life of about three hours **(Williams et al,.2018).**

7.2Dexamethasone as adjuvant to Peripheral nerve block

Mechanism underlying extension of block duration following use of dexamethasone like adjuvant to LA is multidirectional and extremely complex.

Respiratory depression and obstructive airway disease, liver cell failure and hypersensitivity to any common drug delivery excipient.

Dexamethasone in dose of four mg, administered perineurally with LA, prolongs impact of short- and medium-acting LAs by three-five hours and long-acting LAs by seven-nine hours. Furthermore, higher dose of dexamethasone did not result in significant variation in action. In order to prolong duration of analgesia, dexamethasone reduces onset time of block and, according to research, has protective impact on nerve cells. **(Gola et al,.2020).**

When dexamethasone is added to Bupivacaine, former crystallizes in solution, posing potential risk to studied case, rendering this mixture unsuitable for clinical use. According to current research, intravenous administration of dexamethasone has same impact as perineural delivery in terms of prolonged analgesia. **(Emelife et al,.2018)**

Conclusion

our review article has focused in ultra-sound guided supraclavicular brachial plexus block as embryology and anatomy of brachial plexus and detailed the ultra-sound

guided supraclavicular block as it is considered the most important anaesthetic method for upper limb surgeries. Complete details about the technique, indications and complications ofultra-sound supraclavicular block.

The research investigated safety and efficacy of various additives, namely dexmedetomidine, ketamine, fentanyl, and dexamethasone, when added to bupivacaine in ultrasound guided supraclavicular brachial plexus block in order to evaluate onset and duration of sensory and motor block and to estimate the efficacy of each drug in reducing the post operative pain

So, further researches needed using various doses of this adjuvants and using other adjuvants as clonidine, neostigmine and magnesium sulphate

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