Complications of Brachial Plexus Block. A Systematic Review

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Preface

Not all books include a preface, as you can combine the information the preface covers into the Introduction. However, some authors like to separate it. This is written by the author of the book, and appears before the Introduction. The preface usually deals with the background to the book. The reason for it being written. It can also include what it doesn't include as well!

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Dr. Krishna Prasad G V

Contents

ABSTRACT

Background: The brachial plexus block (BPB) is very popular in providing pain relief and operative anesthesia to the upper limb. There are various techniques of BPB depending upon the site of approaching the plexus; however, there has been a controversy related to the choice of the best technique in terms of benefits as well as complications. **Objective:** Thissystematic review was performed to evaluate the data from randomized controlled trials (RCTs) on the rates of complication in each of these techniques of BPB.

Methods: The literature was searched from PUBMED, EMBASE, Google Scholar, and Cochrane Library from 2001 till the year 2020. All the available RCTs that met the criteria were included. Data were independently extracted from the included studies by one of the authors and entered in the Microsoft Excel sheet.

Results: Our search strategy identified 73 RCTs comprising 5819 patients. Of these, the majority of the RCTs were published in the year 2018 (n=10) and performed with the supraclavicular BPB approach (n=21). Neurological complications (n=41) were reported by most of the studies that include Horner syndrome (n=32), paresthesia (n=21), followed by respiratory complications (n=23) comprising hemi-diaphragmatic paralysis in 19 studies, and cardiac complications (n=13), that includes hypotension and bradycardiac events (HBE) (n=11). Other complications such as hoarseness (n=8), phrenic nerve palsy (n=4), and many more complications related to local anesthesia were also reported in studies.

Conclusion: The most common complications reported in most studies areHorner's syndrome, paresthesia, followed by the occurrence of HDP, and HBE. Most of the complications were associated with Interscalene BPB and the

use of dexmedetomidine was found to be associated with the occurrence of HBE.

Keywords: *Approaches, Brachial plexus block, Complications, Shoulder surgery*

INTRODUCTION

Brachial plexus is the network of nerves passing from the spinal cord to supply the sensation and function to the major part of the upper limb. Surgical anesthesia of the arm from the elbow to the hand is performed by injecting the local anesthetic solution around the brachial plexus named as brachial plexus block (BPB). The block is very popular in providing pain relief and operative anesthesia to the upper limb as it avoids the needs of general anesthesia and the risks associated with it.[1]

The brachial plexus can be approached through a needle from various sites along its course. Depending upon the site of approaching the plexus, type of surgical procedure to be performed, condition, and medical comorbidities of the patient, techniques are divided as the axillary block (AXB) where the skin is pierced in the axilla, interscalene block (ISBPB) where the needle pierces in front of the neck and passes between the scalene muscles, infraclavicular block (IBPB) where the skin below the clavicle is pierced, supraclavicular block (SBPB) in which the skin in the root of the neck above the clavicle is pierced, and retroclavicular block (RBPB). The choice of the best technique is very difficult as it depends upon the preference of the practitioner and efficacy of each technique.[2] A Cochrane systematic review compared the effects of blocking the brachial plexus by injecting local anesthetic in the area below the collarbone (the IBPB) with other techniques and concluded that the IBPB is an effective and safe choice for producing anesthesia of the lower arm.[2]

There has been a controversy related to the choice of the best technique for providing surgical anesthesia to the upper limb as each of these techniques have their benefits as well as complications. Since the BPB alters the integrity of the skin, it is associated with several types of complications such as Horner

syndrome, brachial plexus injury, nerve injury (neuropraxia, neurotmesis), complications associated with local anesthetic toxicity (nausea, vomiting, dizziness, arterial puncture, venous puncture), rare instances of serious complications like pneumothorax, phrenic nerve palsy (PNP), and many more.[3,4] There is also evidence from a systematic review that the use of ultrasound (US) during the block procedure decreases the rates of several serious complications such as pneumothorax, PNP, and vascular injury, and increases block efficiency as the use of ultrasound has made these blocks more safe.[1]

We, therefore, have undertaken a systematic review to evaluate the data from randomized controlled trials (RCTs) on the rates of complication in each of these techniques of BPB.

METHODS

This systemic review comparing the complication rates among various techniques of brachial plexus block was performed according to recommendations from the Preferred Reporting Items for Systemic Reviews and Meta-Analyses statements.[5]

Methodology for Literature Search

This systematic literature review was synthesized by searching databases such as PUBMED, EMBASE, Google Scholar, and Cochrane Library from 2001 till the year 2020. The keywords "Brachial plexus block", "complications", "brachial plexus injury, brachial plexus neuropathies", "axillary block", "supraclavicular", "infraclavicular", "ultrasonic-guided", "nerve block" were used to retrieve the related studies. The above-mentioned databases are readily available for the literature search.

Eligibility Criteria

Inclusion Criteria

The databases were searched for published randomized controlled trials (RCTs) and cross-over trials comparing different techniques or approaches of brachial plexus anesthesia. The RCTs involving modification of these techniques such as the use of any drug to alter the local anesthetic duration, the use of ultrasound or nerve stimulator along with block were also included.The clinical evidence was searched in the form of original peer-reviewed journal articles published in the English language. Clinical and experimental studies were included and the references of the reviewed articles were also searched for the relevant studies wherever necessary to increase the yield.

Exclusion Criteria

Conference papers, book reviews, book chapters, case reports, case series, cross-sectional, case-control, cohort, retrospective study designs, animal studies, cadaver studies, letters to editors, commentaries, newspaper and newsletter articles, expert opinions, and theses or dissertations were not used. Articles that are not published in English were excluded. Studies were also excluded based on their methodological quality assessment.

Types of Participants

Participants older than 18 years of age and undergoing surgery of the upper limb with any of the techniques of BPB and demonstrating the complications as their primary or secondary outcome were included.

Types of Intervention

We have included those RCTs in which the different techniques (either two or three) of BPB were compared to each other. The RCTs that have focused on only one of the techniques of BPB and compared the various intervention within one technique were also included.

Various intervention includes:

- Comparison of two or three techniques of BPB (ISBPB, SBPB, IBPB, AXB, and RBPB)
- Comparison of peripheral nerve stimulator guided or ultrasound-guided BPB
- Comparison of different local anesthesia (LA) in BPB (lignocaine, bupivacaine, ropivacaine, and chloroprocaine)
- Comparison of different volumes of LA in BPB
-

- Comparison of addition of some drugs like dexamethasone to LA in BPB
- Comparison of perineural and perivascular LA in BPB
- Comparison of single-shot injection and multiple injections of LA
- Comparison of single injection with continuous catheter.

Data Extraction and Management

Data were independently extracted from the included studies by one author using uniform data extraction and any discrepancies were resolved by discussion. Extracted data were independently entered into an Excel spreadsheet.

Data items extracted

The following information was extracted from each trial:

- The first author of the study, year of publication, number of enrolled patients, American Society for Anesthesiology (ASA) status, clinical setting, duration of follow-up
- Type of LA regimen (lignocaine, bupivacaine, ropivacaine, and chloroprocaine), technique of LA injection (single injection, multiple injection), LA volume and concentration used
- The technique used in the study (ISBPB, IBPB, RBPB, SBPB, and AXB) and the technique of block needle insertion (ultrasound-guided, in-plane, out-of-plane)
- Complications of the techniques, complications related to LA toxicity, and success/failure rate of the study.

Outcome Definitions

Primary outcome measures

The pre-specified primary outcome was the rates of complications (paresthesia/pain, dyspnea, PNP, Horner syndrome, vascular puncture, pneumothorax, and many more) associated with each of the techniques of the BPB.

Secondary outcome measures

ASA status of patients in various RCTs, successful/failed blocks, onset time, duration of anesthesia, and duration of sensory and motor blocks

Statistical Analysis

The articles were stratified based on the type of technique chosen in the study and their related complications. The data obtained was entered in the Microsoft Excel spreadsheet. Characteristics of the retained studies sorted by the first author name and year of publication were presented in a tabular form. These tables will have information relating to the clinical setting of the study, number of patients, duration of follow-up of the study, LA regimen, onset and duration of LA, success/failure rates, techniques used, and the various complications and adverse effects associated with different techniques and LA toxicity respectively.

RESULTS

Comprehensive Literature Search

Our search strategy identified 73 studies. The titles and abstracts of 382 studies were screened for eligibility. After removing duplicates, irrelevant studies, animal studies, and non-English articles (n=141), 241 full-text articles were assessed for eligibility. After reading the full text of these studies, more studies (n=168) were excluded as they were non-RCTs and conducted among children. The remaining 73 RCTs were included in this systematic review. The flow chart of the study inclusion process is shown in [Figure 1].

Description of the Included Studies (n=73)

The study characteristics involving the year of publication, ASA status, clinical setting, number of patients, and the duration of follow-up assessment are shown in [Table 1].

(a) **Year of publication**

A total of 73 studies were included in the systematic review. Majority of the studies were published in the year 2018 (n=10), followed by 2019 (n=9), and 2015 (n=8). The year distribution of the studies is as follows: 2001 (n=1),[6] 2003 (n=3),[7,8,9] 2005 (n=4),[10,11,12,13] 2006 (n=1),[14] 2007 (n=1),[15] 2008 (n=4),[16,17,18,19] 2009 (n=4),[20,21,22,23] 2010 (n=3),[24,25,26] 2011 (n=4),[27,28,29,30] 2012 (n=2)[31,32] 2013 (n=1),[33] 2014 (n=2),[34,35] 2015 (n=8),[36,37,38,39,40,41,42,43] 2016 (n=6),[44,45,46,47,48,49] 2017 (n=3),[50,51,52] 2018 (n=10),[53,54,55,56,57,58,59,60,61,62] 2019 (n=9),[63,64,65,66,67,68,69,70,71] and 2020 (n=7),.[72,73,74,75,76,77,78]

(b) Number of patients

The 73 studies involving a total of 5819 patients were included in the present systematic review.

(c) ASA status 2.2.12

Almost all the studies have given the ASA status of the patients. A total of 27 studies have included patients till ASA III,[6,8,15,16,19,21,23,24,25,29,33,34,35,36,38,44,45,46,47,50,51,52,54,55,56,57,58,67,74] and 29 studies have included patients till ASA II.[7,11,14,18,22,28,31,37,40,42,53,56,59,60,61,62,63,64,65,66,68,69,70,71,72,75,76,77,78] Mean ASA was given in three studies,[17,27,39] and one study was conducted among healthy volunteers.[73]

(d) Duration of follow-up:

At 15 minutes, post-block assessment interval was done in two studies,[30,32] at 30 min, post-block assessment was done in 25 studies.[7,12,13,14,15,19,20,26,35,43,44,45,50,51,52,53,62,64,69,70,71,74,75,76,77]Within 24 hrs, post-block assessment was done in 14 studies,[16,20,33,37,42,49,56,59,60,61,63,66,68,78] and more than 24 hrs post-block assessment was done in rest of the 32 studies.[Table 1]

(e)Type of block drug used and additional use of drugs

Seventeen studies have used combination of two or three block drugs.[14,20,26,27,34,35,37,40,42,46,53,54,55,64,67,74,75] Rest of the studies (n=56) have used one of the following LA drug (bupivacaine, ropivaciane, lidocaine, mepivacaine).A total of 22 studies have use epinephrine as vasoconstrictor.[11,14,15,17,19,20,23,27,29,32,35,36-38,41,44,45,53,54,57,64,73]Additional use ofclonidine,[70] MgSO4,[62,66,68] fentanyl,[56,60,77]dexamethasone,[25,54,76,78] and dexmedetomidine,[55,56,59,60,62,70,75,76,77] were done in several studies [Table 2].

(f)Technique of LA injection

A total of 30 studies,[6,7,8,10,12,13,16,19,21,24,29,30,32-34,36-38,41,42,43,44,49,50,53,68-70,72,78] have used the single technique of LA injection, five studies,[7,11,19,35,71] have used both single and multiple injection techniques, and in rest of them (n=58), multiple injection technique was used [Table 2].

(g)Approach used in studies

A total of 21 studies were based on SBPB approach,[6,22,25,29,35,39,41,42,53,56,59,60,61,66,68,70,71,75,76,77,78]15 studies were based on ISBPB approach,[14,16,21,27,28,30,31,33,38,44,48,49,51,65,72] seven studies depicted the AXB approach,[8,9,11,15,26,32,34] and six studies were based on IBPB approach .[17,19,52,54,62,73]

Rest 24 studies have shown the comparison of two approaches. Comparison of ISBPB and SBPB approaches was done in eight studies,[40,43,46,47,50,57,63,70] ISBPB and AXB in one study,[13] ISBPB, SBPB, and IBPB in one study,[37] AXB and IBPB in three studies,[7,10,12] SBPB, IBPB and AXB in two studies,[23,45] SBPB and IBPB in four studies,[18,20,24,36] IBPB and RBPB in one study,[67] SBPB and CBPB in two studies,[64,74] ISBPB, SBPB and suprascapular in one study,[59]and in one study, name of the BPB,[55] is not given [Table 3].

(h)Technique of block needle insertion

A total of 40 studies,[16,17,19,20,22,23,25,27,28,29,30,31,32,36,37,38,39,40,41,43,44,45,47,48,49,50,51,52,53,54,55,56,57,58,60,61,67,71,72,76] have used the in-plane technique of block needle insertion, both in and out-plane techniques were used in two studies.[18,46] In one of the study, either In-plane or out-plane technique was used,[64] depending on the operator, and in rest of the studies (n=30), they have not

clearly mentioned [Table 3].

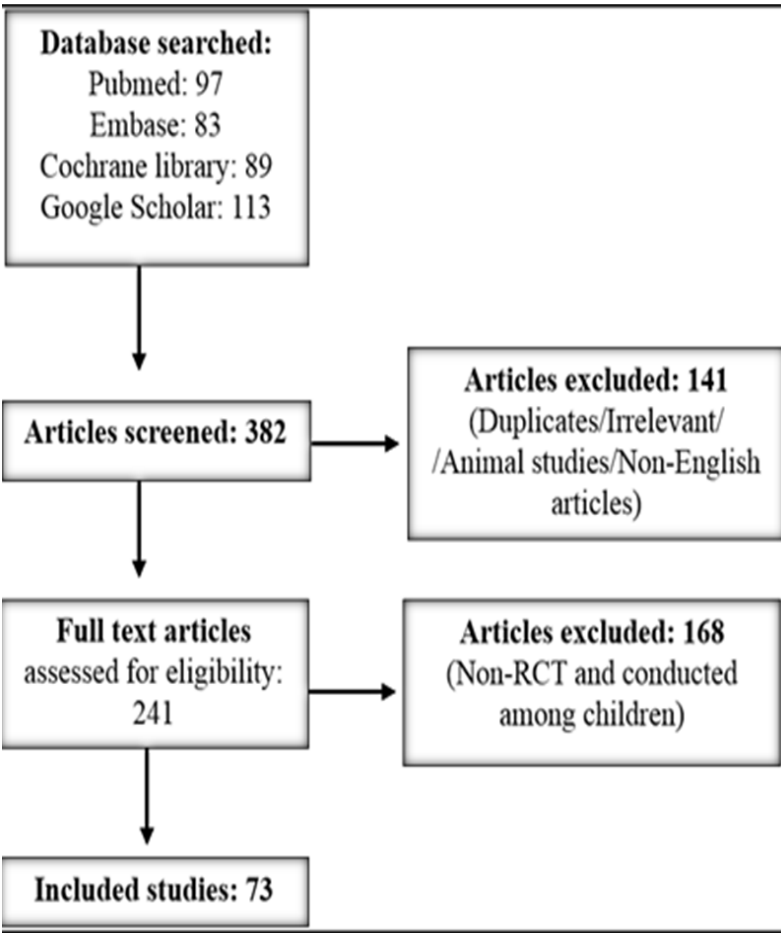

Figure 1: The flow chart of the study inclusion process

Table 1: Showing the characteristics of the included studies (n=73)

Study	Number of patients	ASA (I/II/III)	Clinical setting	Follow-up assessment
Mak PHK et al (2001),[6]	30	I/II/III	Upper limb surgery	10 min
Deleuze A et al (2003),[7]	100	I and II	Arthroscopic shoulder surgery	5, 10, 15, 20, 25, and 30 minutes
Serradell A et al (2003),[8]	114 (38/38/38-36ml/28ml/20 ml group)	17/16/5 (36 ml group) 12/18/8 (28 ml group) 12/18/8 (20 ml group)	Elective distal upper limb surgery	40, 50 and 60 min
March X et al (2003),[9]	100		Elbow/ forearm/ wrist/hand: 9/2/10/28 (Group A) and 4/5/8/30 (Group H)	40 min
Rettig HC et al (2005),[10]	60 (Axillary-30 and IBPB-60)		Upper arm-proximal/ distal/wrist or hand/other: 13/5/9/3(IBPB), 7/4/17/2 (axillary)	5, 10, 15, 20, 30 and 60 min

Liu FC et al (2005),[11]	90 (nerve stimulator-guided and double-injection (ND) group-30), US-guided and double-injection (UD) group-30), and US-guided and single-injection (US) group-30	I/II	Elective surgery of the hand, wrist, or forearm	40 min
Heid FM et al (2005),[12]	60	-	Upper limb surgery distal to the elbow	30 min
Soeding PF et al (2005),[13]	40	-	Upper Limb Surgery	10 and 30 min
Pippa P et al (2006),[14]	60	I/II	Shoulder capsuloplasty	30 min
Chan VWS et al (2007),[15]	NS-62 US-64 USNS-62	I/II/III	Elective hand surgery	30 min
Riazi S et al (2008),[16]	60 40 (group I-20 and group II-20)	7/12/1 (group I) 5/12/3 (group II)	Shoulder surgery	30 min, 60 min, 120 min, 12 hrs and 24 hrs
Dhir and Ganapathy,[17] (2008)	66 (TR-22, ST-22, US-22)	1.8±0.7 (TR) 2.2±0.5 (ST) 2±0.(US)	Elective hand surgery	3 weeks
De Jose Maria B et al (2008),[18]	80 (SBPB-40 and IBPB-40)	I/II 29/11 (group I) 28/11 (group S)		1 week
Tran DQH et al (2009),[19]	88 (single injection-44, double injection-44)	I/II/III 39/5/0-single injection 36/6/2-double injection	Upper limb surgery	5,10,15, 20, 25, 30 min

Koscielniak-Nielsen JZ et al (2009),[20]	120 (Group I-60 and group II-60)		Upper extremity surgery	20 and 30 min
Renes SH et al (2009),[21]	30	I/II/III 3/11/1 (US-ISB) 4/11/0 (NS-ISB)	Elective shoulder surgery	5, 10, 15, 30, 180, and 360 minutes after ISB
Renes SH et al (2009),[22]	60	I/II 13/17 (US) 10/20 (NS)	Elective elbow, forearm, wrist, or hand surgery	5, 10, 15, 30, 180, and 360 min
Tran DQH et al (2009),[23]	120 SBPB (n = 40), IBPB (n = 40), or AXB (n = 40)	I/II/III: 28/10/2 (SBPB) 29/10/1 (IBPB) 26/13/1 (AXB)	Upper extremity surgery of the elbow, forearm, wrist, and hand	
Yang CW et al (2010),[24]	100 (group S-50 and group I-50)	I/II/III: 28/20/2 (group S), 30/20/0 (group I)	Upper limb surgery-Hand/wrist/ forearm/elbow: 16/4/23/8 (SBPB), 20/4/17/9 (IBPB)	-
Parrington SJ et al (2010),[25]	45 (normal saline group-21) (dexamethasone group-24)	I/II/III 6/12/3 (normal saline group) 12/11/1 (dexamethasone group)	Elective hand or forearm surgery Elbow/ forearm/ hand: 0/4/17 (Group 2), 1/2/21 (Group 1)	1, 7 and 14 days
Gianesello L et al (2010),[26]	100	-	Upper limb surgery	30 min
Thomas LC et al (2011),[27]	41 (US group-22) (NS group-19)	2 6±0.5 (US group) 2 6±0.4 (NS group)	Orthopedic shoulder surgery	2 weeks

Lee JH et al (2011),[28]	60 (group-30) (group 10-30)	I/II 13/17 (group 5) 17/13 (group 10)	Arthroscopic rotator cuff repair surgery	30 min, 12 hrs, 24 hrs and 48 hrs

Subramanyam R et al (2011),[29]	72 (lateral approach-35) (medial approach-37)	I/II/III 18/15/2 (lateral approach) 18/16/3 (medial approach)	Hand or wrist: 34 (lateral), 32 (medial) Forearm: 0 (lateral), 5 (medial) Elbow: 1(lateral), 0(medial)	7 days
Sinha SK et al (2011),[30]	30	-	Arthroscopic shoulder surgery	15 min
Behr A et al (2012),[31]	150 (control-50, IMB-50, EMB-50)	I/II-35/15 (control), 38/12 (IMB), 31/1 (ENB)	Arthroscopic surgery	2, 4, 6, 8, 12, 24, and 36 h
Bernucc F et al (2012),[32]	50 PV(n = 25) or PN (n = 25)	-	Upper extremity surgery	10 and 15 min
Kaya M et al (2013),[33]	60 (group 1-30, group 2-30)	I/II/II-10/19/1 (group 1), 13/14/ group 2)	Modified radical mastectomy	24 hrs
Saracoglu S et al (2014),[34]	60	I/II/III	Hand or forearm surgery	90 min
Arab SA et al (2014),[35]	96	I/II/III	Arteriovenous fistula creation or superficialization	20 min and 30min
Yazer MS et al (2015),[36]	64 (SBPB-32, IBPB-32)	I/II/III-15/15/2 (SBPB), 20/10/2 (IBPB)	Hand/wrist/ forearm/elbow: 14/12/2/4 (SBPB) and 13/12/4/3 (TII-IBPB)	30 min and 1 week

Bharti N et al (2015),[37]	60 (SBPB-21, IBPB-20, ISBPB-19)	I:II- 16:4 (SBPB group), 19:1 (IBPB group), 18:2 (ISBPB group)	Upper limb surgery	30 min and 24hrs
Bjørnholdt KT et al (2015),[38]	61 (LIA group-30, ISBPB-31)	I/II/III-5/20/5 (LIA group) 4/23/4 (ISBPB)	Shoulder replacement surgery	24 hrs and 3 days
Singh S et al (2015),[39]	102	Mean ASA: 1.28±0.45 (US),1.21±0.41 (NS)	Upper limb surgery	30 min
Ryu T et al (2015),[40]	ISBPB-47; SBPB group-46	I/II-25/22 (ISBPB), 27/19 (SBPB)	Arthroscopic Shoulder Surgery	20 min
Liu GY et al (2015),[41]	60	-	Distal upper limb surgery	
Kooloth RA et al (2015),[42]	60	I/II	Upper limb surgery	30, 45 min, 1 hr and 24 hours
Petrar SD et al (2015),[43]	64	-	Right-sided upper arm surgery	30 min
Palhais A et al (2016),[44]	40 (20 in each group)	I/II/III-6/12/2 (conventional injection), 13/6/1 (extrafascial injection)	Upper limb surgery	30 min
Stav A et al (2016),[45]	101 (SBPB-37, IBPB-23, AXB-34)	I/II/III-7/1/29 (SBPB), 4/4/15 (IBPB), 6/3/25 (AXB)	Upper limb surgery	30min
Wiesmann T et al (2016),[46]	120	I/II/III	Elective arthroscopic shoulder surgery	1 week
Koh WU et al (2016),[47]	Continuous interscalene (n = 38) or supraclavicular block (n = 37)	I/II/III	Open rotator cuff surgery	30 minutes, 1 hour and 14 hours

Ghodki and Singh (2016),[48]	60 ((NS-30 and US-30 patients)	-	Shoulder arthroscopy	5, 10, 15, 20 min and 1 day (for HDP)
Stundner O et al (2016),[49]	30	-	Shoulder surgery	24 hrs
Kim BG et al (2017),[50]	49 ISBPB-25 SBPB-24	I/II/III-13/10/2 (group I), 15/6/3 (group S)	Shoulder surgery	30min
Albrecht E et al (2017),[51]	70 (intrafascial-35,extrafascial group-35)	I/II/III- 15/8/11 (intrafascial group), 18/1/15 (extrafascial group)	Elective major shoulder surgery	30 min, 1 and 2 days
Oztur NK et al (2017),[52]	100 (group R-50, group C-50)	I/II/III-26/20/4 (group R), 23/18/9 (group C)	Upper limb surgery	30 min
Kang RA et al (2018),[53]	36 (CP group-18, NC-18 group)	I/II-14/4 (CP group), 16/2 (NC group)	Upper limb surgery	10 min and 30min
Bravo D et al (2018),[54]	360 (2mg-119, 5mg-120, 8mg-120)	I/II/III- 65/50/4 (2mg), 66/52/2 (5mg), 60/56/4 (8mg)	Upper extremity surgery (hand/ wrist/forearm/ elbow- 2mg-48/46/17/8, 4mg-65/33/17/5, 8mg-56/36/21/7	1 and 2 weeks
Hong B et al (2018),[55]	102	I/II/III	Upper limb surgery	
Hamed MA et al (2018),[56]	60 (20 in each group)	I/II-18/2 (group D), 17/3 (group F), 17/3 (group C)	Orthopaedic surge	24 hrs
Aliste J et al (2018),[57]	44	I/II/III 3/10/0 (ISB) 8/14/0 (SBPB)	Arthroscopic shoulder surgery	6,12 and 24 hrs

Auyong DB et al (2018),[58]	189	I/II/III 16/41/6 (ISBPB) 11/50/2 (SBPB) 13/47/3(Suprascapuar)	Arthroscopic shoulder surgery	24hrs
Sinha C et al (2018),[59]	90	I/II 35/10 (Group I) 31/14 (Group II)	Forearm/hand: 25/20(Group I), 22/23 (Group II)	48 hrs
Dharmarao PS et al (2018),[60]	80	I/II	Elective upper limb surgeries	24hrs
Mangal V et al (2018),[61]	90	I/II	Elective upper limb surgeries	150 min
Elyazed MAM et al (2018),[62]	105	I/II	Hands, wrist, and forearm surgery	30 min
Karaman Tet al (2019),[63]	62	I/II 14/17 (ISBPB) 16/13 (SBPB)	Upper limb surgery	24hrs
Sivashanmugam T et al (2019),[64]	40 (SBPB-20, Costoclavicular-20)	I/II 13/7 (SBPB), 11/9 (costoclavicular)	Right-sided upper extremity surgery.	30 min
Ayyanagouda B et al (2019),[65]	60 (extrafascial-30, intrafascial-30)	I/II-20/9 (extrafascial), 16/14 (intrafascial)	Proximal upper limb surgeries	-
Kaur S et al (2019),[66]	105 (Group 1=34), (Group II-34), (Group III-31)	I/II 25/10 (group I), 17/18 (group II), 27/8 (group III)	Elective upper limb surgery (forearm and hand)	8hrs, 12 hrs and 24 hrs
Blanco AFG et al (2019),[67]	109 (RBPB-53, IBPB-56)	I/II/III-27/24/2 (RBPB), 22/25/9 (IBPB)	Upper extremity surgery	48 hrs
Elhusein AKA et al (2019),[68]	40 (Group I-20) (Group II-20)	I/II	Elective upper limb surgery	24 hrs

Singh and Singham (2019),[69]	60	I/II 20/10 (ISBPB) 19/11 (SBPB)	Elective and emergency shoulder surgeries	30min
Singh and Singham (2019),[70]	90	I/II 22/8 (CL) 23/7 (CD) 23/7 (DX)	Upper extremity surgeries	30 min
Refaat S et al (2019),[71]	36	I/II	Upper extremity surgeries	30 min
Patel MA et al (2020),[72]	155 (LB 133mg, N=69; LB 266mg, N=15; placebo, N=71).	I/II/III- 15/36/18 (LB 133mg), 14/37/20 (placebo)	Total shoulder arthroplasty or rotator cuff repair	Through 120 hrs, 7th day and 14th day
Kasine T et al (2020),[73]	26	-	Healthy patients	3 weeks
Luo Q et al (2020),[74]	112	I/II/III (SBPB-49.1%, 41.8%, 9.1%) (CBPB-45.5%, 43.6%, 10.9%)	Upper limb surgery	30 min
Sachdev S et al (2020),[75]	60	I/II	Upper limb surgeries	30
Singh N et al (2020),[76]	60	I/II	Elective upper-limb surgery	50
Lotfy ME et al (2020),[77]	90	I/II	Upper limb surgeries	30
Youssef MY et al (2020),[78]	120 (30 in each group)	I/II	Upper limb surgeries	24 hrs

Table 2: Showing the characteristics of the block drug and its related complications (n=73)

Study	Block drug	Technique of local anesthetic injection	Onset time and duration of block	Complications related to local anesthetic toxicity
Mak PHK et al (2001),[6]	Bupivacaine 0.375% 0.5 ml. kg^{-1}	Single	-	-
Deleuze A et al (2003),[7]	40 ml of ropivacaine 0.75% Volume: 5 ml	Single-IBPB Triple-Axillary	Onset of sensory and motor block: 6 ±2 and 17.5 ±3 (axillary) 17±9 and 21±8 (SBPB) Block performance time: 2.5±1.9 min (IBPB) , 6.0±2.8 min (AXB)	Axillary artery and axillary vein puncture: 1 patient (IBPB)
Serradell A et al (2003),[8]	Group 1: 36 (n=38) ml Group II: 28 (n=38) ml Group III: 20 ml (n=38) of mepivacaine 10 mg ml±1	Single	Mean duration of analgesia/ Mean block performance time, min : 246.2 and 7.6 (36 ml group), 244.7 and 6.6 (28 ml group), 230.9 and 6.1(20 ml group)	Venous puncture: 6 (36 ml group), 6 (28 ml group), 7 (20 ml group),

March X et al (2003),[9]	40 ml mepivacaine of 1%	Multiple	Onset time / Block performance time (min): 16 ±8 and 8±4 (Group A), 21 ±9 and 11±4 (Group H) Total anesthetic time (min): 24 ±8 (Group A), 33 ±10 (Group H)	Vascular puncture (%): 22 (Group A), 8 (Group H) (P<0.05)
Rettig HC et al (2005),[10]	Ropivacaine 7.5 mg/ml, at a dose of 0.5 ml/kg (3.75 mg/kg)	Single	Block procedure time (min): 9.2 (IBPB) and 5.3 (axillary)	PONV/blood aspiration: 1/8 patients (IBPB) and nil/6 patients (axillary)
Liu FC et al (2005),[11]	0.5 ml kg-1 of 1.5% lidocaine with 5 µg kg-1 epinephrine	Double injection (ND and UD groups) Single (US group)	Duration of block performed (min): 8.2 ± 1.5 (ND), 6.7 ± 1.3 (UD), 6.5 ± 1 (US) Duration of operation (min): 45.7 ± 12.1 (ND), 46.3±11.5 (UD), 48.7 ± 12.8 (US)	Tourniquet pain/vessels puncture/ hematoma: 7%/10%/3% (ND), 3%/0%/0% (UD), 7%/0%/0% (US)
Heid FM et al (2005),[12]	40ml ropivacaine 0.75% (300mg)	Single	80% of the vertical IBPB patients showed a complete sensory block in the radial nerve area, compared to 36.7% of the HAP	Accidental venous puncture: 1 patient (both groups)

Soeding PF et al (2005),[13]	Ropivacaine (0.75% solution for interscalene block, and 0.6% for axillary block Dose- 3 mg/kg	Single	Duration of block: 10.3±0.6 (control) and 11.2±0.6 (US-guided)	-
Pippa P et al (2006),[14]	Group I: 60ml of bupivacaine 0.25% (with 150µg epinephrine, i.e. 2.5µgml^{-1}) and lidocaine 1% Group II: 30ml of bupivacaine 0.50% (with 150µg epinephrine, i.e. 5µgml^{-1}) and lidocaine 2%.	Multiple	Motor block: 25 min and 15 min in Groups I and II, respectively ($P<0.05$).	Dysphonia: 20 patient
Chan VWS et al (2007),[15]	2% lidocaine with 1:200,000 epinephrine and 0.5% bupivacaine (total 42 ml),	Multiple	The block procedure time: 9.3 ± 4.0 min (group US) vs 11.2 ± 4.4 min (Group NS), and 12.4 ± 4.8 min (Group USNS) ($P = 0.01$)	Local bruising/ pain: 8 patients/10 patients (NS), 2/3 patients (US), 0/3 patients (USNS)
Riazi S et al (2008),[16]	ISBPB of either 5 ml (low volume-group I) or 20ml of ropivacaine 0.5% (standard volume-group II)	Single	-	

Dhir and Ganapathy (2008), [17]	40 millilitres of 15mg/ml mepivacaine with 2.5mg/ml adrenaline Group TR: LA injected with needle' Group ST-catheter; Group US- LS was observed ultrasonographically	Multiple	Total motor block in all nerves after 20min (out of 10): 4.8±2.9 (TR), 6.3±2.2 (ST), 6.8±2 (US). Time to achieve complete motor and sensory block (min) 28.1±8.8 (TR), 23.9±8.7 (ST), 21.1 ±7.8 (US)	-
De Jose Maria B et al (2008), [18]	GA with 8% sevoflurane Block with ropivacaine 0.5%, up to a maximum volume of 0.5 ml/kg)$^{-1}$ Volume of ropivacaine 6 ± 2 ml	Multiple	Mean time: 13 min in IBPB and 9 min in SBPB. The duration of the sensory block was 6.5 ± 2 h and of the motor block was 4 ± 1 h.	Accidental puncture o-f the axillary artery-2 patients (IBPB)
Tran DQH et al (2009), [19]	Single-injection (n = 44) or double-injection (n = 44) 3 ml xylocaine 1% and 35 milliliters of lidocaine 1.5% with epinephrine 5 Kg/ml	Single and double	Onset time, mean, min: 19.4 (single), 19.3 (double) Total anesthesia-related time, mean, min: 24.5 (single), 24.7 (double) Performance time, mean, min 5.1 (single) 5.8 (double)	-

Koscielniak-Nielsen JZ et al (2009),[20]	Equal volumes of ropivacaine 7.5mg/ml and mepivacaine 20 mg/ml with adrenaline 5mg/ml	Multiple	Block performance time (min): 5.0±1.6 (IBPB) and 5.7± 1.6 (SBPB)	Vessel puncture: 1 patient (IBPB) and 1 patient (SBPB)
Renes SH et al (2009),[21]	10 ml of ropivacaine 0.75%	Single	Onset time: 30 min	-
Renes SH et al (2009),[22]	20 ml of 0.75% ropivacaine	Multiple	-	-
Tran DQH et al (2009),[23]	35 ml lidocaine 1.5% with epinephrine 5 Kg/ml (IBPB) 7ml lidocaine 1.5% with epinephrine 5 Kg/ml (AXB) 35ml lidocaine 1.5% with epinephrine 5 Kg/ml (SBPB)	Single	Mean onset time: 18.2min (SBPB), 18.5 min (IBPB), 17.8 min (AXB) Total anesthesia-related time: 23.1 min (SBPB), 23.9 (IBPB), 25.5 min (AXB)	Vascular puncture: 1 (2.5) (SBPB), 1 (2.5) (IBPB), 1 (2.5) (AXB)
Yang CW et al (2010),[24]	30 ml 0.5% ropivacaine	Single	Duration of sensory block: 763±202 (SBPB), 827±175 (IBPB) Duration of motor block: 774±231 (SBPB), 828±210 (IBPB)	Vascular puncture: 8 patients (SBPB), 7 (IBPB)
Parrington SJ et al (2010),[25]	Group 1: 30 ml mepivacaine 1.5% plus 2 ml normal saline. Group 2: 30 ml mepivacaine 1.5% plus dexamethasone 8 mg (4 mg/ml),	Multiple	Median duration of analgesia: 332 mins (Group 2), 228 mins (Group 1) (P = 0.008)	Nausea on POD 1/ vomiting at POD 7/ bruising at injection site POD 14: 10%/0/5% (Group 1), 5%/5%/6% (Group 2)

Gianesello L et al (2010),[26]	0.5% bupivacaine and 2% lidocaine (o.5ml/kg/body weight)	Multiple	Block performance time: Group I-9.8±2.3 and Group II-4±1.2	Venous puncture: 4 patients (Group I) and 6 patients (Group II)
Thomas LC et al (2011),[27]	20 ml of 1.5% mepivacaine and 20 ml of 0.75% ropivacaine, with 3 mg/ml epinephrine	Multiple	Mean duration of sensory and motor block: 19± 6.2 and 20.2±2.1minutes (NS group) and 12±6.2 and 13.5±2.3 minutes (US group) (P<.02 and P<0.03 respectively)	-
Lee JH et al (2011),[28]	5 (Group 5) or 10 ml (Group 10) of 0.75% ropivacaine	Multiple	Anesthesia time: 151 min (Group 5) and 150 mi (Group 10)	-
Subramanyam R et al (2011),[29]	30-ml local anesthetic admixture (1:1 lidocaine 2% bupivacaine 0.5% with 1:200,000 epinephrine)	Single	The rate of ulnar nerve sensory block at 20 mins: 63% in the lateral group and 62% in the medial group	Bruising/ pain: 26%/6% (lateral approach), 16%/14% (medial approach)
Sinha SK et al (2011),[30]	Either 10 (group I) or 20 ml (group II) of ropivacaine 0.5%	Single	Block performance time, mean ±SD, min: 777.1± 120.5 (group II), 744.9± 173.2 (group I)	-

Behr A et al (2012),[31]	29.5 ml of 0.75 % levobupivacaine Patients receive additionally either saline (control group) or intramuscular buprenorphine 0.15 mg (Group IMB) or epineural buprenorphine 0.15 mg (Group ENB)	Multiple	Duration of sensory block and postoperative analgesia: 856.1 ± 215.2 min and 1,049.7 ± 242.2 min (ENB group), 693.6 ± 143.4 and 820.3 ± 335.3 min (IMB group) or 488.3 ± 137.6 and 637.5 ± 72.1 min (saline)	Postoperative nausea and vomiting/ Artery puncture: 1/1 patient (control), 6/0 patients (INB group), 4/0 patients (EMB group)

Bernucc F et al (2012),[32]	Lidocaine 1.5% with epinephrine 5 Kg/ml (Total volume-32 ml)	Single	Total anesthesia-related time: 27.1 min (PV) and 29.0 min (PN) Performance time, min 8.2 (PV), 15.7 (PN) Onset time, min: 18.9 (PV), 13.8 (PN)	Vascular puncture: 6 patients (24%) (PV) and 0 (0%) (PN); (P = 0.01)
Kaya M et al (2013),[33]	30 ml bupivacaine 0.25 % Group 1: single-injection group 2: control group	Single	Duration of surgery (min) 187 ± 30 (group 1), 181 ± 34 (group 2)	Nausea/ vomiting/ antiemetic requirement: 47 %/43%/43% (Group 1), 83 %/57%/73% (Group 2) (P=0.03)
Saracoglu S et al (2014),[34]	70mg lidocaine followed by 150mg bupivacaine 0.5% in 10ml normal saline (total volume 40ml)	Single	Block performance time: 324.33±85.30 (pen+group) and 272.07±103.53 (pen-group) (p=0.01)	Arterial puncture/ venous puncture: 1/3 patients (pen+group), 1/7 patients (pen-group).

Arab SA et al (2014),[35]	Single injection group (SI): 10 ml of 1.5% lidocaine with epinephrine was injected incrementally, followed by another 20 ml of 0.5% ropivacaine. Triple injection group (TI): LA was injected in 3 aliquots of 10 ml each, each composed of 3.5 ml of 1.5% lidocaine with epinephrine and 6.5 ml of 0.5% ropivacaine	Single and triple	Sensory block of all 5 nerves was significantly better in the TI group (all P < 0.035). Successful surgical anesthesia: 40 patients (SI) and 46 patients (TI) Performance time ± SD (min): 4.67 ± 2.09 (SI), 6.51 ± 2.13 (TI)	Vascular puncture: 1 patient (SI) and 0 patient (TI)
Yazer MS et al (2015),[36]	Lidocaine 1.5% with epinephrine 5µg/ml IBPB-volume-35 ml TII-SBPB-half the volume (16ml)	Single	Onset time, min: 8.9 (SBPB), 17.6 (TII-IBPB) Total anesthesia-related time, min: 18.2 (SBPB), 22.8 (TII-IBPB) Performance time, min: 9.5 (2.9) (SPBP), 5.6 (2.3) (TII-IBPB)	-

Bharti N et al (2015),[37]	0.75% plain ropivacaine and 2% lignocaine-adrenaline (1:200,000) mixture as a single injection of 0.5 ml/kg	Single	Onset of motor block/ Block performance time, min: 16.5±7.9/ 5.2±1.4 (SBPB), 15.4±7.2/ 5.6±1.8 min (IBPB), 21.3±7.6/ 5.9±1.6 (ISBPB) Duration of analgesia: 641.2±68.3 min (SBPB), 654.2±88.5 (IBPB) min, 626.5±82.5min (ISBPB)	-
Bjørnholdt KT et al (2015),[38]	Group LIA: local infiltration analgesia -150 ml ropivacaine 0.2 % with epinephrine intra-operatively Group ISC: interscalene brachial plexus catheter-ropivacaine 0.75 %, 7 ml bolus followed by 48-h 5 ml/h infusion.	Single	-	dizziness, haematoma, sweating, stinging in the axilla, pain in axilla (n = 2), pin prick sensation in the forearm and thumb (n=1)

Singh S et al (2015),[39]	40 ml of 0.25% bupivacaine	Multiple	Mean duration of the block: 286.22 ± 42.339 (US), 204.37 ± 28.54 (NS) (p<0.05) The onset of block was faster in the Group US as compared to Group NS (P=0.007)	Accidental vascular punctures: 7 patients (NS), 1 (US) (P < 0.0001
Ryu T et al (2015),[40]	25 ml of LA containing 12.5mlof1%mepivacaine and 12.5 ml of 0.75% ropivacaine	Multiple	Onset time: 20-min Duration of anesthesia-705min in ISBPB and 733min in SBPB	
Liu GY et al (2015),[41]	40-ml bolus of mepivacaine, 1.5%, with epinephrine, 2.5 µg/ml,	Single	Onset time: 5.67 ± 2.58 (US-guided) and 16.97 ± 7.87 (NS)	Intravascular injection: 1 patient (NS group)

Kooloth RA et al (2015),[42]	Group R (Ropivacaine): 20 ml of 0.75% ropivacaine + 10 ml of normal saline (total volume 30 ml) Group B (Bupivacaine):30 ml of 0.5% bupivacaine.	Single	Mean onset time of motor blockade, min: 14.33+4.92 (Group R), 15.30+5.01 (Group B) Mean duration of motor blockade, min: 480.43±55.26 (Group R), 507.70±56.07 (Group B)	PONV: Group R-2 (6.67%), Group B-4(13.33%)
Petrar SD et al (2015),[43]	30 ml of 0.5% ropivacaine	Single	Sedation for block: 20 (63%) (SBPB), 23 (72%) (ISBPB)	-
Palhais A et al (2016),[44]	20 ml bupivacaine 0.5% with epinephrine 1:200000	Single	Onset time of motor and sensory blocks: 8 and 12 min (conventional) and 17 and 19 min (extrafascial) Duration of motor and sensory block: 1134 and 1026 min (conventional) and 980 and 922 min (extrafascial)	-

Stav A et al (2016),[45]	40 ml of bupivacaine 0.5% with adrenaline 1:200,000	Multiple	Duration: 25.35±9.65 min (AXB), 18.32±6.27 min (SBPB) and 19.48± 7.88 min (IBPB)
Wiesmann T et al (2016),[46]	10 ml of ropivacaine 0.2% followed by continuous application of 4 ml of ropivacaine 0.2%	Multiple	Onset time: 30min Block performance time, min: 7.2±4 (ISBPB) and 8.4±4 (SBPB)
Koh WU et al (2016),[47]	20 ml ropivacaine 0.375%	Multiple	Onset time: 30min Duration of anesthesia-164.7 min
Ghodki and Singh (2016),[48]	10 ml of 0.5% bupivacaine for both groups	Multiple	Sensory onset time/ Block performance time/block duration: 19 min/8 min/548.6 min (NS) and 12min/4.3 min/ 570.1min (US)
Stundner O et al (2016),[49]	Ropivacaine 0.75% (either 20 or 5ml) plus the contrast dye gadopentetate dimeglumine	Single	-
Kim BG et al (2017),[50]	20 ml of 0.375% ropivacaine	Single	Post-operative analgesia: 868 min (SBPB) and 800 min (ISBPB)
Albrecht E et al (2017),[51]	Ropivacaine 0.5% 20 ml through the catheter in 5 ml increments	Multiple	-

Oztur NK et al (2017),[52]	2–4 ml of 1% lidocaine 2 groups: a coracoid approach group (group C) and a retroclavicular approach group (group R)		Onset time, min/ Block performance time, min: : 15.4 ± 6/2.8 ± 1.6 (group R), 18.2 ± 5.1/6.2 ± 2.2 (Group C) Total anesthesia-related time, min: 17.9 ± 2.1 (Group R), 23.9 ± 2.2 (Group C)	Vascular puncture: 0 (Group R) and 1 patient (2%) (Group C)
Kang RA et al (2018),[53]	12.5 ml of 0.75% ropivacaine and 12.5 ml of 2% lidocaine with 1:200,000 epinephrine Group CP: LA was injected in corner pocket' Group NC: LA inserted inside the neural cluster	Single	-	-
Bravo D et al (2018),[54]	35 ml of lidocaine 1%-bupivacaine 0.25% with epinephrine 5 µg/ml Group I, II and III: 2, 5, or 8 mg of preservative-free perineural dexamethasone.	Multiple	Duration of postoperative analgesia, sensory block and motor block (hours): 2mg-20.0±5.7, 16.6±4.6, 14.9±4.5 4mg-22.7±6.0, 18.0±5, 16.1±4.9 8mg-22.0±7.4, 17.3±4.8, 15.3±4.5 respectively Performance time (min) 6.2±2.3 (2mg), 6.3±2.4 (4mg), 6.7±2.6 (8mg)	Vascular puncture: 6 (5.0%) (2mg group), 4 (3.3%) (4mg group), and 3 (2.5%) (8mg group)

Hong B et al (2018),[55]	25ml of LA (1:1 mixture of 1% lidocaine and 0.75% ropivacaine) D group: sedation with dexmedetomidine (0.7–0.8 mg/kg/hr) M group: midazolam (3 mg of midazolam if over 60 kg, 2 mg of midazolam if less than 60 kg)		Time to first request for analgesic (min): D group-616.9± 158.2, M-group-443.7±127.2	PONV/dizziness/dry mouth/headache: D group-12.2%/8.2%/8.2%/0, M group-23.4%/0/2.1%/2.1%
Hamed MA et al (2018),[56]	0.5 ml/kg up to a maximum of 40 ml (the dose of bupivacaine was 1.5 mg/kg). Group C: isobaric bupivacaine 0.5%. Group D: 1 mg/kg of dexmedetomidine along with equal volumes of 0.5% isobaric bupivacaine. Group F: 1 mg/kg of fentanyl along with equal volumes of 0.5% isobaric bupivacaine.	Multiple	Onset of motor and sensory block: 6.85 ± 2.4 and 5.75 ± 2.2 (Group D), 13.7 ± 3.3 and 11.8 ± 3.4 (Group F), 18.4 ± 5.2 and 16.3 ± 4.8 (Group C) Duration of motor and sensory block: 777 ± 74.6 and 819 ± 76.6 (Group D), 465.5 ± 46.8 and 500.2 ± 37.2 (Group F), 420.5 ± 44.4 and 473.9 ± 36.8 (Group C)	PONV: 2 patients (fentanyl group)

Aliste J et al (2018),[57]	ISBPB-20 ml of levobupivacaine 0.5% and epinephrine 5µg/ml Small volume SBPB-3 and 17 ml were deposited at the corner pocket and posterolateral to the brachial plexus	Multiple	Performance time, min-7.7 (ISBPB), 7.3 (SBPB) Onset time, min: 10.4 (ISBPB), 24.4 (SBPB)	PONV: 1 (4.5) (ISBPB), 1 (4.5%) (SBPB)
Auyong DB et al (2018),[58]	15 ml, 0.5% ropivacaine	Multiple	-	Vomiting, n (%): 9 (15%) (ISBPB), 5 (8%) (SBPB), 2 (3%) (suprascapular)
Sinha C et al (2018),[59]	20 cc 0.5% levobupivacaine. Group I: 1 µg/kg dexmedetomidine Group II: 2 µg/kg dexmedetomidine	Multiple	The average time for onset and duration of sensory and motor blockade was similar in both the groups.	-
Dharmarao PS et al (2018),[60]	Group A: 30 ml of 0.5% ropivacaine with 1 µg kg-1 dexmedetomidine Group B: 30 ml of 0.5% ropivacaine with 1 µg kg-1 fentanyl	Multiple	Onset of sensory blockade: 13.95±1.34 min (group A), 14.18±1.41 min (group B). The duration of motor blockade: 649.56±42.73 min (group A), 456.75±32.93 min (group B).	Nausea/ Vomiting: 7.5% (Group A), 5% (Group B)

Mangal V et al (2018),[61]	20 ml 0.75% ropivacaine Group A: 2 ml 0.9% normal saline Group B: dexmedetomidine (1 µg/kg body weight)	Multiple	Sensory and motor block: 613.34 ± 165.404 min and 572.7 ± 145.709 min in group B and 543.7 ± 112.089 min and 503.26 ± 123.628 min in group A; P < 0.01). Duration of analgesia: 593.19 ± 114.44 min (group A), 704.8 ± 178.414 min (group B); P < 0.001).	-
Elyazed MAM et al (2018),[62]	35 ml ropivacaine 0.5% diluted with 4 ml normal saline 0.9%. Group I: Magnesium sulfate 150 mg Group II: dexmedetomidine 100 µg	Multiple	Dexmedetomidine group provided the longest duration of analgesia as compared to ropivacaine group (P = 0.000) The mean onset time: 20.23 ± 3.34 (ropivacaine group), 20.77 ± 2.55 min (mgso4 group), and 17.26 ± 2.60 min (dexmedetomidine group) (P = 0.000).	PONV: 8.5% (ropivacaine and mgso4 groups) and 11.4% (dexmedetomidine group),

Karaman Tet al (2019),[63]	20 ml of 0.25% bupivacaine	Multiple	Onset time of sensory block (min): 11.55 (ISBPB), 12. 28 (SBPB) Duration of surgery: 120 min (ISBPB) and 140 min (SBPB)	-
Sivashanmugam T et al (2019),[64]	20ml of an equal mixture of 0.5% bupivacaine and 2% lidocaine with 1:200000 epinephrine.	Multiple	Onset time: 30 min	-
Ayyanagouda B et al (2019),[65]	Skin infiltration of 1–3 ml 1% lignocaine 20 ml 0.5% ropivacaine in 5 ml increments by extrafascial (Group E) or intrafascial (Group I) approach	Multiple	Duration of surgery: 84±24.65 min (Group E) and 90±25.38 (Group I); Sensory and motor onset time: 10±2.3 min and 7.10±1.936 (Group I), 17±1.8 and 15.69±2.625 (Group E)	-

Kaur S et al (2019),[66]	Group I = 27 ml of 0.5% ropivacaine Group II = 27 ml of 0.5% ropivacaine + 250 mg mgso4 Group II = 27 ml of 0.5% ropivacaine + 2 mg.kg^{-1} ketamine.	Multiple	Onset of motor and sensory block: 20.26±1.69 and 15.61±1.39 min (Group I), 21.11±1.52, 15.65±1.62 min (Group II), 21.00±1.26, 15.64±1.27 min (Group III) Duration of motor and sensory block: 4.51±0.70 and 4.51±0.70 min (Group I), 5.67±0.72 and 5.67±0.72 min (Group II), 4.14±0.59 and 4.14±0.59 min (Group III)	Nystagmus: 5 Hallucination: 7 patients (Group III) patients (Group III) Nausea/ vomiting: 2 patients (Group III) Hematoma: 2 patients (Group I). 2 patients (Group II) and 3 patients (Group III)
Blanco AFG et al (2019),[67]	20ml of 0.5% ropivacaine and 20ml of 1.5% mepivacaine	Multiple	Mean performance time: 4.8±2.0min (RBPB) and 5.2±2.3min (IBPB)(p=0.06)	Arterial puncture/pain: n=1.9%/3.8% (RBPB) and 7.1%/7.1% (IBPB)

Elhusein AKA et al (2019),[68]	Group I- 28 ml 0.5% bupivacaine and 2 ml 0.9% normal saline Group II- mixture of 28 ml 0.5%bupivacaine and 2 ml of mgso4 containing 200 mg mixed with 1000 unit hyaluronidase	Multiple	Onset of sensory and motor block: faster in patients in group (II) than groups (I) Duration of sensory and motor block: longer in group (II) than in group (I)	-
Singh and Singham (2019),[69]	30 ml of 0.375% injection bupivacaine.	Single	Block performance time (Sec): 190.54±20.28 (ISBPB), 220.64±25.72 (SBPB) (P<0.001) Duration of analgesia (min): 715.32±25.27 (ISBPB), 725.44±15.58 (SBPB)	-
Singh and Singham (2019),[70]	Group control (CL): Ropivacaine 0.5% (30 ml) + normal saline (1 ml), Group Clonidine (CD): Ropivacaine 0.5% (30 ml) + injection Clonidine (150 µg), Group Dexmedetomidine (DX): Ropivacaine 0.5% (30 ml) + injection Dexmedetomidine (100 µg).	Single	Onset of sensory and motor block (min): 3.93±0.98, 11.06±2.53 (CL), 3.1±0.54, 8.30±4.86 (CD), 2.5±0.73, 6.56±0.971 (DX) Duration of motor block (min)/ Duration of analgesia: 349.43±39.99/ 410.56±25.4 (CL), 408.86±42.63/472.7±28.67 (CD), 559.7±18.69/701.5±35 (DX)	

Refaat S et al (2019),[71]	30ml 0.5% bupivacaine	Single injection, Double injection, Intracluster injection	Onset of block (min): 18.00± 2.45 (Gs), 12.58±1.83 (Gd), 8.17±1.64 (Gic) (P <0.001) Duration of block (min): 125.83±43.32 (Gs), 444.17±64.73(Gd), 310±50.0 (Gic) (P<0.001)	-
Patel MA et al (2020),[72]	Group I- LB 133mg, Group II-LB 266mg, or Group III- saline placebo (20ml total volume each)	Single	-	Nausea/ headache/ constipation/ pruritis: 17/7/6/3 (GI), 3/1/2/1(GII), 26/3/9/11 (GIII)
Kasine T et al (2020),[73]	20 ml lidocaine 20 mg/ml with epinephrine 5 µg/ ml.	Multiple	Onset time: needle tip tracking- 23.6±13.2 min; without needle tip tracking- 27.0±21.0 min Block duration: needle tip tracking-128.2±39.5 min; without needle tip tracking- 143.2±48.0 min	-

Luo Q et al (2020),[74]	SBPB and CBPB-11.5 ml) of a 1:1 mixture of 2% lidocaine and1 % ropivacaine initially and then remaining 11.5 ml	Multiple	Performance time (s): 251.69± 43.17 (SBPB), 274.55±45.62 (CBPB) (p=0.01) Duration of surgery: less in CBPB	Vascular puncture (yes/no): 1/54 (SBPB), 2/5 (CBPB)
Sachdev S et al (2020),[75]	Group L: 29 ml of 0.5% levobupivacaine+1ml of normal saline. Group LD: 29ml of 0.5% levobupivacaine + 1ml of dexmedetomidine 1ml(100mcg).	Multiple	Onset of sensory- and motor block: 12.4±3.1 min, 15.9±2.7 min (Group L), 20.5±3.8 min, 22.1±3.2 min (Group LD). The duration of sensory and motor block and duration of analgesia was longer in Group LD than Group L	
Singh N et al (2020),[76]	30 ml of 0.5% ropivacaine Group 1 (n = 20): 1 µg/kg of dexmedetomidine, group 2 (n = 20): 8 mg of dexamethasone in addition to ropivacaine, while group 3 (n = 20): only ropivacaine	Multiple	Onset of sensory and motor block: group 1 (13.5 ± 4.1 and 17.0 ± 4.1 min) and group 2 (15.6 ± 3.6 and 18.5 ± 3.7 min) as compared to group 3 (20.1 ± 5.3 and 24.9 ± 5.6 min; P < 0.001) Block duration: significantly longer in group 1 and group 2 Duration of analgesia: prolonged in group 1 and 2 than group 3. (P < 0.001)	

Lotfy ME et al (2020),[77]	Group C: 30ml0.5%bupivacainewith 1mlnormal saline, groupf: 30ml bupivacaine 0.5% with fentanyl 50µg (1ml), Group D:30ml bupivacaine 0.5% with dexmedetomidine 75µg (1ml).	Multiple	Group D showed significantly rapid onset and longer duration of sensory and motor block, prolonged duration of anesthesia and analgesia Duration of surgery (min): 109.8±29.4 (Group C), 98.3±30.9 (Group F), 109.7±33.4 (Group D),	Nausea and vomiting: 0 (Group C), 10% (Group F), 3.3% (Group D) Pruritus: 0 (Group C), 6.7% (Group F), 0(Group D)
Youssef MY et al (2020),[78]	Group B: 20ml bupivacaine (0.5%) plus 2ml of saline; Group K: 20ml bupivacaine (0.5%) and ketamine 1.5mg/kg; Group D: 20ml bupivacaine (0.5%) and dexamethasone 8mg; Group E: 20ml bupivacaine and epinephrine (5µg/ml).	Single	Group D showed a shorter onset of sensory and motor blocks compared with the other groups. Duration of analgesia (h): 7.98±0.28 (Group B), 8.00±0.00 (Group K), 8.40±2.19 (Group D), 21.57±1.36 (Group E) ($p<0.001$)	Nausea and vomiting: 2 (6.7) (Group B), 1 (3.3) (Group K), 2 (6.7) (Group D), 0 (Group E)

PONV: Postoperative nausea and vomiting

Table 3: Different types of BPB techniques and their related complications

Study	Approach used	Technique of block needle insertion	Complications	Successful/failed blocks	Outcome of the study
Mak PHK et al (2001),[6]	SBPB	-	HDP: total-51%, partial-39%, No paralysis-51%	-	Risk of unilateral HDP is high with SBPB
Deleuze A et al (2003),[7]	IBPB And AXB	-	Horner's syndrome: 2 patients (IBPB)	Success rate was 90% and 88% in groups IBPB and AXB	A single shot IBPB is equally effective as a triple-nerve stimulation Axillary block

Rettig HC et al (2005),[10]	Vertical IBPB and axillary blocks	-	Horner's syndrome: 1 patient (IBPB) and nil (axillary) Shortness of breath: 1 patient (IBPB) and nil (axillary) Paraesthesia/ dysaesthesia: 4 (IBPB) and 3 (axillary)	Complete blockade: 97% (IBPB) and 77% (AXB).	IBPB approach provides a more complete block than the AXB
Liu FC et al (2005),[11]	AXB	-	Paraesthesia: 3 (10) (ND), 0 (0) (UD), 0 (0) (US) p = 0.03	Success rate: 90% in ND and UD groups , 70% in US group	US-guided AXB, using either single- or double-injection technique, provided excellent results
Heid FM et al (2005),[12]	Vertical IBPB and high axillary plexus block	-	Horners' sign 30min after the injection: I patient (HAP)	-	Vertical IBPB demonstrated a partially higher success rate and a faster onset
Soeding PF et al (2005),[13]	US-guided ISBPB, and AXB	-	Paraesthesia: higher in the control group (P=0.012) as compared to US group	-	US guidance reduces the incidence of paraesthesia

Pippa P et al (2006),[14]	Winnie - ISBPB and Pippa proximal cranial needle approach.	PNP: 0 (Group I) and 8 (Group II) (P=0.002) Bradycardia and hypotension:0 (Group I) and 20 (Group II) Horner's syndrome: 18 patients in Group II	Excellent: 28 (group I), 19 (group II) Failure: 0 (group I) and 1 (group II)	The lower concentration of the anesthetic solution avoids complications while increased volume provides analgesia
Chan VWS et al (2007),[15]	AXB (nerve-stimulator real-time ultrasound guidance and combined US and NS (USNS)	Transient post-block paresthesia (< five days): 13 patients in both Groups US and NS and nine in Group USNS	Block success rate-82.8% (US), 80.7% (USNS, 62.9% (NS) (P = 0.0).	US guidance, with or without concomitant nerve stimulation, significantly improves the success rate of AXB
Riazi S et al (2008),[16]	US-guided In-plane ISBPB	Hypoxia and respiratory distress: 1 patient (Group II) Ipsilateral Horner's syndrome: 3 patients (Group II) Hiccups lasting for 3 days: 1 patient (Group II) Post-block hoarseness: 3 patients (Group II)		Use of low-volume US-guided ISBPB is associated with fewer respiratory and other complications

Dhir and Ganapathy (2008),[17]	US-guided continuous IBPB	In-plane	Paraesthesia- 2 patients of ST group (Tingling and numbness in the thumb region on day 4-1 patient and numbness over the incision site that recovered in 3 weeks-1 patient.)	Block success: 96% (US), 58% (ST), 59% (TR) (P<0.0005)	Post-operative block success:3 (TR), 15 (ST), 20 (US)
De Jose Maria B et al (2008),[18]	US-guided SBPB and IBPB	In-plane (SBPB) and Out-of-plane (IBPB)	-	Failed block-5 in IBPB and 2 in SBPB	The supraclavicular approach of the brachial plexus was faster
Tran DQH et al (2009),[19]	US-guided IBPB	In-plane	Horner's syndrome,-n (%): 2 (4.5) (single injection), 1 (2.2) (double injection) Paresthesia, n (%): 4 (9.1) (single injection), 4 (9.1) (double injection)	-	The double-injection IBPB provides no significant advantages
Koscielniak-Nielsen JZ et al (2009),[20]	SBPB and IBPB	In-plane	Paraesthesia: 8 patients (IBPB) and 22 (SBPB) (P=0.003) Horner syndrome: Nil (IBPB) and 17 patients (SBPB) (P<0.0001) HDP: Nil (IBPB) and 7 patients (SBPB) (P<0.0001)	Partial block failures: 4 (group I) Partial-12 and one complete failure (Group S)	IBPB had a faster onset, better surgical effectiveness and fewer adverse events

Renes SH et al (2009),[21]	US-guided ISB along with GA 2 groups (US and NS)	-	US-ISB: 2 patients with complete paresis, NS-ISB: 12 patients showed complete and 2 patients had partial HDP. .Ventilatory function was reduced in the NS-ISB group.	Block success rate: 100% (US) and 93 (NS)	US-guided ISB reduces the incidence of HDP
Renes SH et al (2009),[22]	US-guided SBPB	In-plane	HDP: 0 patient (US group), 15 patients show complete and 1 patient showed partial HDP (P<0.0001) (NS group) Horner syndrome: 7 patients (US group), 8 patients (NS group)	Block failures: 2 (NS group)	US-guided SBPB is not associated with HDP
Tran DQH et al (2009),[23]	US-guided SBPB, IBPB and AXB	In-plane (all three)	Paresthesia: 4 (10%) (SBPB), 3 (7.5%) (IBPB), 6 (15%) (AXB) Horner syndrome: 15 (37.5) (SBPB), 2 (5) (IBPB), 0 (0) (AXB) (P<0.001)	Similar success rates for the 3 groups (95%-97.5%).	US results in similar success rates for all 3
Yang CW et al (2010),[24]	SBPB and IBPB	-	Horner syndrome: 27 patients (SBPB), 4 (IBPB) Dyspnea: 3 patients (SBPB), 0 (IBPB) Pneumothorax: 2 patients (SBPB), 0 (IBPB)	Complete failure: 1 (group S) and 0 (group I)	The IBPB approach may be preferred due to lesser complications

Parrington SJ et al (2010),[25]	SBPB	In-plane	Numbness/tingling-on POD 14: 5 (21%) (Group 1), 8 (44%) (Group 2)		The addition of dexamethasone to mepivacaine prolongs the duration of analgesia
Gianesello L et al (2010),[26]	AXB	-	Accidental paresthesia: 2 patients (Group I) and 2 patients (Group II)	-	No serious complications in either of the groups
Thomas LC et al (2011),[27]	US-ISBPB and NS-ISBPB	In-plane	Paresthesia-1 (US group), 1 (NS group); Pain upon injection: 0 (US group), 2 (NS group); Neurologic Complications: Numbness >2 wk-1 (US group), 0 (NS group); Radiating pain >2 wks-4 (US group), 6 (NS group); Motor weakness>2 wks-2 (US group), 0 (NS group);	Block success rate: 95% (US group), 91% (NS group)	US-guided ISBPB is safe and effective
Lee JH et al (2011),[28]	US-guided ISBPB	In-plane	HDP: 10 (33%) (Group 5), 18 (60%) (Group 10) (P<0.05) Complications: 2 (6.7%) (Group 5), 4 (13.3%) (Group 10)	-	ISBPB with 5 ml LA showed reduce incidence of HDP

Subramanyam R et al (2011),[29]	US-guided SBPB by lateral or medial needle approach	In-plane	Paresthesias in operative extremity: 1 (3) (lateral approach), 4 (11) (medial approach) Weakness in operative extremity: 2 (6) (lateral approach), 3 (8) (medial approach),	-	Rates of sensory and motor block is similar in all groups
Sinha SK et al (2011),[30]	US-guided ISBPB	In-plane	HDP after 15 min: 14 of 15 patients in each group; At discharge: 13 of 15 patients in each group	-	Decreasing the volume for ISBPB from20 to 10 ml did not reduce the incidence of HDP
Behr A et al (2012),[31]	ISBPB	In-plane	Respiratory depression: 0 (control), 2 patients (INB group), 0 (EMB group) Laryngeal nerve block: 1 patient (control), 1 patients (INB group), 0 (EMB group)		Epineural buprenorphine prolonged postoperative analgesia of MIB

Bernucc F et al (2012),[32]	PV and PN US-guided AXB	In-plane	Paresthesia: 2 patients (8%) (PV) and 13 patients (52%) (PN); (P = 0.001)	No	Both have comparable success rates and total anesthesia-related times
Kaya M et al (2013),[33]	ISBPB Group 1: single-injection group 2: control group	-	Urinary retention: 0 (Group 1), 1 (3 %) (Group 2) Horner's syndrome 2 (7 %) (Group 1), 0 (Group 2)	-	ISBPB in patients undergoing MRM improved pain scores
Saracoglu S et al (2014),[34]	AXB	-	-	-	Successful block: 24/30 patients (Pen+group) and 6/30 patients (Pen-group)
Arab SA et al (2014),[35]	US-SBPB (Single vs triple injection)	-	Symptomatic HDP: 0 (SI) and 1 patient (TI) Horner syndrome: 2 patients (SI) and 3 patients (TI)	Successful anesthesia: 87% –single injection, 96%-multiple injection	TI technique for SBPB resulted in improved onset and more complete sensory block

Yazer MS et al (2015),[36]	US-guided targeted intracluster injection SBPB and IBPB	In-plane	Paresthesia: 6 (18.7%) (SBPB), 1 (3.1%) (TII-IBPB) Horner syndrome:17 (53.1%) (SBPB), 1 (3.1%) (TII-IBPB) Block-related pain (scale 0–10): 2 [0–7] (SBPB), 3 [0–9] (TII-IBPB)	Similar success rate in both groups (93.7-96.9%)	Both techniques provide comparable success rates
Bharti N et al (2015),[37]	US-guided SBPB, IBPB and C-6 ISBPB	In-plane	Transient phrenic nerve palsy: 2 patients (10%) (ISBPB)	Success rate: 86% (SBPB), 90% (IBPB) and 84% (ISBPB)	ISBPB has longer onset time and incidence of PNP
Bjørnholdt KT et al (2015),[38]	ISBPB	In-plane	Severe dyspnoea and pulmonary embolism: 1 patient (ISBPB group)	Failed blocks-7/27 (ISBPB)	LIA provided inferior analgesia but lesser complication then ISBPB
Singh S et al (2015),[39]	US-guided-SBPB and NS-SBPB	-	-	Successful block-90% (US group), 73.1% (NS group)	SBPB is safer and faster

Ryu T et al (2015),[40]	Comparison of ISBPB and SBPB groups	In-plane-ISBPB	Horner's syndrome: 59.6% (ISBPB group) and 19.6% (SBPB group), P<0.001). Hypotensive bradycardiac events: 12.8% (ISBPB) and 4.3% (SBPB) Hoarseness-10.6% (ISBPB), 4.3% (SBPB)	-	SBPB produces a better motor blockade and a lower incidence of Horner's syndrome than ISBPB
Liu GY et al (2015),[41]	US-guided SBPB and NS-SBPB	In-plane	Lung puncture and pneumothorax: 1 patient (NS-group)	-	US-guided SBPB is feasible and almost have no complications
Kooloth RA et al (2015),[42]	SBPB	-	Horner's syndrome: Group R -1 (3.33%), Group B- 3(10%)	-	SBPB using 0.5% ropivacaine is similar to 0.5% bupivacaine.

Petrar SD et al (2015),[43]	US-guided SBPB and ISBPB	In-plane	HDP: 11 (34%) (SBPB) and 1 (3%) (ISBPB) (P=0.001) Complete or partial paralysis: (44%) (SBPB) and (13%) (ISBPB) Dyspnea: 8(25%) (SBPB) and 5(16%) (ISBPB)	-	The incidence of HDP is less in ISBPB as compared to SBPB
Palhais A et al (2016),[44]	US-guided ISBPB	In-plane	HDP: 90% (conventional) and 21% (extrafascial) (P<0.0001). Hoarseness: 35% (conventional) and 5% (extrafascial) (P<0.02). Claude-Bernard-Horner syndrome: 35% (conventional) and 20% (extrafascial). Paraesthesia: 30% (conventional) and 0% (extrafascial).	-	US-guided ISBPB with an extrafascial injection reduces the incidence of HDP
Stav A et al (2016),[45]	US-guided SBPB, IBPB and axillary	In-plane	Transient Horner syndrome: 3 patients (SBPB)	Failed block: 10 (SBPB), 10 (IBPB), 16 (AXB)	All 3 approaches produce similar anesthesia

Wiesmann T et al (2016),[46]	Comparison of continuous SBPB and ISB	Out of plane-ISB, In-plane –SBPB	HDP: 43% in ISBPB, 24% in SBPB, (P = 0.047). Hoarseness- 6 patients in each group Horner syndrome-12 patients in ISBPB and 2 patients in SBPB (POD 1) After 1 week-dyspnoea (1 patient in each group), hoarseness (1 patient in SBPB)	-	Significantly greater incidence of phrenic nerve palsy in ISB group
Koh WU et al (2016),[47]	Comparison of continuous SBPB and ISB	In-plane approach for both	HDP: 63% (ISBPB) Horner's syndrome: 37% (ISBPB) vs 14% (SBPB); p = 0.04] Complete loss of sensation of the upper extremity: 32% (ISBPB) vs 68% (SBPB); p = 0.004].	-	Continuous supraclavicular block can be an effective modality for postoperative analgesia after open rotator cuff repair
Ghodki and Singh (2016),[48]	US-guided ISBPB and NS-ISBPB	In-plane	HDP: POD1- Group NS (12 patients), Group US (none); (p<0.0001) Horner syndrome: Group NS (6 patients) and Group US (2 patients)	Success rate: 100% (US) and 99% (NS)	Success rate: 100% (US group) and 99% (NS group)

Stundner O et al (2016),[49]	US-guided ISBPB	In-plane	HDP: 53% (n=8) and 27% (n=4) in the 20 and 5 ml groups	-	ISBPB is associated with epidural spread irrespective of injection volume
Kim BG et al (2017),[50]	US-guided ISBPN and SBPB	In-plane for both	HDP-No/ partial/complete: 2/0/23 patients (ISBPB); 8/2/14 patients (SBPB) (p=0.021); In the PACU-2/2/21 patients (ISBPB); 9/0/15 patients (SBPB) (P=0.024) Horner's syndrome: 0 (ISBPB) and 2 (SBPB) Hoarseness: 1 (ISBPB) and 0 (SBPB) Dyspnoea: 2 (ISBPB) and 1 (SBPB) Fingertip numbness: In the PACU-25 patients (ISBPB); 24 patients (SBPB)	-	SBPB is associated with a lower incidence of diaphragmatic paresis

Albrecht E et al (2017),[51]	US-guided continuous ISBPB	In-plane	HDP- POD 1-extrafascial group (15%) and intrafascial group (41%) (P=0.01); POD 2-extrafascial group (0%) and intrafascial group (6%) (P=0.016)	Failed block: 1 patient in extrafascial group	Placement of the catheter tip immediately outside of the brachial plexus sheath reduced the incidence of HDP
Oztur NK et al (2017),[52]	US-guided IBPB	In-plane	Paresthesia during block performance: 0 (Group R), 6 (12%) (Group C)	Block success: 96% (group R), 90% (group C)	The IBPB is associated with reduced performance time and less paresthesia
Kang RA et al (2018),[53]	SBPB	In-plane	HDP: 5 patients (CP) and 12patients (NC group) (P=0.019) No paresis/partial paresis/complete paresis: 13/4/1 (CP group) and 5/9/4 (NC group)	Successful block-100% in both groups	HDP incidence is reduced when LA is injected at the corner-pocket
Bravo D et al (2018),[54]	US-guided IBPB	In-plane	Paresthesia: 4 (3.4%) (2mg group), 3 (2.5%) (4mg group) and 1 (0.8%) (8mg group)	Success rate was similar in all the three groups	2, 5, and 8 mg of dexamethasone provide clinically equivalent sensorimotor and analgesic duration

Hong B et al (2018),[55]	Brachial plexus block	In-plane	Bradycardia: 3 (6.1) 0 (0)	-	
Hamed MA et al (2018),[56]	SBPB	In-plane	Hypotension: 2 patients (dexmedetomidine group) and 1 patient (control group) Bradycardia: 1 patient (dexmedetomidine group)	-	Addition of dexmedetomidine is better in prolongation of the duration of SBPB block
Aliste J et al (2018),[57]	US-guided ISBPB and small volume SBPB	In-plane	HDP (30 min after block): 21 (95) (ISBPB), 2 (9%) (SBPB) (P<0.001) Horner syndrome: 3 (13.6) (ISBPB), 1 (4.5%) (SBPB) Paresthesia: 2 (9.1) (ISBPB), 1 (4.5) (SBPB)	-	Small volume SBPB results in less incidence of HDP as compared to ISBPB
Auyong DB et al (2018),[58]	ISBPB, SBPB and suprascapular	In-plane	Horner syndrome: 29% (ISBPB), 24% (SBPB), 8% (Suprascapular) [P = 0.005]. Hoarseness: 22% (ISBPB), 21% (SBPB), 8% (suprascapular) [P = 0.04]. Subjective dyspnea 6% (ISBPB), 3% (SBPB), 2% (Suprascapular).	-	Pulmonary function is best preserved with the anterior suprascapular nerve block

Sinha C et al (2018),[59]	SBPB		Bradycardia: 2 patients (Group I), 8 patients (Group II) (p=0.04) Hypotension: 2 patients (Group I), 6 patients (Group II)	-	Increasing the dose of dexmedetomidine increases the rate of complications
Dharmarao PS et al (2018),[60]	US-guided SBPB	In-plane	Bradycardia: 12.5% (Group A), 0 (Group B) (p=0.05) Hypotension: 2.5% (Group A), 0 (Group B)	-	Dexmedetomidine prolongs the duration of sensory and motor block
Mangal V et al (2018),[61]	US-SBPB	In-plane	Bradycardia: 4.54% (group B), 0 (group A) Horner syndrome: 11.35 (group B), 9.3% (group A)	-	Addition of dexmedetomidine prolongs the duration of analgesia.
Elyazed MAM et al (2018),[62]	US-guided IBPB		Hypotension: 14.2% (dexmedetomidine group), other groups-0% Bradycardia: 20% (dexmedetomidine group), other groups-0%	-	Dexmedetomidine provided quicker onset and longer duration of blocks
Karaman Tet al (2019),[63]	US-guided ISBPB and SBPB	In-plane	Horner's syndrome (n): 8(25.8%) (ISBPB), 1(3.4%) (SBPB) (p=0.015)	Block failure- 0 in both groups	US-guided SBPB is as effective as ISBPB

Sivashanmugam T et al (2019),[64]	Comparison of SBPB and CBPB	SBPB and CBPB-either in-plane or out-of-plane	Ipsilateral PNP-5% in CBPB and 45% in SBPB (P=0.008). Impaired diaphragmatic excursion-SBPB-33.7%, CBPB-10.7% (P=0.003) Deep breathing (SBPB-36.3% vs. CBPB group-6.6%, P=0.014)	Success rate-100% in both groups	CBPB has a lower incidence of ipsilateral PNP
Ayyanagouda B et al (2019),[65]	US-guided ISBPB	-	HDP-17% (Group E), 46% (Group I) (P < 0.0001). Paraesthesia-31% (Group I) and 0% (Group E) Hoarseness-31% (group I) and 3.4% (Group E) Horners syndrome-27.6% (Group I) and 20.7% (Group E)	-	US-guided ISBPB through extrafascial approach reduces the incidence of HDP
Kaur S et al (2019),[66]	SBPB	-	-	-	The addition of MgSO4 to ropivacaine in SBPB has a lesser incidence of side effects
Blanco AFG et al (2019),[67]	IBPB and RBPB	In-plane	Paresthesia n=5.7% (RBPB group) n=1.8% (IBPB) Horner's: n=1.9% (RBPB group), n=1.8% (IBPB)	Successful block-94.3% (RBPB), 91.1% (IBPB)	RBPB approach for brachial plexus anesthesia was similar to ICB approach

Elhusein AKA et al (2019),[68]	US-guided SBPB	In-plane	Tachycardia: 5 patients (group I) and 2 patients (group II)	-	Combination of both MgSO4 with hyaluronidase decrease analgesic requirements
Singh and Singham (2019),[69]	SBPB and ISBPB	-	Horner's syndrome: 25% (ISBPB), 3.4% (SBPB), (p=0.01) PNP: 21.4% (ISBPB), 3.44% (SBPB), (p=0.03) Hoarseness: 17.8% (ISBPB), 0% (SBPB), (p=0.01)	ISBPB-95.3% SBPB-97.2%	SBPB technique has an equal success rate and provides similar analgesic effects
Singh and Singham (2019),[70]	SBPB		Pneumothorax: 6.6% (CL), 3.3% (CD), 3.3% (DX) Horner's syndrome: 3.3% (CL), 3.3%) (CD), 6.6% (DX). (P=0.02)		Dexmedetomedine and Clonidine prolong the duration of analgesia
Refaat S et al (2019),[71]	US-guided SBPB	In-plane	Horner syndrome: 1 patient (Gd)	-	Intra-cluster technique showed rapid onset with adequate postoperative analgesia

Patel MA et al (2020),[72]	ISBPB	In-plane	Tachycardia/ sinus tachycardia): 1 (GI), 1 (GII), 1 (GIII) Nervous system disorders (Dysgeusia/ Paresthesia/ dizziness/motor dysfunction): 5 (GI), 1 (GII), 4 (GIII) Muscle twitching/ Tinnitus/visual impairment: 3/0/0 (GI), 1/0/0 (GII), 2/1/1 (GIII)	-	Single-injection BPB with LB 133mg provided analgesia through 48hours post-surgery
Kasine T et al (2020),[73]	IBPB	In-plane	Horner syndrome: 2 individuals (without needle tip tracking)	Block success rate-81% with and 69% without needle tip tracking	No significant differences between active needle tip tracking and the control procedures were found
Luo Q et al (2020),[74]	USg u i d e dfor both SBPB and CBPB	-In-plane	Horner syndrome-(yes/no): 16/39 (SBPB), 0/55 (CBPB) (p <0.01)		Multi-drug injection resulted in similar block dynamics for both techniques
Sachdev S et al (2020),[75]	SBPB		H y p o t e n s i o n :- 1 patient (LD) bradycardia: 2 patients (LD)		Dexmedetomidine added with l e v o b u p i v a c a i n e prolongs the duration of sensory as well as motor block
Singh N et al (2020),[76]	USg u i d e d SBPB	-In-plane	H y p o t e n s i o n :- 1 patient (dexmedetomidine group)		Dexmedetomidine and dexamethasone prolong' block duration.

Lotfy ME et al (2020),[77]	US-guided SBPB	Hypotension: 0-(Group C), 0 (Group F), 6.7% (Group D) Bradycardia: 0 (Group C), 0(Group F), 17.5% (Group D) (p<0.001)	Dexmedetomidine hastens the onset and prolongs the duration of blocks
Youssef MY et al (2020),[78]	US-guided-SBPB	-	- Dexamethasone has a longer duration of sensory and motor blocks

ISB: Interscalene Block; GA: general anesthesia; NS-ISBPB: nerve stimulation ISB, US-ISB: Ultrasound-guided ISBPB; US-SBPB: Ultrasound-guided supraclavicular brachial plexus block; POD: Postoperative day; CBPB: Costoclavicular brachial plexus block; PNP: Phrenic nerve palsy; HDP: Hemidiaphragmatic paralysis; NS: nerve stimulator; IBPB: Infraclavicular brachial plexus block; HAP: high axillary plexus block; AXB: Axillary block; MIB: Middle interscalene brachial plexus block; PV: perivascular (PV; PN: perineural; RBPB: Retroclavicular brachial plexus block.

Description of the Outcome Measures

A. Primary outcome measures

Complications reported in various studies (n=73)

1. Complications related to BPB [Table 3]

(a) Neurological complications: The majority of the studies (n=41) reported neurological complications. A neurologic complication was defined as neurological symptoms within the operative site brachial plexus that was related to brachial plexus irritation but were unrelated to the surgical procedure as determined by the neurologist, including Horner syndrome, numbness, paresthesia, radiating pain, motor weakness, and many more.

The 41 studies reported more than one neurological complications Among these, more than half of the studies (n=32) reported Horner

(b) Respiratory complications: A total of 23 studies have reported respiratory complications. Among them, the most common ones are hemidiaphragmatic paralysis (HDP) (n=19), followed by pneumothorax (n=3), any other respiratory complications. HDP was observed in 19 studies.[6,20,21,22,28,30,35,43,44,46,47,48,49,50,51,53,57,64,65]Diaphragmatic movement reduction of more than 75%, no movement, or paradoxical movement was considered to be "complete paresis". Diaphragmatic movement reduction between 25% and 75% was considered to be "partial paresis", and diaphragmatic movement of less than 25% was considered to be "no paresis. Three studies reported the complication of pneumothorax,[11,24,70] in which the majority of them belong to the SBPB technique. Other respiratory complications such as dyspnea,[24,38,43,46,50,58] reduce ventilator function,[21] shortness of breath,[10] deep breathing,[64] hypoxia and respiratory distress,[16] respiratory depression,[31]

pulmonary embolism,[38] and pneumothorax with lung puncture,[41] were also observed in the studies.

(c) Cardiac complications: Thirteen studies denoted cardiac complications. Among these,bradycardia and hypotension was reported in 11 studies,[14,40,56,75,76,77,55,59,60,61,62] and tachycardia/sinus tachycardia was shown in two studies.[68,72]

(d) Hoarseness: Eight studies,[16,40,44,46,50,58,65,69] reported the incidence of hoarseness among patients undergoing surgery and one study reported laryngeal nerve block with the use of ISBPB technique.[31]

(e) Phrenic nerve palsy: It was reported in four studies.[14,37,64,69]

(f) Other complications: Patel MA et al in their study reported visual impairment, ear and labyrinth disorders (Tinnitus), and muscle twitching with the ISBPB technique.[72] Urinary retention was also reported with the ISBPB technique by Kaya M et al.[33]

1. **Complications related to LA [Table 2]**

(a) Vascular puncture: Twenty

studies,[7,8,9,10,11,12,18,20,23,24,26,31,32,34,35,39,52,54,67,74] measured the incidence of vascular punctures, and a vascular puncture was determined by the presence of frank blood in the hub of the needle or aspiration of blood when the needle was attached to tubing and a syringe.

(b) Postoperative nausea and vomiting (PONV): It was reported in 15 studies.[10,25,31,33,42,55,56,57,58,60,62,66,72,77,78]

(c) Pain and bruising at the injection site: Burning pain,[29,38] tourniquet pain,[11] and axillary,[15] were observed in the studies. Apart from this, bruising was reported by Parrington SJ et al,[25] Chan VWS et al,[15] and Subramanyam R et al.[29]

(d) Other complications: Hematoma,[11,66,38] intravascular injection,[41] constipation,[72] pruritis at the site of injection,[72,77] hallucination and nystagmus by,[66] dry mouth[55] dizziness,[38,55] headache,[55,72] and dysphonia,[14] were reported as other complications in various studies.

B. Secondary outcome measures

(a) Block performance time: Twenty one studies,[7,8,9,15,19,20,26,30,32,34,35,36,37,46,48,52,54,57,67,74,69] reported block performance time. Performance time was measured by the stopwatch by the anesthesiologist performing the block from needle insertion until finishing local anesthetic injection in these studies[Table 2].

DISCUSSION

A revolution came in the field of peripheral nerve blocks after the introduction of BPB as it has decreased the need forgeneral anesthesia (GA) and the complications associated with it. BPB was first performed by Halsted in 1884, and then Crile in 1887.[79] The present systematic review was conducted to compare the complications of the 73 RCTs that have used any of the techniques for blocking brachial plexus.

One of the advances in the field of regional anesthesia was the introduction of US which is considered as the "gold standard" of regional anesthesia. The first report about the application of the US was published in 1989 by Ting and Sivagnanratnam.[80] The US-guidance predicts a more accurate and efficient deposition of LA due to the visibility of the neural targets, the vascular structures, and the spread of LA.[81] In our systematic review, most of the studies (n=38) have utilized the US for increasing the efficiency of the block procedure. Renes SH et al,[21] Thomas LC et al,[27] and Ghodki and Singh,[48] found higher success rate with the US-guided ISBPB group (100% vs 95% vs 100%) as compared to NS-ISBPB group (93% vs 91% vs 99%) respectively. Renes SH et al,[21] and Ayyanagouda B et al,[65] concluded that US-guided ISBPB reduces the incidence of HDP. Liu GY et al,[41] and Karaman T et al,[63] found that US-guidance reduces the risk of pneumothorax, is feasible, and almost has no complications. Yuan Ja-Min in their systematic review concluded that blocks performed using US guidance were more likely to be successful (risk ratio (RR) for block success 0.36, 95% CI 0.23–0.56, P <0.00001), decreased incidence of vascular puncture during block performance (RR 0.13, 95% CI 0.06–0.27, P <0.00001), decreased the risk of complete hemi-diaphragmatic paresis (RR 0.09, 95% CI 0.03–0.52, P=0.0001).[1]

In the present systematic review, a total of 30 studies,[6,7,8,10,12,13,16,19,21,24,29,30,32,33,34,36,35,36,37,38,41,42,43,44,49,50,53,68,69,70,72,78] have used the single-injection technique of LA. There has been controversy regarding the technique of LA injection as some authors were in favor that the success rate of multiple injections was better than the single-injection technique in blocking the brachial plexus. Even, the duration of anesthesia was rapid in multiple injections rapidly than one injection.[82,83,84] Park SK et al in their systematic review found that multiple injection technique may be better based on the analysis of the spread of peripheral nerve block,[85] but another systematic review conducted by Albrecht et al concluded that single injection is better than multiple injections as it takes less time and causes less paraesthesia,[86] whereas, four studies,[10,11,19,35] included in our systematic review found that both injection techniques have equivalent effects. Refaat S et al found that the intracluster technique for SBPB showed rapid onset with adequate postoperative analgesia and minimal complications as compared to single and double injection techniques.[71]

In the present systematic review, many studies have used adjuvants such as clonidine,[70] MgSO4,[62,66,68] fentanyl,[56,60,77] dexamethasone,[25,54,76,78] and dexmedetomidine,[55,56,59-62,70,75,76,77] to LA to prolong the duration of block. Parrington SJ et al,[25] and Youssef MY et al,[78]found that the addition of dexamethasone to LA prolongs the duration of analgesia and respective blocks. Kaur S et al,[66] and Elhusein AKA et al,[68] stated that the addition of MgSO4 has a lesser incidence of side effects and also decreases the analgesic requirements. When dexmedetomidine added with LA, all the studies,[55,56,59,60,61,62,70,75,76,77] found that the adjuvant prolongs the duration of sensory and motor blocks, as well as the duration of postoperative analgesia. Similar findings were found by various studies conducted in the past.[87,88,89] Dexmedetomidine is an α2 agonist and a newer congener of clonidine but in our review, almost all the studies,[55,56,59-62,75,76,77] except Singh and Singham,[70] found hypotension and bradycardia as the complication when dexmedetomidine was

added as an adjunct to LA.

Complications associated with BPB

Although BPB is the most common block used for upper limb surgery, it is not free from complications. These complications can be devastating for the patients as well as for the performing anesthesiologist. We found that the most common complication found among most of the studies was neurological (n=41) followed by respiratory (n=23) and cardiac complications (n=13).

(1) Neurological complications

We found that more than half of the studies (n=41) reported neurological complications. During surgery, nerves are sometimes injured causing neurological complications. These complications are well-recognized since the early days. Most of the neurological complications resolve on its own without any treatment. Serious permanent nerve injury following the block is very rare.[3] The most common neurological complication found in our systematic review is Horner syndrome (n=32) followed by paresthesia (n=21) and tingling/numbness (n=4). The detailed elaboration of these complications along with their studies are:

(a) Horner syndrome: It is a neurologic condition consisting of a triad of miosis, ptosis, and anhidrosis. The sympathetic outflow to the ipsilateral head and neck is interrupted due to the spread of the LA to the prevertebral spaces causing Horner syndrome.[90] The incidence of Horner syndrome following the ISBPB technique ranges from 20% to 90%. Despite using the same approach and same LA regimen, the incidence of Horner syndrome varies between the studies,[90,91] which may be due to the mal-distribution of LA in the brachial plexus sheath.[92]

A total of 32 studies,[7,10,12,14,16,19,20,21,23,24,33,35,36,40,42,44,45,46,47,48,50,57,58,61,63,65,67,69,70,71,73,74] have depicted the incidence of Horner syndrome. Among them, 18 studies compared two or three techniques of BPB

and the rest (n=14) have focused on only one approach of BPB. Six studies,[14,16,33,44,48,65] that reported the complications of Horner syndrome were related to the ISBPB technique alone. These studies were conducted by Riazi S et al,[16] (lower incidence of Horner syndrome with low-volume LA (5ml) as compared to the high volume (20ml), Kaya M et al,[33] (more with single-injection technique), Ghodki and Singh,[48] (more with the NS group as compared to the US group), Palhais A et al,[44] and Ayyanagouda B et al.[65] Palhais A et al,[44] and Ayyanagouda B et al,[65] found a lesser incidence of Horner syndrome with extrafascial group (20% and 20.7%) as compared to the intrafascial group (35% and 27.6%) respectively. Six studies have reported the complication of Horner syndrome in studies related to the SBPB technique. These six studies are: Renes SH et al,[21] Arab SA et al,[35] (more with triple injection technique as compared with single-injection technique), Kooloth RA et al,[42] (more with the group using bupivacaine as compared to ropivacaine), Mangal V et al,[61] (more incidence with dexmedetomidine group), Singh and Singham,[70] (more incidence with the Dexmedetomidine group as compared to clonidine group), and Refaat S et al.[71] Horner syndrome was reported in the IBPB technique only in two studies conducted by Tran DQH et al,[19](more with single-injection technique) and Kasine T et al.[73] A systematic review conducted by Schubert AK et al found that the SBPB had a significantly lower incidence of Horner's syndrome than the ISBPB (7.57% versus 28.20%).[93] This agrees with the findings of our systematic review also. Seven studies have compared the ISBPB and SBPB techniques of which, six of them (Ryu T et al,[40] Wiesmann T et al,[46] Koh WU et al,[47] Aliste J et al,[57] Karaman Tet al,[63] and Singh and Singham,[69] found higher incidence with ISBPB and only one showed higher incidence in SBPB.[50] A systematic review done by Park SK et al compared the US-guided SBPB and IBPB found a greater incidence of Horner syndrome with US-guided SBPB (32.1%) as compared to US-guided IBPB.[85]Even in our systematic review,when the SBPB technique was compared with IBPB in

three studies,[20,24,36] all of the studies found a higher incidence of Horner syndrome with SBPB as compared to IBPB. In three of the studies, IBPB was compared with AXB. Out of which, two studies,[7,10] have shown a greater incidence of Horner syndrome with IBPB but the third study,[12] has showna higher incidence with the AXB. In two studies,[23,45] SBPB, IBPB, and AXB were compared, both of them found higher incidence with SBPB, whereas, Auyong DB et al compared ISBPB, SBPB, and suprascapular and found higher incidence with ISBPB.[58] Blanco AFG et al have compared IBPB and RBPB and found equal incidence in both studies.[67] The Cochrane systematic review compared the risk of Horner syndrome with IBPB and other techniques and found that other techniques have 12.1% chances of Horner syndrome as compared to IBPB (2.2%) and the difference between them is also significant ($p<0.0001$).[2] A study conducted by Neal JM et al reported that the incidence of Horner syndrome in SBPB technique can be reduced to 90% with the use of US as it reduces the requirement of LA due to exact positioning of the needle around the nerve which in turn reduces the escape of the LA towards the paravertebral spaces, hence reduces the incidence of Horner syndrome.[91] The study of the SBPB technique included in our review also agrees with this point and found a greater incidence with NS-SBPB as compared to US-SBPB.[22] However, Luo Q et al found a higher incidence with US-guided SBPB as compared to US-guided CBPB ($p <0.01$).[74] Stasiowski M et al assessed the development of Horner syndrome after ISBPB found a significantly higher incidence in younger patients.[90] However, we have not included studies conducted in patients less than 18 years of age.

(b) Paresthesia: It refers to the persistent anesthesia that extends even after the expected duration of anesthesia. It manifests as a burning or prickling sensation in the hands, legs, or any part of the body. Paresthesia can happen after the administration of a peripheral nerve block such as the BPB. The incidence of transient paraesthesia can be as high as

8–10% after the BPB.[11]

We found that a total of 21 studies,[8,9,10,11,13,15,17,19,20,23,26,27,32,36,44,52,54,57,65,67,72]have reported paresthesia as their complication. Of these 21 studies, seven studies were based on the comparison of the two techniques, and the rest (n=14) are based on individual techniques. Six studies,[8,9,11,15,26,32] were conducted on the AXB technique and reported this complication. These were conducted by Serradell A et al,[8] (more incidence of paresthesia/dysesthesia with 20ml LA group followed by 36 ml and 28ml), March X et al,[9] Liu FC et al,[11] (more incidence in nerve stimulator-guided and the double-injection group as compared to US-guided double and single-injection groups, p=0.03), Chan VWS et al,[15] (13patients in both Groups US and NS and nine in Group USNS AXB techniques, Gianesello L et al,[26] (equal incidence with electrical nerve stimulation and fascial pop technique of AXB), and Bernucc F et al,[32] (more incidence with perineural AXB as compared to perivascular AXB). Four studies,[17,19,52,54] have reported paraesthesia with the IBPB technique. A systematic review done by Albrecht E et al,[86] concluded that the rate of procedural paraesthesia was less with one injection than multiple injections, relative risk (95% CI) 0.6 (0.4–0.9), p = 0.004, whereas, Tran DQH et al,[19] found equal incidence with single and double injection techniques with IBPB. Four studies,[27,44,65,72] have reported the incidence with the ISBPB technique. Palhais A et al (0 vs 30%),[44] and Ayyanagouda B et al,[65] (0% vs 31%) have compared the extrafascial and intrafascial approaches respectively and were in favor that the extrafascial injection reduces the incidence of paresthesia. Seven studies have compared the two techniques of BPB.

The findings of a systematic review conducted by Park SK et al,[85] concluded that procedure-related paresthesia and adjacent nerve-related complications were more frequent in SBPB as compared to IBPB. Another systematic review conducted by Albrecht et al,[86] also found that paraesthesia

was less common with the IBPB approach as compared to the SBPB approach. Two studies,[20,36] in our systematic review have compared the SBPB with the IBPB technique and found a greater incidence with the SBPB technique in both studies. Yazer MS,[36] et al also found a greater incidence with the SBPB (18.7%) as compared to the IBPB (3.1%). Even, Koscielniak-Nielsen JZ et al,[20] have found a statistically significant greater incidence with the SBPB as compared to the IBPB (P=0.003).

Aliste J et al,[57] found a greater incidence with the ISBPB technique as compared to the SBPB. When the AXB was compared with the IBPB in the Rettig HC study,[10]a greater incidence of paresthesia was seen with IBPB. Soeding PF et al,[13] compared ISBPB and AXB and found greater incidence in control AXB as compared to US-guided AXB (P=0.012). Blanco AFG,[67] found a greater incidence with RBPB as compared to IBPB. A comparison of the three techniques (SBPB, IBPB, AXB) was done by Tran DQH et al,[23] and found a greater incidence of the complication with AXB.

(c) Tingling/Numbness: Numbness/tingling is lost, reduced, or abnormal sensations in which either the sensation of the body part is lost or a person feels a sensation of pins-and-needles/prickling. It is usually a temporary sensation that returns to normal after sometimes.

We have evaluated the incidence of tingling/numbness following BPB and found that only four studies,[17,25,27,50]have reported this complication.Dhir and Ganapathy,[17] found tingling and numbness with the IBPB technique. In Parrington SJ et al study of the SBPB, a greater incidence of tingling and numbness was noted in the group in which dexamethasone was added.[25] Thomas LC found greater chances of numbness with the US-ISBPB as compared to the NS-ISBPB.[27] Kim et al found equal incidence with the ISBPN and SBPB techniques.[50]

Motor weakness: Two studies,[27,29] have found motor weakness as their complication. Thomas LC et al,[27] found more weakness with the US-ISBPB (2%) as compared to the NS-ISBPB (0%). Subramanyam R et al,[29] have reported more weakness with the medial approach (8%) as compared to the lateral approach (6%) of SBPB.

(2) Respiratory complications: A total of 23 studies,[6,20,21,22,28,30,35,43,44,46,47,48,49,50,51,53,57,64,65]reported respiratory-related complications.Among them, the most common ones are HDP (n=19), followed by pneumothorax (n=3), any other respiratory complications.

(a) Hemidiaphragmatic paralysis (HDP): HDP occurs due to blocking of ipsilateral phrenic nerve blocks which decreases the pulmonary functions of the patient.[94] In the case of surgery of the shoulder, the incidence of HDP is reported to be 1 per 2069 (0.048%).[95]We found that 19 studies reported the complication of HDP in our systematic review. Among these 19 studies, most of them belong to the ISBPB technique. According to Urmey WF et al, ISBPB is found to be associated with a 100% incidence of HDP and 25-32% reduction in the spirometric measures of the pulmonary function,[94] which restricts the use of this technique among respiratory insufficiency patients. The first case of HDP following ISBPB was reported by Bashein et al. in 1985.[96]

A systematic review conducted by Park SK et al commented that the occurrence of HDP because of PNP is an integral complication of ISBPB, its incidences associated with SBPB cannot be neglected.[85] Another systematic review conducted by Schubert AK et al found that the patients with SBPB had a significantly lower incidence of HDP than the ISBPB (42.60 versus 78.75%).[93] This holds true with our review also as we foundthat eight studies,[21,28,30,44,48,49,51,65] have reported the complication of HDP with ISBPB approach. Among these, two RCTs,[21,48] have divided the ISBPB patients into 2 groups: Ultrasound group (US) and neural stimulation (NS) and in

both of these, greater incidence of HDP was seen with NS group as compared to US group.

Many studies have tried to alter the volume of LA and found the effect on the incidence of complications. Lee JH et al have compared the effects of 5ml and 10ml LA on complications and found that 5 ml LA showed a lesser incidence of HDP (33%) to 10ml (60%).[28] Similarly, Stundner O et al found a lesser incidence of HDP with 5 ml group (27%) when compared with 20ml group (53%),[49] whereas, Sinha SK et al concluded that decreasing the volume from20 to 10 mL did not reduce the incidence of HDP.[30] Palhais A et al,[44] (21% vs 90%), Ayyanagouda B et al,[65] (17% vs 46%), and Albrecht E et al,[51] (15% vs 41%) have compared between the extrafascial and intrafascial approaches respectively and both of them were in favor that the extrafascial injection reduces the incidence of HDP.

Three studies have reported the complication of HDP with SBPB approach.[6,22,53] Renes found a lesser incidence with the US group as compared to the NS-SBPB group.[22] When the SBPB and ISBPB were compared, four studies,[46,47,50,57] have depicted higher incidence of HDP in the ISBPB technique and only Petrar has shown the lesser incidence with the ISBPB technique.[43] When the SBPB was compared with the IBPB,[20] and the CBPB,[64]a greater incidence was seen with the SBPB in both studies. Owing to the serious respiratory complications associated with ISBPB technique, it should be avoided in patients with respiratory insufficiency.

(b) Pneumothorax: Pneumothorax is a collapsed lung in which air leaks into the space present between the lungs and the chest wall.The onset of clinical manifestations usually takes time (up to 24 hours). The prevalence of pneumothorax after the SBPB ranges from 0.5 to 6%.[97] Its association with BPB administration is due to the positioning of the apex of the lung which is medial and posterior to the brachial plexus.

Three studies related to the SBPB technique reported the complication of pneumothorax.[11,24,70]Pneumothorax is a very dreaded complication that is most commonly specific to the SBPB technique.[3] Yang CW et al found a greater incidence of pneumothorax with the SBPB as compared to the IBPB.[24]Shi-ping Luh found evidence of pneumothorax in 25% of patients after the SBPB technique by using X-rays.[98]Even, our review found a greater incidence of pneumothorax with the SBPB technique and more specifically SBPB technique with neural stimulation as compared to the US-guided SBPB,[41] as the use of US have reduced the incidence of this complication to a great extent. Singh and Singham found a greater incidence with the control group as compared to clonidine and dexmedetomidine groups with SBPB technique.[70]

(c) Other respiratory complications: Dyspnea was seen in six RCTs.[24,38,43,46,50,58] Respiratory complications are also found higher with the ISBPB technique (n=5). Respiratory depression and reduce ventilator function were seen in Renes SH et al,[21] and Behr et al,[31] studies with ISBPB. Riazi S et al,[16] found lower incidence of respiratory distress with low-volume LA (5ml) as compared to the high volume (20ml) with the US-guided ISBPB technique. Dyspnea and pulmonary embolism in Bjørnholdt KT et al with the ISBPB technique.[38] Shortness of breath was seen in Rettig HC et al,[10] with SBPB and IBPB technique respectively. Deep breathing was observed in Sivashanmugam T et al study with the SBPB technique.[64] Yang CW et al,[24] found a greater incidence of dyspnea with the SBPB technique as compared to the IBPB. Petrar SD et al,[43] and Kim BG et al,[50] compared the SBPB and the ISBPB techniques but found contrasting results. The former found a lesser incidence of dyspnea with the ISBPB technique and the latter found with the SBPB technique.

(3) Cardiac disorders: Thirteen studies reported cardiac complications, of which eleven studies,[14,40,56,75,76,77,55,59,60,61,62] demonstrated hypotensive and bradycardiac events and two

studies showed tachycardia/sinus tachycardia with ISBPB and SBPB technique respectively.[68,72] We found that among thirteen studies, eight are related to the SBPB technique only.
(a) Hypotension and bradycardiac events (HBE): It is defined as a decrease in heart rate of more than 30/min in less than 5 minutes a decrease in systolic blood pressure of more than 30 mm Hg in less than 5 minutes. The possible etiology responsible for HBE are carotid sinus hypersensitivity, Bezold-Jarisch reflex, orthostatic hypotension, venous air embolism, LA toxicity or epidural/subarachnoid spread of LA.[99]

Eleven studies reported the occurrence of HBE following BPB.[14,40,56,75,76,77,55,59,60,61,62] Pippa P et al,[14] found a greater incidence in the group receiving a lesser volume of LA with the ISBPB technique**.** Ryu T et al,[40] found a greater incidence with the ISBPB group (12.8%) when compared with the SBPB (4.3%). Hong B et al,[55] also found the complication of bradycardia with BPB. Hamed MA et al,[56] Sinha,[59] Dharmarao PS et al,[60] Mangal V et al,[61] Elyazed MAM et al,[62] Sachev S et al,[75] Singh N et al,[76] and Lotfy ME et al,[77]found incidence of bradycardia and hypotension more in the group receiving dexmedetomidine as compared to the control group,[61,75] or other adjuncts such as dexamethasone,[76] fentanyl,[56,60,77] MgSO4,[62] and clonidine,[70] with SBPB technique. Sinha C et al found more incidence with the group receiving a higher dose of dexmedetomidine with SBPB technique.[59]
(4) Hoarseness: Hoarseness is a rare complication of nerve block caused due to the blockade of the recurrent laryngeal nerve (RLN). The blockade also results in RLN palsy. In the present systematic review, eight studies,[16,40,44,46,50,58,65,69] have reported hoarseness as their complication and one study reported laryngeal nerve block,[31] with the use of ISBPB technique). Among the eight studies, three of them related to only the ISBPB technique. Riazi S et al found a greater incidence with high volume (20ml) LA group as compared to low-volume LA group of the ISBPB technique.[16] Palhais A et al,[44] (35% and 5%) and Ayyanagouda B et al,[65] (31% and

3.4%) found a lesser incidence of hoarseness with extrafascial group as compared to intrafascial group of ISBPB technique respectively. Five studies reported the complication while comparing two techniques. The incidence of the RLN block during the supraclavicular approach is seen in only 1.3% of patients.[100]With regard to hoarseness, Schubert AK et al found no significant difference between SBPB and ISBPB,[93] whereas, Ryu T et al,[40] Kim et al,[50] and Singh and Singham,[69] found higher incidence with ISBPB technique (10.6%, 1%, 17.8%) as compared to SBPB technique (4.3%. 0% and 0%) respectively, whereas, Wiesmann T et al,[46] found equal incidence after one week when ISBPB and SBPB were compared. Auyong DB et al compared ISBPB, SBPB, and suprascapular techniques and found a greater incidence with ISBPB technique (22%).[58]

(5) Phrenic nerve palsy: An inevitable consequence of the ISBPB technique is PNP which sometimes results in HDP and restricts the use of this technique in patients with respiratory difficulties. The high occurrence of PNP with this technique is because of the close proximity of the phrenic nerve to the site of injection of the ISBPB technique. According to the data from the case series, the incidence of PNP after the ISBPB technique ranges from 1 in 2,000 up to 1 in 100.[95]

In our review, we found that PNP was reported by four studies,[14,37,64,69] of which three studies,[14,37,69] found higher incidence with the ISBPB technique. Pippa P et al found a greater incidence in the group receiving a lesser volume of LA (P=0.002) with the ISBPB technique.[14] Bharti N et al,[37] and Singh and Singham,[69] found a greater incidence with the ISBPB technique when compared with the SBPB and SBPB, IBPB respectively. Sivashanmugam T et al found a greater incidence with the SBPB technique (45%) as compared to the CBPB (5%).[64] A systematic review conducted by El-Boghdadly K et al concluded that "the safest option to avoid phrenic nerve block would be to avoid performing an interscalene block" altogether".[101] The potential cause of PNP is direct damage of the phrenic nerve, intraneural injection, deposition of LA to the phrenic nerve (transient PNP). The occurrence of PNP

after ISBPB was seen in various case series published in the literature.[102,103,104] But none of the studies have reported the complication with US-ISBPB as the US helps in the visibility of the nerve. The mechanism of PNP may be attributed to the chemical, ischemic or mechanical trauma caused by LA, or its needle.

(6) Other complications: Patel MA et al in their study reported visual impairment, tinnitus, and muscle twitching with the ISBPB technique.[72] Urinary retention was also reported with the ISBPB technique by Kaya M et al.[33]

(7) Complications related to LA toxicity: LA toxicity is a well-known complication of anesthesia-related procedures. The chances of this toxicity is greater with brachial plexus anesthesia as compared to others because a larger dose of LA is required in this technique and the injection site is in close proximity with the large blood vessels of the head, neck, and axillary regions. When administered in the recommended concentrations and correctly, LA procedures are safe. Toxicity occurs due to inadvertent injection of the LA to the blood vessels and absorption of the LA from the peripheral sites, administration of high concentration of LA, or intraneural injection. The complications associated with LA are:

(a) Vascular puncture: Vascular puncture refers to the injury of blood vessels either through crushing, stretching, or tearing of the blood vessels due to the needle. It is determined by the presence of frank blood in the hub of the needle or aspiration of blood when the needle was attached to the tubing and a syringe. Twenty studies,[7,8,9,10,11,12,18,20,23,24,25,26,31,32,34,35,39,52,54,67,74] measured the incidence of vascular punctures. March X et al,[9] Serradell A et al,[8] Liu FC et al,[11] Gianesello L et al,[26] Bernucc F et al,[32] and Saracoglu S et al,[34] reported vascular puncture with AXB technique. Deleuze A et al,[7] De Jose Maria B et al,[18] and Bravo D et al,[54] reported the incidence with the IBPB technique. Oztur NK et al,[52] also reported the

complication but with the coracoid approach IBPB technique. Behr A et al reported with the ISBPB technique.[31] Singh S et al,[39] and Arab SA et al,[35] reported with the SBPB technique but Singh S et al with NS-SBPB technique.[39] Heid FM et al,[12] (IBPB and AXB), Tran DQH et al,[23] (IBPB, SBPB, and AXB), and Koscielniak-Nielsen JZ et al,[20] (SBPB and IBPB) reported equal incidence of the vascular puncture in groups but Yang CW et al,[24] reported more incidence with SBPB as compared to IBPB and Blanco AFG et al,[67] reported more incidence with IBPB as compared with RBPB. Luo Q et al reported more incidence with CBPB as compared to the SBPB technique.[74] Blood aspiration during block was reported in the Rettig HC et al with IBPB technique.[10]

(b) Postoperative nausea and vomiting (PONV): The administration of LA may manifest as nausea and vomiting in some patients. It was reported in 15 studies.[10,25,31,33,42,55,56,57,58,60,62,66,72,77,78] Parrington SJ et al,[25] Kooloth RA et al,[42] Kaur S et al,[66] reported incidence of PONV in low volume LA group, ropivacaine group and ketamine group (2 $mg.kg^{-1}$ ketamine with LA) with SBPB technique respectively. Hamed MA et al,[56] Dharmarao PS et al,[60] Elyazed MAM et al,[62] and Lotfy ME et al,[77] with SBPB technique Youssef MY et al,[78] reported with the SBPB technique. Rettig HC et al,[10] with the IBPB group. Behr et al reported with more incidence with intramuscular buprenorphine the ISBPB group.[31]. Kaya M et al,[33] Auyong DB et al,[58] and Patel MA et al,[72] reported more incidence of PONV with the ISBPB technique. Hong B et al,[55] reported more incidence with the midazolam group as compared to the dexmedetomidine group. Aliste J et al,[57] found equal incidence with ISBPB and SBPB

(c) Transient burning pain and bruising at the injection site: Burning pain was reported in two studies,[29,38] with SBPB and ISBPB techniques respectively, tourniquet pain,[11] axillary pain,[15] with AXB techniques. Bruising was reported by Chan VWS et al,[15] Parrington SJ et al,[25] and Subramanyam R et al.[29] Subramanyam R et al reported the incidence of bruising

in low volume LA group and lateral approach with SBPB technique respectively.[29]

(d) Other complications: Hematoma was reported in three studies,[11,38,66]with SBPB, ISBPB, and AXB techniques respectively. The intravascular injection was reported only in one RCT,[41] constipation by Patel MA et al,[72] pruritis at the site of injection by Patel MA et al,[72] and Lofty ME et al,[77] with ISBPB and SBPB techniques respectively. Hallucination and nystagmus by Kaur S et al,[66] dry mouth by Hong B et al,[55] dizziness by Hong B et al,[55] and Bjørnholdt KT et al,[38] the headache was reported by Hong B et al,[55] and Patel MA et al,[72] dysphonia was reported by Pippa P et al.[14]

In the present systematic review, we found that although ISBPB is the most common technique of anesthesia and pain management for the procedures involving the upper limb, it constitutes several inevitable consequences such as the occurrence of Horner syndrome, HDP, PNP, Hoarseness, respiratory complications, and PONV. Owing to the highest rates of complications associated with the ISBPB technique, alternate blocks should be searched. Even Guo C et al in their systematic review concluded that US-guided SBPB could become a feasible alternative to ISBPB in shoulder surgery.[105]

Limitations

Although we performed an extensive literature search, several pitfalls do exist as we have only included the RCTs that were published in the English language only. Secondly, we have only included one type of study design (RCT). In our review, most of the RCTs have a small sample size (<60 per group) and the number of RCTs constituting a larger sample size were very less. Some RCTs were performed by the same group of authors,[19,23,21,22,69,70] which might introduce some bias in the systematic review. Hence, the above-mentioned points should be kept in mind while performing further systematic reviews on this vital topic.

CONCLUSION

To conclude, the most common complications reported in 73 RCTs are Horner's syndrome, paresthesia, followed by the occurrence of HDP, and cardiac complications. With regard to various techniques of BPB, ISBPB leads the list due to the association of several inevitable complications such as Horner syndrome, HDP, PNP, and hoarseness. Pneumothorax and cardiac complications are mostly associated with SBPB, and paresthesia with AXB technique. The occurrence of cardiac complications is found more when dexmedetomidine is used as adjunct to LA for prolonging the duration of analgesia.

Although US-guidance is a blessing for the anesthesiologist for performing regional anesthesia, the possibility of various dreaded complications associated with specific techniques should be kept in mind and their alternative should be searched.

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