Protocol: Comparative efficacy of sedation or analgesia methods for reduction of anterior shoulder dislocation: a systematic review and network meta-analysis

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1. Introduction

Shoulder dislocation accounts for 50% of all dislocations and is the most common type of dislocation [1]. Most shoulder dislocations are anterior (90-98%) [1]. The pain due to the dislocation triggers muscle spasms around the shoulder. An important factor for the reduction of shoulder dislocation is moderate relaxation of the muscles around the shoulder [2]. Hence, sedation and analgesia are used for reduction of shoulder dislocation frequently [3].

As for the comparison between intravenous sedation and intra-articular anesthetic injection, previous systematic reviews reported that there were no significant differences in the success rate of reduction and patient satisfaction [4-6]. They also revealed intra-articular anesthetic injection had fewer complications, shorter length of hospital stay, and lower medical costs than intravenous sedation [4-6]. Recently, ultrasound-guided peripheral nerve blocks have been used for the reduction of shoulder dislocation. There have been several randomized control studies (RCT) comparing ultrasound-guided peripheral nerve block with intravenous sedation [7-9], but no systematic review compared among the three modalities.Therefore, it remains unclear what is the best method of sedation and analgesia for reduction of shoulder dislocation.

We will conduct a network meta-analysis to compare the efficacy and safety among intravenous sedation, intra-articular anesthetic injection, and peripheral nerve block for reduction of anterior shoulder dislocation.

2. Research question

P: The patients who need reduction of anterior shoulder dislocation
I: “Intra-articular anesthetic injection”, “Intravenous sedation”, “Peripheral nerve block”, “Placebo”, or “No intervention”
O: Immediate success rate of the reduction, Patient satisfaction, Length of hospital stay (minutes)

3. Method

3.1 Inclusion criteria of the articles for the review

3.1.1 Type of studies

We will include randomized controlled trials that assess sedation or analgesia methods for reduction of anterior shoulder dislocation. We will not apply language or country restrictions. We will include all papers including published, unpublished articles, abstract of conference and letter. We will exclude crossover trials,quasi-experimental studies and quasi-randomized trials. We will not exclude studies based on the observation period or publication year.

3.1.2 Study participants

Inclusion criteria:

Participants who were older than 15 years, and had a diagnosis of anterior shoulder dislocation as a result of the physical examination or X-ray of the shoulder.

Exclusion criteria:

Patients who cannot be obtained informed consent, allergies to any study medications, multiple trauma, associated fractures of the humerus (except Hill-Sachs lesion and Bankart lesions), hemodynamic instability, respiratory distress

3.1.3 Intervention

Intravenous sedation (IVS): Participants were injected with sedatives intravenously. Any type and dosage of sedatives is acceptable (ex: propofol, etomidate,benzodiazepines, barbiturates, ketamine, dexmedetomidine).

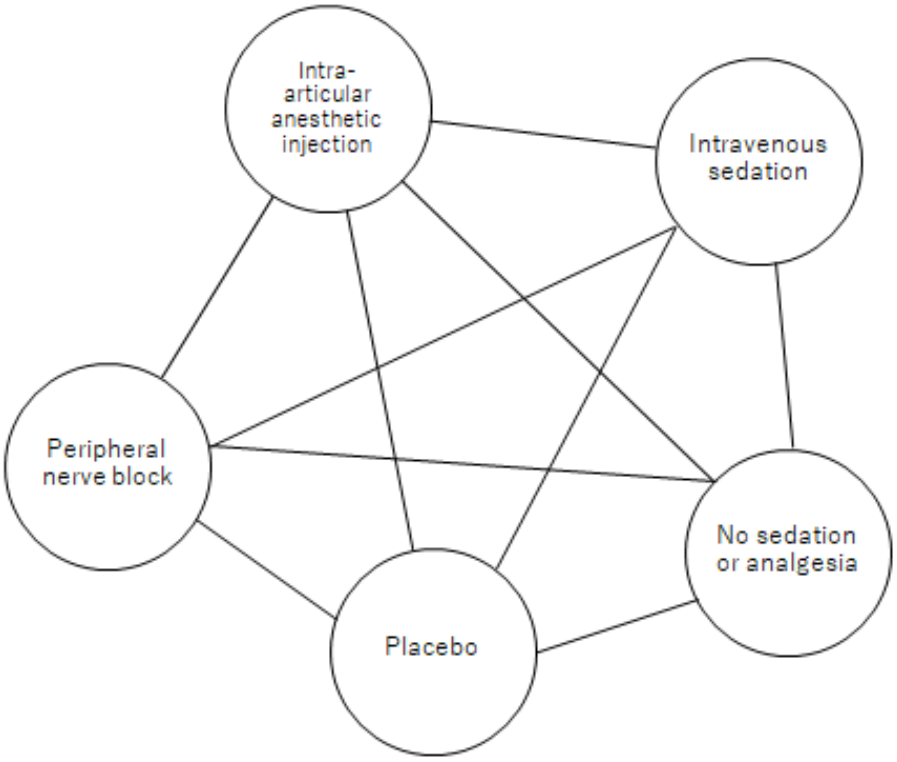
Analgesics may be used in combination (ex: opioid, acetaminophen, nonsteroidal anti-inflammatory agents, pethidine, meperidine).

Intra-articular anesthetic injection (IAA): Participants were injected with local anesthetics into the glenohumeral joint. Any medications and dosing is acceptable (ex: lidocaine, prilocaine, mepivacaine, ropivacaine, bupivacaine).

Peripheral nerve block (PNB): Participants were injected with local anesthetics into the brachial plexus in the interscalene position or the suprascapular nerve. Any medications and dosing is acceptable (ex: lidocaine, prilocaine, mepivacaine, ropivacaine, bupivacaine).

Placebo

No sedation or analgesia



3.2 Type of outcomes

3.2.1 Primary outcomes

1. Immediate success rate of the reduction

Definition: The success rate was as defined by the study authors (ex: at first attempt, at first reduction technique). we will accept a few attempts of reduction.

2. Patient satisfaction

Definition: Patient satisfaction with shoulder reduction procedure. Interview the patient on a scale of several levels of satisfaction. We will allow other definitions.

Period: After reduction, in a situation where the patient is awake. We will adopt the satisfaction data following order: during reduction, post-reduction, and post-intervention satisfaction.

3. Length of hospital stay (minutes)

Definition: Length of hospital stay was as defined by the study authors (ex: between entry into a room in the ED to discharge, between beginning of the procedure to discharge, between initial physician assessment to discharge). Ideally, the time between the start of the intervention and when the patient is allowed to discharge by medical staff.

3.2.2 Secondary outcomes

1. All adverse events

Definition: Definition of adverse events are set by original authors. Incidence proportion of all

adverse events
Period: During follow up period

2. Pain score
Definition: Interview the patient for pain score. We will adopt numeric rating scale (NRS) or visual analog scale (VAS) scale for pain score. We allow other definitions.
Period: Time from arrival at the hospital to discharge. Post-intervention pain score data extraction is the priority. Next priority is the post-reduction pain score.

3. Time required for reduction (minutes)
Definition: Time from the start to the end of reduction

4. The number of reduction attempts
Definition: Numbers of times physicians have attempted reduction
Period: Time from the start to the end of reduction

5. Total success rate of the reduction
Definition: Divide patients of successful reduction by total patients.
Period: Time from the start to the end of reduction

3.3 Search method
3.3.1 Electronic search
We will search the following databases:
1. The Cochrane Central Register of Controlled Trials (CENTRAL);
2. MEDLINE via PubMed;
3. EMBASE via Embase.com;
See Appendix 1, 2, and, 3 for the search strategies.

3.3.2 Other resources
We will also search the following databases for ongoing or unpublished trials:
1. The World Health Organization International Clinical Trials Platform Search Portal (ICTRP);
2. ClinicalTrials.gov;
See Appendix 4, 5 for the search strategies.
3. Google scholar;
We will use Google Scholar to search for literature citing the included studies .

We will check the reference lists of studies, including international guidelines as well as the reference lists of eligible studies and articles citing eligible studies. We will ask the authors of original studies for unpublished or additional data.

3.4 Data collection and analysis
3.4.1 Selection of the studies
Two independent reviewers (MH and KK) will check the title and abstract. All extracts by the two reviewers will be considered for full-text review. The full text will then be used by the same two independent reviewers to determine if it can be included in the review. If the study is an abstract only and it is not clear whether it meets the criteria for review, the original author will be contacted.

Any disagreements between the two reviewers should be discussed and resolved. If necessary, discuss with a third reviewer (NK).

3.4.2 Data extraction and management

Two reviewers (MH and KK) will perform independent data extraction of the included studies using standardized data collection form. We will use a pre-checked form using 10 randomly selected studies. The form will include the information on study design, study population, interventions and outcomes. Any disagreements will be resolved by discussion, and if this fails, a third reviewer will act as an arbiter (NK).

3.5 Assessment of risk of bias in included studies

Two reviewers (MH and KK) will work independently using the Risk of Bias 2 tool. Any disagreements between the two reviewers should be discussed and resolved. If necessary, discuss with a third reviewer (NK).

3.6 Measures of treatment effects

We will pool the odds ratio, relative risk ratios and risk difference with the 95% confidence intervals (CIs) for the following binary variables: the immediate success rate of the reduction, the total success rate of the reduction.

We will pool the standardized mean differences and the 95% CIs for the following continuous variables: length of hospital stay (minutes), patient satisfaction, pain score, the time required for reduction (minutes), and the number of reduction attempts.

We will summarize adverse events based on the definition by the original article, but we will not perform meta-analysis.

3.7 Unit of analysis issues

Only randomized controlled trials will be validated, and cluster randomized trials and crossover trials will not be included.

For the integration of the mean and standard deviation of continuous variables, we follow the method of the Cochrane Handbook [10].

8. Handling of missing data

3.8.1 Missing outcomes

Outcomes for dichotomous data

We will perform the intention-to-treat (ITT) analysis for all dichotomous data. We will also include missing participants for analysis. For those who dropped out from the study early, they are assumed to have the same rates of negative outcome on the basis of the rates of those who completed the study. We will underestimate the treatment effect by this method. We will describe how to impute missing data in each study. We will conduct the sensitivity analysis for imputation for missing data.

Outcomes for continuous data

We will not impute missing data based on the recommendation by Cochrane handbook [10]. We will perform meta-analysis about the available data in the original study.

2. Missing data
We will ask not-presented data to the original authors.

3. Missing statistics
When original studies only report standard error or p-value, we will calculate the standard deviation based on the method by Altman [11]. If we don't know these values when we contact the authors, standard deviation will be calculated by confidence interval and t-value based on the method by Cochrane handbook [10] , or validated method [12]. Validity of these methods will be analyzed by sensitivity analysis.

3.9 Assessment of heterogeneity
We will evaluate the statistical heterogeneity by visual inspection of the forest plots and calculating the I2 statistic (I2 values of 0% to 40%: might not be important; 30%to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity). When there is substantial heterogeneity (I2> 50%), we will assess the reason for the heterogeneity. Cochrane Chi2test (Q-test) will be performed for I2 statistics, and P value less than 0.10 will be defined as statistically significant.

3.10 Assessment of reporting bias
We will search the clinical trial registry system (ClinicalTrials.gov and ICTRP) and will perform extensive literature search for unpublished trials. We will assess the potential publication bias by visual inspection of the funnel plot. An Egg test will be performed as well. We will not conduct the test when we find less than 10 trials or trials which have similar sample sizes. We will assess the potential publication bias by visual inspection of the funnel plot.

3.11 Meta-analysis
We will perform statistical analyses using R software version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) and OpenBUGS (MRC Biostatistics Unit, University of Cambridge, Cambridge, United Kingdom).
For each outcome, we will conduct a network meta-analysis with both a fixed effect model and a random-effects model to estimate direct evidence and indirect evidence. If a network meta-analysis is inappropriate because of small sample size issues or violation of the model assumptions (exchangeability and consistency) , we will conduct a pairwise meta-analysis or a narrative synthesis.

3.12 Subgroup analysis
To elucidate the influence of effect modifiers on results, we will evaluate the subgroup analyses of the primary outcomes on the following factors when sufficient data are available.
1. (For participants) First time shoulder dislocation or recurrent

3.13 Sensitivity analysis
We will undertake the following sensitivity analyses for the primary outcomes to assess whether the results of the review are robust to the decisions made during the review process.
1. Exclusion of non-double blind studies.
2. Exclusion of studies using imputed statistics.

3. Exclusion of studies with high or some concern in the overall assessment of ROB.
4. Exclusion of studies that do not meet the ideal outcome.

4. Summary of findings table

Two reviewers (MH and NK) will evaluate the certainty of evidence using Confidence in Network Meta-analysis (CINeMA) [10, 13]. Disagreements between the two reviewers will be discussed, and if this fails, a third reviewer (NY) will be acting as an arbiter, if necessary. We will present the summary of findings table for the following outcomes[14].

1. Immediate success rate of the reduction
2. Patient satisfaction
3. Length of hospital stay (minutes)

5. Conflict of Interest

The authors declare no conflicts of interest.

6. Support

This work does not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix 1: CENTRAL (Cochrane Library) search strategy

([mh "shoulder dislocation"] OR ("shoulder" NEXT dislocation*):ti,ab OR ("closed" NEXT reduction*):ti,ab OR ("glenohumeral near" NEXT dislocat*):ti,ab) AND ([mh "injections, intra articular"] OR [mh anesthetics] OR [mh anesthesiology] OR [mh "conscious sedation"] OR [mh "hypnotics and sedatives"] OR [mh "anesthesia, intravenous"] OR [mh "nerve block"] OR [mh "brachial plexus"] OR ("intra" NEXT articular*):ti,ab OR ("local" NEXT anesthesia*):ti,ab OR sedation*:ti,ab OR sedatives*:ti,ab OR "nerve block":ti,ab OR intraarticular*:ti,ab OR ("regional" NEXT anesthesia*):ti,ab OR isbpb*:ti,ab OR ("brachial" NEXT plexus*):ti,ab OR interscalene*:ti,ab)

Appendix 2: MEDLINE (PubMed) search strategy

#1 "shoulder dislocation"[mh]
#2 "shoulder dislocation*"[tiab]
#3 "closed reduction*"[tiab]
#4 glenohumeral near dislocat*[tiab]
#5 "anterior dislocation of shoulder*"[tiab]
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 "injections, intra articular"[mh]
#8 "anesthetics"[mh]
#9 "anesthesiology"[mh]
#10 "conscious sedation"[mh]
#11 "hypnotics and sedatives"[mh]
#12 "anesthesia, intravenous"[mh]
#13 "nerve block"[mh]
#14 "brachial plexus"[mh]
#15 "intra articular*"[tiab]

#16 "local anesthesia*"[tiab]
#17 "sedation*"[tiab]
#18 "sedatives*"[tiab]
#19 "nerve block"[tiab]
#20 "intraarticular*"[tiab]
#21 "regional anesthesia*"[tiab]
#22 "isbpb*"[tiab]
#23 "brachial plexus*"[tiab]
#24 "interscalene*"[tiab]
#25 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR#24
#26 "randomized controlled trial"[pt]
#27 "controlled clinical trial"[pt]
#28 "randomized"[tiab]
#29 "drug therapy"[sh]
#30 "placebo"[tiab]
#31 "randomly"[tiab]
#32 "trial"[tiab]
#33 "groups"[tiab]
#34 "animals"[mh]
#35 "humans"[mh]
#36 #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 NOT (#34 NOT #35)
#37 #6 AND #25 AND #36

Appendix 3: EMBASE (Embase.com) search strategy

S1 'shoulder dislocation'/exp
S2 'shoulder dislocation*':ti,ab
S3 'closed reduction*':ti,ab
S4 glenohumeral NEAR/2 dislocat*
S5 S1 OR S2 OR S3 OR S4
S6 'injections, intra articular'/exp
S7 'anesthetics'/exp OR 'anesthesiology'/exp
S8 'conscious sedation'/exp
S9 'hypnotics and sedatives'/exp
S10 'anesthesia, intravenous'/exp
S11 'nerve block'/exp
S12 'brachial plexus'/exp
S13 'intra articular*':ti,ab
S14 'local anesthesia*':ti,ab
S15 sedation*:ti,ab
S16 sedatives*:ti,ab
S17 'nerve block':ti,ab
S18 intraarticular*:ti,ab
S19 'regional anesthesia*':ti,ab

S20 isbpb*:ti,ab
S21 'brachial plexus*':ti,ab
S22 interscalene*:ti,ab
S23 S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22
S24 S5 AND S23

Appendix 4: ICTRP search strategy

Condition:
shoulder dislocation OR closed reduction OR glenohumeral dislocation OR anterior dislocation of the shoulder
Intervention:
intra articular OR anesthesiology OR sedation OR sedatives OR intravenous anesthesia OR local anesthesia OR nerve block OR intraarticular OR brachial plexus OR regional anesthesia OR interscalene OR local anesthesia

Appendix 5: ClinicalTrials.gov search strategy

Condition or disease:
shoulder dislocation OR closed reduction OR glenohumeral dislocation OR anterior dislocation of shoulder
Intervention:
intra articular OR anesthesiology OR sedation OR sedatives OR intravenous anesthesia OR local anesthesia OR nerve block OR intraarticular OR brachial plexus OR regional anesthesia OR interscalene OR local anesthesia

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