# Efficacy of liposomal bupivacaine in regional anesthesia: a systematic review

Supplementary table 1: risk of bias assessments of included studies

|  |  |
| --- | --- |
| Baja 20018 | |
| Randomization process | Some concerns |
| Justification | Allocation concealment and randomization process not reported, patient baseline characteristics not reported |
| Deviation from intended intervention | Some concerns |
| Justification | Blinding not clear, protocol deviation not clear |
| Missing Outcome data | Some concerns |
| Justification | No consort diagram |
| Measurement of outcome | Some concerns |
| Justification | Observer blinding not reported |
| Selection of reported results | Some concerns |
| Justification | Trial not registered |
| Conflict of interest | Low |
| Justification | No conflict of interest |

|  |  |
| --- | --- |
| Belsh 2018 | |
| Randomization process | Some concerns |
| Justification | Allocation concealment and randomization process not reported, patient baseline characteristics not reported |
| Deviation from intended intervention | Some concerns |
| Justification | Patient blinded, clinician blinding not stated, not clear if there were protocol deviation |
| Missing Outcome data | Some concerns |
| Justification | No consort diagram |
| Measurement of outcome | Some concerns |
| Justification | Observer blinding not reported |
| Selection of reported results | Low |
| Justification | Trial registered NCT02607579 |
| Conflict of interest | Some concerns |
| Justification | Author is on the advisory board of the LB manufacturer |

|  |  |
| --- | --- |
| De Miersman 2017 | |
| Randomization process | Some concerns |
| Justification | Allocation concealment and randomization process not reported, patient baseline characteristics not reported |
| Deviation from intended intervention | Some concerns |
| Justification | Patient blinded, clinician blinding not stated, not clear if there were protocol deviation |
| Missing Outcome data | Some concerns |
| Justification | No consort diagram |
| Measurement of outcome | Low |
| Justification | Observer blinded |
| Selection of reported results | Some concerns |
| Justification | Trial not registered |
| Conflict of interest | Low |
| Justification | No conflict of interest |

|  |  |
| --- | --- |
| Gatherwright 2018 | |
| Randomization process | Some concerns |
| Justification | Allocation concealment and randomization process not reported, patient baseline characteristics not reported |
| Deviation from intended intervention | Some concerns |
| Justification | Blinding not clear, protocol deviation not clear |
| Missing Outcome data | Some concerns |
| Justification | No consort diagram |
| Measurement of outcome | Some concerns |
| Justification | Observer blinding not reported |
| Selection of reported results | Some concerns |
| Justification | Trial not registered |
| Conflict of interest | Low |
| Justification | No conflict of interest |

|  |  |
| --- | --- |
| Ha 2019 | |
| Randomization process | Some concern |
| Justification | Allocation concealment not described |
| Deviation from intended intervention | Some concerns |
| Justification | Patient blinding not clear, practitioner not blinded, 3 patients with missing data were excluded from the control group |
| Missing Outcome data | Some concerns |
| Justification | 16 patients excluded, 4 due to missing data |
| Measurement of outcome | Low |
| Justification | Observer was not aware of the allocation |
| Selection of reported results | Low |
| Justification | Trial registered NCT02662036 |
| Conflict of interest | Low |
| Justification | Funding not related to liposomal bupivicaine |

|  |  |
| --- | --- |
| Hutchins 2015 | |
| Randomization process | Some concern |
| Justification | allocation concealment not described |
| Deviation from intended intervention | Low |
| Justification | Surgeon blinded, patient blinding not clear, no deviation |
| Missing Outcome data | Low |
| Justification | Two patients excluded due to change in surgical plan |
| Measurement of outcome | Low |
| Justification | Observer was not aware of the allocation |
| Selection of reported results | Low |
| Justification | Trial registered NCT02289079 |
| Conflict of interest | Some concerns |
| Justification | Author is a consultant for the LB manufacturing company |

|  |  |
| --- | --- |
| Hutchins 2016 | |
| Randomization process | Low |
| Justification | Random number list and seal envelope technique |
| Deviation from intended intervention | Low |
| Justification | Patient blinded, practitioner not blinded, no protocol deviation reported |
| Missing Outcome data | Low |
| Justification | One patient excluded due to surgery changes |
| Measurement of outcome | Low |
| Justification | Observer was not aware of the allocation |
| Selection of reported results | Low |
| Justification | Trial registered NCT02287623 |
| Conflict of interest | Some concerns |
| Justification | Author is a consultant for the LB manufacturing company |

|  |  |
| --- | --- |
| Nair 2020 | |
| Randomization process | Some concerns |
| Justification | Allocation concealment and randomization process not reported, patient baseline characteristics balanced |
| Deviation from intended intervention | Low risk |
| Justification | No protocol deviation |
| Missing Outcome data | Low risk |
| Justification | all enrolled patients were completed |
| Measurement of outcome | Low risk |
| Justification | Assessors blinded |
| Selection of reported results | Low risk |
| Justification | Trial registered NCT03303794 |
| Conflict of interest | Low |
| Justification | No conflict of interest |

|  |  |
| --- | --- |
| Nedeljkovic 2020 | |
| Randomization process | Some concerns |
| Justification | Allocation concealment not reported, patient baseline characteristics balanced |
| Deviation from intended intervention | Some concerns |
| Justification | Authors reported protocol deviations in the dosage of liposomal bupivacaine given |
| Missing Outcome data | Low risk |
| Justification | 12 out pf 186 patients lost to follow up and further 50 were not excluded in the efficacy analysis due to protocol deviation, this was balanced |
| Measurement of outcome | Low risk |
| Justification | Assessors blinded |
| Selection of reported results | Low risk |
| Justification | Trial registered NCT03176459 |
| Conflict of interest | Some Concerns |
| Justification | The investigators received research funding from the drug manufacturers |

|  |  |
| --- | --- |
| Purcell 2019 | |
| Randomization process | Low |
| Justification | Block randomization and allocation according to ID number |
| Deviation from intended intervention | Low |
| Justification | The patient, surgeon, intraoperative and postoperative nurses all blinded |
| Missing Outcome data | Low |
| Justification | 4 patients excluded due to cancellation and preopreative medications |
| Measurement of outcome | Low |
| Justification | Observer was blinded to the medication assignment |
| Selection of reported results | Low |
| Justification | Trial registered NCT02947178 |
| Conflict of interest | Low |
| Justification | No conflict of interest |

|  |  |
| --- | --- |
| Shariat 2018 | |
| Randomization process | Some concerns |
| Justification | Randomized, allocation concealment not reported |
| Deviation from intended intervention | Low |
| Justification | Patient and clinician blinded |
| Missing Outcome data | Some concerns |
| Justification | 3 patients lost out of 42 |
| Measurement of outcome | Low |
| Justification | Assessor blinded |
| Selection of reported results | Low risk |
| Justification | Trial registered NCT01977352 |
| Conflict of interest | Low |
| Justification | No conflict of interest |

|  |  |
| --- | --- |
| Van Boxstael 2018 | |
| Randomization process | Some concerns |
| Justification | Allocation concealment and randomization process not reported, patient baseline characteristics not reported |
| Deviation from intended intervention | Some concerns |
| Justification | Patient blinded, clinician blinding not stated, not clear if there were protocol deviation |
| Missing Outcome data | Some concerns |
| Justification | No consort diagram |
| Measurement of outcome | Some concerns |
| Justification | Observer blinding not reported |
| Selection of reported results | some concerns |
| Justification | Trial not registered |
| Conflict of interest | Low |
| Justification | No conflict of interest |

|  |  |
| --- | --- |
| Vandepitte 2017 | |
| Randomization process | Low |
| Justification | Computer generated sequence, opaque envelope technique |
| Deviation from intended intervention | Low |
| Justification | Patient and clinician blinded, no protocol deviation |
| Missing Outcome data | Some concerns |
| Justification | 2 patients lost to follow up in the control group |
| Measurement of outcome | Low |
| Justification | Evaluator blinded to the assignment |
| Selection of reported results | Low risk |
| Justification | Trial registered NCT02554357 |
| Conflict of interest | High |
| Justification | Study funded by the liposomal bupivacaine manufacturer |

| Supplementary table 2: additional characteristics of included studies | | | | |
| --- | --- | --- | --- | --- |
|  | Publication medium | Regular postoperative analgesia | Additional analgesia related procedures | Conflict of interest |
| Baja 2018 | Conference abstract | Not reported | None | None |
| Belsh 2018 | Conference abstract | Not reported | Periarticular liposomal bupivacaine infiltration | Author is on the advisory board of the LB manufacturer |
| De Meirsman 2017 | Conference abstract | Not reported | None | None |
| Gatherwright 2018 | Journal paper | Not reported | Infiltration to the breast | None |
| Ha 2019 | Journal paper | Acetaminophen, celecoxib, gabapentin, OxyContin | Thoracic paravertebral block | Funding not related to the LB manufacturer |
| Hutchins 2015 | Journal paper | Acetaminophen and ibuprofen | None | Author is a consultant for the LB manufacturing company |
| Hutchins 2016 | Journal paper | Ketolorac | None | Author is a consultant for the LB manufacturing company |
| Nair 2020 | Trial registration | Not reported | Periarticular infiltration with the same drug mixture | None |
| Nedeljkovic 2020 | Journal paper | Acetaminophen and ibuprofen |  | Several authors received research fundings from the LB manufacturing company |
| Purcell 2019 | Journal paper | Acetaminophen, celecoxib, aspirin, sustained release oxycodone | None | None |
| Shariat 2018 | Trial registration | Not reported | None | None |
| Van Boxstael  2018 | Conference abstract | Not reported | None | None |
| Vandepitte 2017 | Journal paper | Acetaminophen, ibuprofen, dexamethasone | None | Study funded by the liposomal bupivacaine manufacturer |
| LB: liposomal bupivacaine | | | | |