Prolongation of Subarachnoid Block With Concomitant Use of Intravenous Dexmedetomidine: An Evidence-based Review

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A failed subarachnoid block due to prolonged surgical duration continues to be a challenging problem for anesthesia providers. This evidence-based review updates a 2013 systematic review describing the use of intravenous dexmedetomidine as an extrathecal spinal adjunct capable of extending the duration of a subarachnoid block. Eight randomized controlled trials published after the 2013 systematic review met the inclusion criteria. The evidence continues to support the use of intravenous dexmedetomidine as an effective method for prolonging the duration of motor and sensory blockade and postoperative analgesia in a subarachnoid block, with minimal side effects. This updated review reported a more consistent use of assessment tools measuring motor and sensory recovery, expanded the volume of evidence related to postoperative analgesia, and further validated the safe and efficacious use of intravenous dexmedetomidine in extending the duration of a subarachnoid block. Future studies are needed to evaluate the rescue benefit of intravenous dexmedetomidine in failed subarachnoid blocks converted to general anesthesia resulting from prolonged surgical times.

Keywords: Dexmedetomidine, duration, intravenous, spinal, subarachnoid.

The subarachnoid block (SAB) is a safe, quick, and effective form of regional anesthesia with predictable and reliable therapeutic benefits. Despite these positive attributes, a major disadvantage of the SAB is the limited methods for extending the duration of the anesthetic intraoperatively to address the needs of prolonged surgical procedures. Anesthesia providers have resorted to using higher local anesthetic doses, combined spinal-epidural block techniques, or intrathecal adjunct medications (epinephrine, phenylephrine, neostigmine, and clonidine) to extend the duration of an SAB. Higher doses of local anesthetics can predispose a patient to a “high spinal” complication, whereas combined spinal-epidural techniques can be technically difficult and time-consuming to perform. Authors of a 2013 systematic review with meta-analysis described the use of intravenous (IV) dexmedetomidine as an extrathecal spinal adjunct capable of extending the duration of an SAB.

Dexmedetomidine is a highly selective α2 agonist with spinal antinociceptive (visceral and somatic) properties that produces a synergistic effect with intraspinal local anesthetics. A supraspinal mechanism of action of IV dexmedetomidine has not been clearly defined. One group postulated that IV α2 agonists inhibit the activity of the locus coeruleus in the brain, leading to the disinhibition of noradrenergic nuclei. The reduced noradrenergic outflow is thought to strengthen the inhibitory nociceptive effect on the spinal cord. This evidence-based review evaluates the efficacy and safety of using IV dexmedetomidine in SAB cases and provides an update to the 2013 systematic review with meta-analysis.

History and Review of the Literature
• History. The overall failure rate for SABs has been reported to be 0.6%, with about one-fourth of all failed SABs attributed to prolonged surgical times. Spinal anesthetic failure resulting in a general anesthetic conversion negates the positive effects of regional anesthesia. The reported benefits of an SAB include decreased incidence of venous thrombosis, reduction in intraoperative blood loss, and decline in postoperative narcotic requirements, leading to lower rates of postoperative nausea and vomiting, postoperative ileus, and constipation. Extending the duration of the SAB could avoid these unnecessary general anesthetic conversions in those cases in which prolonged surgical time is the predominant factor for spinal anesthetic failure.

The IV α2 agonists, clonidine and dexmedetomidine, have been reported to be effective in prolonging the duration of an SAB. Dexmedetomidine has 8 to 10 times higher binding affinity for the α2 receptor than does clonidine. This higher α2 receptor selectivity for IV dexmedetomidine reduces the severity of hemodynamic side effects (bradycardia and hypotension) and is capable of extending the duration of an SAB longer than clonidine. A lower side effect profile combined with improved SAB duration has led to the dissemination of
research regarding the use of IV dexmedetomidine as an extrathecal adjunct.

Authors of a systematic review published in 2013 suggested that IV dexmedetomidine could be an effective spinal adjunct for prolonging the duration of regional blockade and postoperative analgesia in patients receiving an SAB (Table 1). This systematic review by Abdallah et al contained 7 intermediate to high-quality (Jadad score of 3 or higher) randomized controlled trials (RCTs) examining 364 subjects, equally distributed between placebo and IV dexmedetomidine treatment groups. Primary outcome measures in their review were duration of motor and sensory block, postoperative analgesia, and adverse-related effects (bradycardia, hypotension, respiratory depression, and postoperative sedation).

The authors described a comprehensive search strategy and appraisal of articles in their review. In the review by Abdallah et al, dosing of dexmedetomidine was highly variable between studies and the standardization of assessment measures for sensory and motor block duration lacked consistency. The authors indicated that a high level of heterogeneity (I² > 85%) was also present in all 7 RCTs, which could lessen the generalizability of the results of the systematic review. Using the ratio of means as the measure, there was an increase in motor and sensory block duration and time to first analgesic request favoring the addition of IV dexmedetomidine to the SAB. Ratio of means is derived by dividing mean differences from the control and intervention groups to calculate a ratio that describes the magnitude of effect in continuous data. Bradycardia was the only complication reported in the dexmedetomidine-treated groups.

**Review of the Literature.** This new evidence-based review updates the earlier systematic review with meta-analysis examining the safety and efficacy of IV dexmedetomidine on the block characteristics of a spinal anesthetic.

**The PICO Question.** The PICO (patient or population, intervention, comparison, outcome) question guiding the search for evidence was as follows: “In patients undergoing spinal anesthesia (P), does intravenous dexmedetomidine (I) effectively and safely prolong the motor (O) and sensory (O) blockade duration and postoperative analgesia (O) of a neuroaxial anesthetic?”

**Search Strategy.** Evidence included only those studies published subsequent to the sources included in the systematic review with meta-analysis. The search for evidence (2012-2015) was conducted using PubMed, The Cochrane Database of Systemic Reviews, and Google Scholar. The ancestry approach and the PubMed-related citations feature were used to locate other sources. Search terms included spinal, subarachnoid block, dexmedetomidine, intravenous, anesthesia, analgesia, pain prevention, and duration. Evidence was limited to full-text, English-language systematic reviews and studies published in peer-reviewed journals examining motor and sensory blockade duration, side effects, and postoperative analgesia benefits.

Studies were included regardless of the local anesthetic used for the SAB. All methods and dosing regimens for IV dexmedetomidine were included in this review. Sources were included based on reviewing the title, abstract, and full text of possible sources. Evidence was appraised using the method offered by Melnyk and Fineout-Overholt.

**Critical Appraisal of Literature.** Eight sources, all RCTs (480 subjects), met the inclusion criteria (Figure). These RCTs are described in Tables 2 and 3.

### Table 1. Summary of Systematic Review With Meta-Analysis Examining Characteristics of Spinal Anesthetics With Concomitant Use of Intravenous Dexmedetomidine

<table>
<thead>
<tr>
<th>Type of evidence</th>
<th>Dexmedetomidine method of dosing, number of studies</th>
<th>N</th>
<th>Motor block duration (ROM, 95% CI)</th>
<th>Sensory block duration (ROM, 95% CI)</th>
<th>Time to first analgesic request (ROM, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 RCTs</td>
<td>Bolus, 2; Bolus + maintenance, 5</td>
<td>364</td>
<td>1.21 (1.17-1.25)</td>
<td>1.38 (1.34-1.42)</td>
<td>1.60 (1.53-1.67)</td>
</tr>
</tbody>
</table>

Potential sources: 79
Sources meeting criteria based on title: 19
Sources meeting criteria based on abstract: 13
Sources meeting criteria based on full text: 8
<table>
<thead>
<tr>
<th>Evidence source and level of evidence, 13</th>
<th>Total number of subjects and groups (subjects per group)</th>
<th>Dexmedetomidine before subarachnoid block</th>
<th>Dose of bupivacaine</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jung et al, 16 2013 Level II</td>
<td>60; NS (n = 20); dexmedetomidine, 0.25 μg/kg bolus (n = 20); dexmedetomidine, 0.5 μg/kg bolus (n = 20)</td>
<td>No</td>
<td>12 mg&lt;sup&gt;0&lt;/sup&gt;</td>
<td>Desired sample size based on results of power analysis. Recovery to knee flexion used, not MBS. No observer training described. Double blinded.</td>
</tr>
<tr>
<td>Reddy et al, 21 2013 Level II</td>
<td>75; NS (n = 25); dexmedetomidine, 0.5 μg/kg bolus (n = 25); clonidine, 1 μg/kg bolus (n = 25)</td>
<td>Yes</td>
<td>15 mg 0.5%</td>
<td>Desired sample size based on results of power analysis. Randomization method not described. No statistical difference in motor block from controls. Initial SAB sensory level was 2 dermatomes higher than control. Double blinded.</td>
</tr>
<tr>
<td>Harsoor et al, 15 2013 Level II</td>
<td>50; NS (n = 25); dexmedetomidine, 0.5 μg/kg bolus, and 0.5 μg/kg/h infusion (n = 25)</td>
<td>Yes</td>
<td>12.5 mg&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Desired sample size based on results of power analysis. Loss of temperature sensation used, but exact method not described. Initial SAB sensory level was 2 dermatomes higher for control subjects. Double blinded.</td>
</tr>
<tr>
<td>Dinesh et al, 14 2014 Level II</td>
<td>100; NS (n = 50); dexmedetomidine, 1 μg/kg bolus, and 0.5 μg/kg/h infusion (n = 50)</td>
<td>No</td>
<td>15 mg 0.5%</td>
<td>Desired sample size based on results of power analysis. Initial SAB sensory level was 1 dermatome higher than control. Observer training not described. Reported a time for complete sensory S1 regression. Shivering 10% higher in control group. Blinding method not described.</td>
</tr>
<tr>
<td>Lee et al, 19 2014 Level II</td>
<td>60; NS (n = 20); dexmedetomidine, 0.5 μg/kg bolus (n = 20); dexmedetomidine, 1 μg/kg bolus (n = 20)</td>
<td>Yes</td>
<td>12 mg 0.5%</td>
<td>Desired sample size based on results of power analysis. 5 of 20 subjects did not reach initial MBS of 3 (2 of 20 controls; 1 in dexmedetomidine, 0.5 μg/kg, group; and 2 in dexmedetomidine, 1 μg/kg, group). Observer training not described. Double blinded.</td>
</tr>
<tr>
<td>Kim et al, 17 2014 Level II</td>
<td>90; NS (n = 30); dexmedetomidine, 1 μg/kg bolus, and 0.5 μg/kg/h infusion (n = 30); ketamine, 0.2 mg/kg bolus, and 0.5 mg/kg/h infusion (n = 30)</td>
<td>No</td>
<td>10 mg 0.5%</td>
<td>No power analysis conducted. Observer training not described. Used MBS (1-6) rating scale with endpoint of 4. Blinding method not described.</td>
</tr>
<tr>
<td>Park et al, 20 2014 Level II</td>
<td>45; NS (n = 15); dexmedetomidine, 0.5 μg/kg bolus (n = 15); dexmedetomidine, 1 μg/kg bolus (n = 15)</td>
<td>No</td>
<td>6 mg&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Desired sample size based on results of power analysis. Three patients lost to attrition because of insufficient anesthesia level resulting in less than the desired sample of 15 subjects. No initial MBS set point from SAB recorded. Low-dose (6-mg) bupivacaine given. Observer training not described. Maximum block level not described. No difference in groups for time-to-first request of analgesic. No statistical difference in motor block duration between control and dexmedetomidine groups. Blinding method not described.</td>
</tr>
<tr>
<td>Kumar et al, 18 2015 Level II</td>
<td>100; NS (n = 50); dexmedetomidine, 1 μg/kg bolus, and 0.5 μg/kg/h infusion (n = 50)</td>
<td>No</td>
<td>15 mg 0.5%</td>
<td>No power analysis conducted. No exclusion/inclusion criteria described. Initial SAB sensory level was 1 dermatome higher than control. Observer training not described.</td>
</tr>
</tbody>
</table>

Table 2. Summary of Randomized Control Trials Describing Spinal Block Characteristics with the Concomitant Use of Intravenous Dexmedetomidine

Abbreviations: MBS, motor Bromage scale; NS, normal saline; RCT, randomized controlled trial; SAB, subarachnoid block; TDR, 2-dermatome regression.

<sup>a</sup> Authors in all studies reported using a hyperbaric solution of bupivacaine.
<sup>b</sup> Bupivacaine concentration not disclosed.
<sup>c</sup> Results from medications examined in the study other than dexmedetomidine were not included in the table.
Primary outcome measures of the RCTs included the duration of motor and sensory blockade, postoperative analgesia, and side effects (bradycardia and hypotension) when IV dexmedetomidine was administered simultaneously with an SAB. No difference was noted in demographic characteristics between the treatment and control groups, and randomization techniques in each of the RCTs were described in detail with the exception of 1 study. Three RCTs failed to describe details about blinding methods. All the RCTs included in this review were published outside the United States.

Authors of 2 RCTs failed to conduct a power analysis to determine a sample size for outcomes measured. Park et al performed a power analysis (α = .05, β = 0.2) but had 3 subjects withdraw because of an insufficient anesthetic level, leaving the RCT underpowered based on the author’s calculated sample size, as they did not take into account subject attrition. Authors of 6 RCTs performed a power analysis using a 15% difference in either duration of analgesia or time to 2-dermatome regression (TDR) of at least 20 minutes as measured outcomes.

Dosing of dexmedetomidine was either a bolus only or a bolus plus a maintenance infusion. Intravenous dexmedetomidine administration in 4 studies was commenced after the SAB was placed. Two RCTs omitted the preload IV fluid bolus before SAB placement. In the other 6 RCTs, a fluid bolus dose, decreased HR at all time intervals. Atropine administered for HR < 50/min in 4 of 25 in dexmedetomidine group. No IV fluid bolus given before SAB. No statistical difference seen in MAP between groups. No difference in MAP and HR between groups. 6 subjects in the dexmedetomidine group. ATRO was used for HR < 50/min in 4 of 25 in dexmedetomidine group. lowest HR, instances of bradycardia (< 50/min), lowest SBP (20% decrease from baseline), and DBP intraoperatively were in the dexmedetomidine group. Treatment with atropine was not disclosed.

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean motor recovery time (min)</th>
<th>Mean sensory block recovery time (min)</th>
<th>Postoperative analgesic benefits</th>
<th>Heart rate/mean arterial pressure effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jung et al, 2013</td>
<td>DMB</td>
<td>TDR</td>
<td>Not evaluated</td>
<td>Dexmedetomidine, 0.5-μg bolus dose, decreased HR at all time intervals.</td>
</tr>
</tbody>
</table>
|                  | NS = 135 (60-180)             | NS = 75 (45-120)                      |                                 | Atropine administered for HR < 50/min in 5 of 20 subjects in dexmedetomidine, 0.5 μg/kg, group.  
|                  | α, 2013                       |                                      |                                 | No IV fluid bolus given before SAB. No statistical difference seen in MAP between groups.  
|                  |                               |                                      |                                 | No difference in MAP and HR between groups.  
|                  |                               |                                      |                                 |                                      |
| Reddy et al, 21  | MBS (3-1)α                     | TDR                                   | Mean time to first analgesic request (min): NS = 41 (SD = 29); dexmedetomidine = 243 (SD = 57)  
|                  | NS = 139 (SD = 32); dexmedetomidine = 146 (SD = 32) | NS = 95 (SD = 17); dexmedetomidine = 149 (SD = 21)  
|                  |                               |                                      |                                 | Atropine administered for HR < 50/min in 4 of 25 in dexmedetomidine group.  
|                  |                               |                                      |                                 | Low MAP was treated in 2 of 25 subjects in dexmedetomidine group.  
|                  |                               |                                      |                                 | Lowest HR, instances of bradycardia (< 50/min), lowest SBP (20% decrease from baseline), and DBP intraoperatively were in the dexmedetomidine group.  
|                  |                               |                                      |                                 | Treatment with atropine was not disclosed.  
|                  |                               |                                      |                                 |                                      |
| Harsoor et al, 15| MBS (3-0)                      | TDR                                   | Mean paracetamol use (g): NS = 2.7 (SD = 0.6); dexmedetomidine = 1.87 (SD = 0.6)  
|                  | NS = 231 (SD = 32); dexmedetomidine = 256 (SD = 53) | NS = 54 (SD = 18); dexmedetomidine = 112 (SD = 14)  
|                  |                               |                                      |                                 | Mean diclofenac use (mg): NS = 117 (SD = 41); dexmedetomidine = 77 (SD = 56)  
|                  |                               |                                      |                                 | Treatment with atropine was not disclosed.  
|                  |                               |                                      |                                 |                                      |
| Dinesh et al, 14 | MBS (3-0)                      | TDR                                   | Mean time to first analgesic request: NS = 3 h; dexmedetomidine = 5.27 h  
|                  | NS = 131 (SD = 10); dexmedetomidine = 220 (SD = 17) | NS = 102 (SD = 15); dexmedetomidine = 137 (SD = 11)  
|                  |                               |                                      |                                 |                                      |

Table 3 continues ➔
with knee flexion. Recorded endpoints for motor recovery had MBS scores that varied from 0 to 14,15,18-21 and 4. Observer training in motor and sensory block assessment was identified in only 2 studies.15,21 Sedation from IV dexmedetomidine using a bolus plus maintenance method could have an impact on the validity and reliability of sensory and motor recovery times because subject participation is required. Of these 5 studies,2 studies indicated Ramsey sedation scores during the postoperative period that were equal to those of the control group. One RCT described 5 of 20 subjects with a Ramsey sedation score above 5 in the dexmedetomidine, 1 μg/kg/h, group with a sedation regression time (< 3) recorded at 90 minutes. Two RCTs did not disclose or evaluate Ramsey sedation scores during IV dexmedetomidine administration.

Postoperative analgesia assessment was analyzed in 4 studies.14,15,20,21 Assessment tools used in the studies varied widely and included visual analog score (VAS), time to first analgesic request, and 24-hour dosage requirements of postoperative pain medications. The VAS scores in the first 24-hour postoperative period were recorded in 1 study,20 whereas time to a VAS score above 3 was the endpoint in another study.15 Observer training evaluating postoperative analgesia outcomes was detailed in only 2 of these studies.15,21

Discussion of the State of Art
The 8 RCTs had a considerable amount of variability in the initial maximum sensory level achieved by the SAB.

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean motor recovery time (min)</th>
<th>Mean sensory block recovery time (min)</th>
<th>Postoperative analgesic benefits</th>
<th>Heart rate/mean arterial pressure effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al,19 2014</td>
<td>MBS (3-1)c NS = 99 (SD = 34); dexmedetomidine, 0.5 μg/kg = 133 (SD = 43)b; dexmedetomidine, 0.25 μg/kg = 130 (SD = 50)b</td>
<td>MBS (3-1)c NS = 58 (SD = 23); dexmedetomidine, 0.5 μg/kg = 86 (SD = 24)b; dexmedetomidine, 1 μg/kg = 93 (SD = 31)d</td>
<td>Not evaluated</td>
<td>No difference in MAP and HR between groups</td>
</tr>
<tr>
<td>Kim et al,17 2014</td>
<td>MBS (4)f NS = 124 (SD = 19); dexmedetomidine = 145 (SD = 22)b</td>
<td>MBS (4)f NS = 99 (SD = 11); dexmedetomidine = 122 (SD = 14)b</td>
<td>Not evaluated</td>
<td>No difference in MAP and HR between groups</td>
</tr>
<tr>
<td>Park et al,20 2014</td>
<td>MBS (3-0)c NS = 80 (SD = 32); dexmedetomidine, 0.5 μg/kg = 94 (SD = 51); dexmedetomidine, 1 μg/kg = 80 (SD = 39)</td>
<td>MBS (3-0)c NS = 80 (SD = 32); dexmedetomidine, 0.5 μg/kg = 97 (SD = 28); dexmedetomidine, 0.25 μg/kg = 115 (SD = 28)d</td>
<td>TDR (cold) NS = 82 (SD = 21); dexmedetomidine, 0.5 μg/kg = 90 (SD = 23)d; dexmedetomidine, 1 μg/kg = 98 (SD = 29)d</td>
<td>TDR (pinprick) NS = 82 (SD = 21); dexmedetomidine, 0.5 μg/kg = 90 (SD = 23)d; dexmedetomidine, 1 μg/kg = 98 (SD = 29)d</td>
</tr>
<tr>
<td>Kumar et al,18 2014</td>
<td>MBS (3-0)c NS = 131 (SD = 10); dexmedetomidine = 221 (SD = 17)d</td>
<td>MBS (3-0)c NS = 131 (SD = 10); dexmedetomidine = 221 (SD = 17)d</td>
<td>TDR (cold) NS = 169 (SD = 12); dexmedetomidine = 270 (SD = 21)d</td>
<td>TDR (pinprick) NS = 169 (SD = 12); dexmedetomidine = 270 (SD = 21)d</td>
</tr>
</tbody>
</table>

Table 3. Findings of Evidence Sources Examining Spinal Block Characteristics With Concomitant Use of Intravenous Dexmedetomidine
Abbreviations: DBP, diastolic blood pressure; DMB, time to recovery of knee flexion; HR, heart rate; IV, intravenous; MAP, mean arterial pressure; MBS, motor Bromage scale; NS, normal saline; SAB, subarachnoid block; SBP, systolic blood pressure; TDR, 2-dermatome sensory regression; VAS, visual analog score.
a Values expressed as a median (range).
b P < .05 (control vs intervention)
c Initial MBS required with endpoint recorded for motor duration. Grade 0 indicates no paralysis; 1, unable to raise extended leg; 2, unable to flex knee; and 3, unable to flex ankle.
d P < .0001 (control vs intervention).
e P < .001 (control vs intervention).
f MBS scale from 1-6 with no initial motor block level reported. Return level of 4 was the endpoint (1 indicated complete block, while 6 was no paralysis).
g P value not reported.
Authors of 4 RCTs\textsuperscript{14,16,18,21} reported a 1- to 2-dermatome sensory block level that was higher in the dexmedetomidine groups. In 2 studies,\textsuperscript{17,19} no difference in the highest block level was identified. One RCT\textsuperscript{20} failed to disclose a maximum sensory block level, whereas authors of another RCT\textsuperscript{15} reported block levels that were 2 levels higher in the control group compared with the intervention group. Dexmedetomidine administration before the placement of SAB had no influence on the initial sensory level.\textsuperscript{14-21} Maximum sensory level variability between the dexmedetomidine and control groups could have an impact on motor recovery duration times with higher block levels prolonging the duration of motor recovery.\textsuperscript{2} The TDR was recorded from maximum sensory level, so the variability in block level had less influence on this outcome.\textsuperscript{14-21}

- **Sensory Block Duration.** Authors of all 8 RCTs\textsuperscript{14-21} used a TDR assessment tool to measure sensory recovery. Each of the 8 RCTs was statistically significant in extending the duration of sensory blockade (see Table 3).\textsuperscript{14-21} Several authors\textsuperscript{16,19} indicated that extending the sensory block by 30 minutes was a clinically significant difference. Of the 8 RCTs, only 2 studies\textsuperscript{17,20} reported a TDR of less than 30 minutes when dexmedetomidine was compared with the normal saline control group. Of these 2 RCTs, Park et al\textsuperscript{20} used a 6-mg dose of bupivacaine in the SAB, with no initial maximum level reported involving cases of less than 2 hours in duration. Considering this dose, assessment of TDR from a sacral-level SAB explains why initial maximum levels were not disclosed in this study. Overall, sensory blockade duration beyond 30 minutes using the TDR tool was not affected by the method (bolus or bolus plus maintenance), timing (before or after SAB placement), or the dexmedetomidine dose.\textsuperscript{14-21}

- **Motor Block Duration.** In 6 of the 8 RCTs, the concomitant use of IV dexmedetomidine with SAB produced a statistically significant difference in the duration of motor blockade (see Table 3).\textsuperscript{14-21} In 4 RCTs, motor block duration exceeded control values by more than 30 minutes.\textsuperscript{14,16,18,19} Two authors indicated that a 30 minute prolongation in duration was clinically significant for prolonging motor blockade.\textsuperscript{16,19} Of these 4 studies, 1 study\textsuperscript{16} involved bolus-only dosing of dexmedetomidine, and 3 RCTs used bolus plus maintenance dosing.\textsuperscript{14,18,19} Authors of 1 RCT\textsuperscript{19} reported that an MBS of 3 (complete paralysis) was not achieved in 5 subjects. One RCT\textsuperscript{15} administered dexmedetomidine before the SAB was placed, and this was the only study in which the maximum sensory block level did not exceed the control group. The results of 4 RCTs failed to demonstrate a prolongation in the motor block duration beyond 30 minutes when dexmedetomidine was compared with the control groups.\textsuperscript{15,17,20,21} Recorded block duration times were initiated at the time of the SAB placement.\textsuperscript{14-21} Dosing of dexmedetomidine as a bolus plus maintenance after SAB placement produced the longest duration of motor blockade among the 8 RCTs.\textsuperscript{14-21}

Dosing of dexmedetomidine as a bolus with a maintenance infusion had the greatest effect on the duration of motor and sensory blockade.\textsuperscript{14-21} Starting bolus doses of dexmedetomidine of 0.5 to 1 μg/kg, followed by an infusion of dexmedetomidine of 0.5 μg/kg/h, prolonged the motor and sensory characteristics of an SAB the longest.\textsuperscript{14,18,19} Authors of 1 RCT\textsuperscript{19} used a bolus of 1 μg/kg plus maintenance infusion dosing of 0.5 μg/kg/h with motor and sensory block recovery times of less than 30 minutes between the dexmedetomidine and control groups. Bolus-only dosing of dexmedetomidine at 1 μg/kg was also shown to extend the motor and sensory blockade of an SAB but not to the same extent as bolus plus a maintenance infusion.\textsuperscript{16}

- **Postoperative Analgesia.** Only 1 RCT\textsuperscript{20} failed to find a statistically significant difference between the dexmedetomidine and control group in VAS in the first 24 hours (see Table 3). Total 24-hour pain medication dosage requirements were reported in 1 RCT\textsuperscript{14} with a significant reduction in the use of paracetamol, diclofenac, and tramadol in a comparison of dexmedetomidine with the control group. Additionally, time for the first analgesic request was prolonged by more than 2 hours in 2 RCTs.\textsuperscript{14,21} The addition of IV dexmedetomidine to spinal anesthesia in patients undergoing surgery improved the duration and intensity of postoperative analgesia when measured by VAS,\textsuperscript{15} pain medication dosage requirements,\textsuperscript{14} or time-to-the-first-analgesic-request assessment tools.\textsuperscript{14,21}

- **Adverse Hemodynamic and Respiratory Effects.** Authors of 8 RCTs measured mean arterial pressure and heart rate parameters before, during, and after dexmedetomidine administration.\textsuperscript{14-21} Bradycardia (heart rate < 50/min) requiring treatment with atropine was reported in 2 RCTs.\textsuperscript{15,16} In 1 of these RCTs\textsuperscript{16} reporting atropine treatment, dexmedetomidine was administered before the SAB,\textsuperscript{15} whereas in the other RCT, dexmedetomidine was given after placement of the SAB and without the administration of a preload fluid bolus.\textsuperscript{16} Five RCTs reported no statistical difference in either mean arterial pressure or heart rate data when comparing dexmedetomidine and control groups with each other.\textsuperscript{15,21} In the 8 RCTs,\textsuperscript{14-21} no respiratory-related complications were reported in any of the IV dexmedetomidine groups.

Results from this evidence-based update\textsuperscript{14-21} are similar to the findings published in an earlier systematic review.\textsuperscript{3} Calculated pooled mean differences from evidence sources\textsuperscript{3,14-21} in this updated review confirm this comparative conclusion (Table 4). This updated review of 8 RCTs published subsequent to the systematic review reported a more consistent use of assessment tools measuring motor and sensory recovery, expanded the volume of evidence related to postoperative analgesia, and further validated the safe and efficacious use of IV dexmedetomidine in extending the duration of an SAB.
of an SAB. Intravenous dexmedetomidine does not cause a 
therapeutic level of sedation while also extending the duration 
sedated during the operation. Intravenous dexmedetomi-
dine has not been studied as a “rescue” method when surgery is unexpectedly prolonged, but dexmedetomidine has not been studied as a “rescue” method when surgery is unexpectedly prolonged, but future studies should examine this use. Clinicians must weigh the risk and benefits in selecting IV dexmedetomidine as a primary SAB adjunct in cases that may be unexpectedly prolonged and require a conversion to general anesthesia.

Patients receiving an SAB often have a desire to be sedated during the operation. Intravenous dexmedetomidine has the added benefit of providing this intraoperative level of sedation while also extending the duration of an SAB. Intravenous dexmedetomidine does not cause significant respiratory depression and provides a dependable and titratable level of intraoperative sedation with a wide safety margin.22

Studies are needed examining postoperative pain reduction outcomes. We found only 4 RCTs14-21 and 3 studies in the systematic review3 examining duration of postoperative analgesia. Additionally, future studies using consistent assessment tools for motor and sensory block recovery, equivalent SAB local anesthetic doses, and similar IV dexmedetomidine dosing regimens across a broad class of patients are needed. Such studies could add to the generalizability and potentially reduce the heterogeneity of research results when IV dexmedetomidine is evaluated for the extension of sensory and postoperative analgesia in an SAB.

**Conclusion**

A major disadvantage of the SAB is the inability to extend the duration of the anesthetic intraoperatively to address the needs of prolonged surgical procedures. Methods to address this problem include using intrathecal adjuncts, combined spinal-epidural techniques, and higher SAB local anesthetic doses.2 The results of the systematic review with meta-analysis3 and the 8 subsequently published RCTs14-21 indicate that IV dexmedetomidine is probably an effective alternative method for prolonging the duration of motor and sensory blockade and postoperative analgesia with minimal side effects. Intravenous dexmedetomidine has not been studied as a “rescue” method when surgery is unexpectedly prolonged, but future studies should examine this use. Clinicians must weigh the risk and benefits in selecting IV dexmedetomidine as a primary SAB adjunct in cases that may be unexpectedly prolonged and require a conversion to general anesthesia.

Patients receiving an SAB often have a desire to be sedated during the operation. Intravenous dexmedetomidine has the added benefit of providing this intraoperative level of sedation while also extending the duration of an SAB. Intravenous dexmedetomidine does not cause significant respiratory depression and provides a dependable and titratable level of intraoperative sedation with a wide safety margin.22

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**Table 4.** Pooled Mean Differences Evaluating Subarachnoid Block Characteristics With Concurrent Use of Intravenous Dexmedetomidine

<table>
<thead>
<tr>
<th>Source</th>
<th>Dexmedetomidine dosing method (No. of studies)</th>
<th>Subjects (N)</th>
<th>Motor recoverya (min)</th>
<th>Sensory recoverya (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdallah et al, 20133</td>
<td>Bolus (n = 2)</td>
<td></td>
<td>364</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Bolus + Maintenance (n = 7)</td>
<td>53</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Updated RCTs14-21</td>
<td>Bolus (n = 3)</td>
<td></td>
<td>480</td>
<td>40b</td>
</tr>
<tr>
<td></td>
<td>Bolus + Maintenance (n = 5)</td>
<td></td>
<td></td>
<td>46b</td>
</tr>
</tbody>
</table>

Abbreviations: RCT, randomized controlled trial; +, plus.

a Calculated pooled mean differences did not include one study14 because a median value was reported. Median differences from this study were motor (30 minutes) and sensory (45 minutes).

b Mean differences were calculated using the dexmedetomidine group with the largest difference in motor and sensory times between the control groups.

**REFERENCES**

1. Schug SA, Saunders D, Kurowski I, Paech MJ. Neuraxial drug admin-
vingson Elsevier; 2010:1623-1628.
3. Abdallah FW, Abrahimi A, Brull R. The facilitatory effects of intrave-
nous dexmedetomidine on the duration of spinal anesthesia: a system-
4. Kalso E, Poyhiä R, Rosenberg P. Spinal antinociception by dexme-
detomidine, a highly selective alpha 2-adrenergic agonist. Pharmacol 
Toxicol. 1991;68(2):140-143.
5. Gertler GB, Brown HC, Mitchell DH, Silvus EN. Dexmedetomi-
6. Samuels ER, Szabadi E. Functional neuroanatomy of the norad-
Conversion of spinal anaesthesia into general anaesthesia: an evalu-
ation of more than 35,000 spinal anesthetics. Minerva Anestesiol. 2010;76(9):714-719.
8. Modig J. Influence of regional anaesthesia, local anesthetics, and symp-
ton Elsevier; 2010:2705-2709.
10. Bedder MD, Kozody R, Palahnuk RJ, Cumming MO, Pucci WR. Clo-
11. Friedrich JO, Adhikari NK, Beyene J. The ratio of means method as an alternative to mean differences for analyzing continuous outcome 
12. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-
13. Melnyk BM, Fineout-Overholt E. Evidence-Based Practice in Nursing 
and Healthcare: A Guide to Best Practice. 2nd ed. Philadelphia, PA: Lipp-
cott Williams & Wilkins; 2011.
14. Dinesh CN, Sai Tej NA, Yatish B, Pujari VS, Mohan Kumar RM, 
Mohan CV. Effects of intravenous dexmedetomidine on hyperbaric 
15. Harsoor S, Rani DD, Yalamuru B, Sudheesh K, Neetha S. Effect of 
supplementation of low dose intravenous dexmedetomidine on char-
acteristics of spinal anaesthesia with hyperbaric bupivacaine. Indian J

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