Original article

Block characteristics of Dexmedetomidine as an adjuvant to local anaesthetic in Infraclavicular brachial plexus block using peripheral nerve stimulator and ultrasound

Ujma Shrestha, Sushila Lama Moktan, Sanjay Shrestha

Abstract

Introduction: Dexmedetomidine has been frequently used in regional anaesthesia to improve the quality of blocks. Addition of dexmedetomidine to local anaesthetics has been shown to hasten the onset of both sensory and motor blocks and also prolong the duration of analgesia. The objective of this prospective comparative study was to assess the change in characteristics of infraclavicular brachial plexus block after adding Inj. Dexmedetomidine to 2% Lignocaine with Adrenaline.

Methods: Sixty-six patients, scheduled for upper limb surgeries under ultrasound guided infraclavicular brachial plexus block were randomly allocated to two groups. Group LS received Inj. Lignocaine 2% with Adrenaline, 7mg/kg diluted to 30 ml with saline and Group LD received Inj. Dexmedetomidine 0.75 mcg/kg in addition to Inj. Lignocaine 2% with Adrenaline, 7mg/kg again diluted to a total volume of 30 ml. The parameters studied were: onset of sensory and motor blocks and duration of analgesia.

Results: Sixty patients completed the study. The demographic variables and motor block were similar between both groups. The mean time to onset of sensory block was significantly faster in Group LD compared to Group LS (9.80±4.85 min vs 12.30±3.97 min, p=0.033). The duration of analgesia was also found to be prolonged in Group LD compared to Group LS (286.73±55.38 min vs 226.53±41.19 min, $p < 0.001$).

Conclusion: Addition of 0.75 mcg/kg of Dexmedetomidine to 2% Lignocaine with Adrenaline hastens the onset of sensory block and prolongs the duration of analgesia in ultrasound guided and peripheral nerve stimulator guided infraclavicular block.

Keywords: analgesia; dexmedetomidine; infraclavicular brachial plexus block; lignocaine; sensory block.

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Introduction

Brachial plexus block (BPB) is an excellent choice of anaesthesia for surgeries of upper extremities as it provides excellent analgesia and reduces the unwanted side effects of general anaesthesia.[1] Infraclavicular block (ICB), a type of BPB, is re-gaining popularity with the development of ultrasound technology as it is quick to locate the plexus at the level of the cord with this approach. It also provides a complete block of the upper extremity below the shoulder and decreases the incidence of pneumothorax.[2] Various agents like opioids, dexamethasone, clonidine, ketorolac have been added perineurally to improve the quality and prolong the effect of the block, as the local anaesthetics (LA) when used alone have brief duration of action.[3-5]

Dexmedetomidine, an alpha-2 agonist, inhibits the neuronal conduction by blocking hyperpolarization activated cation currents and produces analgesia.[6] Different doses of dexmedetomidine have been added perineurally but the effective dose is yet to be decided. Higher doses of dexmedetomidine like 1-2 mcg/kg prolong the duration of analgesia but at the cost of more side effects like bradycardia and hypotension.[7]

This study aims to compare the onset of sensory and motor blocks and the duration of analgesia with the addition of 0.75 mcg/kg dexmedetomidine to 2% lignocaine with adrenaline in ultrasound and peripheral nerve stimulator (PNS) guided ICBs. The secondary objectives are to study the side effects of the procedure and the drug used.

Methods

This was a prospective, double-blinded comparative study conducted in Kathmandu Medical College Teaching Hospital (KMCTH) from November 2017 to September 2018. After obtaining ethical approval from the Institutional Review Committee of KMCTH and written informed consent from the patients, this study was conducted in 66 American Society of Anaesthesiology (ASA) I or II patients of 18-70 years of age, scheduled for unilateral upper limb surgeries. Patients who did not give consent, had suspected neuropathies or coagulopathy, known hypersensitivity to local anaesthetic or dexmedetomidine, history of drug or alcohol abuse, those already on alpha-2-agonists or expected surgery duration of more than two hours were excluded from the study. The sample size was calculated based on number of patients presenting to KMCTH for upper limb surgeries using a confidence interval (CI) of 95% using the standard formula:

$$N=Z^2\ pq/e^2$$
$$= (1.96)^2 \text{ X } 0.19 \text{ X } 0.81 / (0.1)^2$$
$$=59$$

Where, N= sample size, p= prevalence of surgeries under BPB in KMCTH of one year (19.42% of total surgeries), q= 1-p, e= margin of error(10%), Z= 1.96 at 95% Confidence Interval.

Taking 20% for block failure and drop-outs, 72 participants were planned to be enrolled in the study, utilising simple randomisation. Computer generated random number list was used for group allocation which was prepared by the co-investigator and was concealed in serially numbered sealed opaque envelopes which were opened only at the time of intervention.

Pre-anaesthetic evaluation of the patients was done on the day before the surgery and an informed consent was taken for enrollment in the study. In the operating room, electrocardiography, non-invasive blood pressure monitor and pulse oximeter were attached to the patient and baseline hemodynamics were recorded. Intra-venous cannulation was done with 18 G cannula and 5 ml/kg of crystalloid was given. ICB was performed on the side of the surgery using ultrasound (USG) and PNS by the principal investigator, who was blinded to the nature of the drug. The study drug was prepared aseptically by another anaesthesiologist just before the procedure. Among the 72 patients approached, four patients did not give consent and two did not meet the inclusion criteria, hence, 66 patients were included. Group LS (n=33) received 7 mg/kg of Inj. Lignocaine 2% with Adrenaline (Lox 2% Adrenaline (1:200000)™; Neon Laboratories Ltd) diluted to 30 ml with saline and Group LD (n=33) received 0.75 mcg/kg of Inj. Dexmedetomidine (Xamdex™:100 mcg/ml; Themis Medicare Ltd, Abbott-Manufacturer) in addition to Inj. Lignocaine 2% with Adrenaline, 7 mg/kg again diluted to total volume of 30 ml with saline. Ultrasound guided ICB was performed under strict aseptic conditions using high frequency linear probe (5–10 MHz) "EXAGO™" (New York, USA) portable ultrasound along with PNS, "Stimuplex R HNS 12" (B Braun Medical Inc., USA).

The ultrasound probe was used to identify the pectoralis muscles and cross sectional view of the axillary vessels by placing it in a para-sagittal orientation medial to the coracoid process on the anterior wall of the chest. A subcutaneous local anesthetic infiltration was done at the site of injection with 1 ml of the prepared drug. Once the posterior, medial and lateral cords of the brachial plexus were identified by USG, a sterile 21 G, 4" Stimuplex A™ needle (B Braun Medical Inc., USA), was inserted using an in-plane approach following which a motor response of the limb was sought initially to 1.0 mA and then to 0.4 mA stimulation. If the motor response was still present, the local anesthetic mixture was slowly injected, first in the area of the lateral and posterior cord and then in the region of the medial cord with frequent aspirations to avoid inadvertent intravascular injection (**Figure 1**).

The ICB was considered successful when the distribution of radial, median, musculocutaneous and ulnar nerves were blocked by the original injection within 20 minutes. Sensory blockade was assessed every three minutes and motor blockade every five minutes for the first 20 minutes following the administration of the injection. Sensory block was assessed by loss of sensation to pin prick using a blunt 23 G needle in the four nerve areas using a 3-point scale:[8]

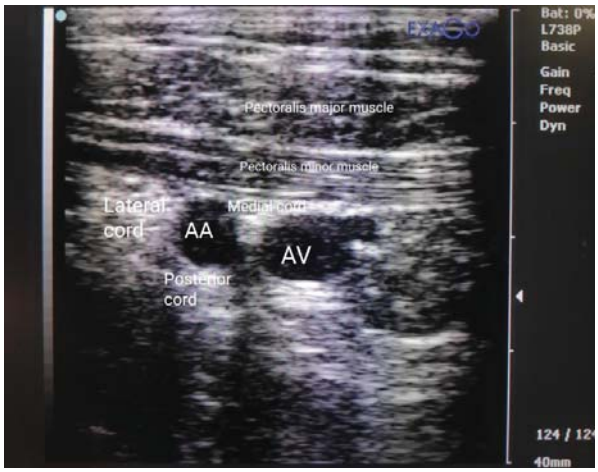

Figure 1. Ultrasound image of the infraclavicular region where ICB is given (AA=axillary artery, AV=axillary vein)

Grade 0= normal sensation
Grade 1= loss of sensation to pin prick (analgesia)
Grade 2= loss of sensation of touch (anaesthesia)

Onset of sensory block was defined as the time from injection of local anaesthetic to loss of sensation to pin-prick (Grade 1).

Motor block was assessed as per the following criteria:[9]
Grade 1: Patient able to flex and extend the forearm
Grade 2: Patient able to flex or extend only the wrist and fingers
Grade 3: Patient able to flex or extend only the fingers
Grade 4: Patient unable to move the forearm, wrist and fingers

Onset of motor block was defined as the time from injection of local anaesthetic to the reduction in motor power to Grade 3 or 4.

The block was considered inadequate if the onset of sensory and motor block was not achieved within 20 minutes or if any supplemental local anaesthetic or analgesics were required for completion of the surgery. These cases were recorded for further evaluation and additional analgesia was provided with Inj. Fentanyl and when required, was converted to general anaesthesia. Heart rate, blood pressure [systolic, diastolic and mean arterial pressure (MAP)], oxygen saturation and respiratory rate were recorded every five minutes till the end of surgery. The total volume of intravenous fluid administered was recorded in both groups. Possible side effects like hypotension (defined as fall in >30 % of the MAP of the baseline), bradycardia (defined as a heart rate of <50/min), respiratory depression (defined as respiratory rate <8/min or fall in Oxygen saturation of

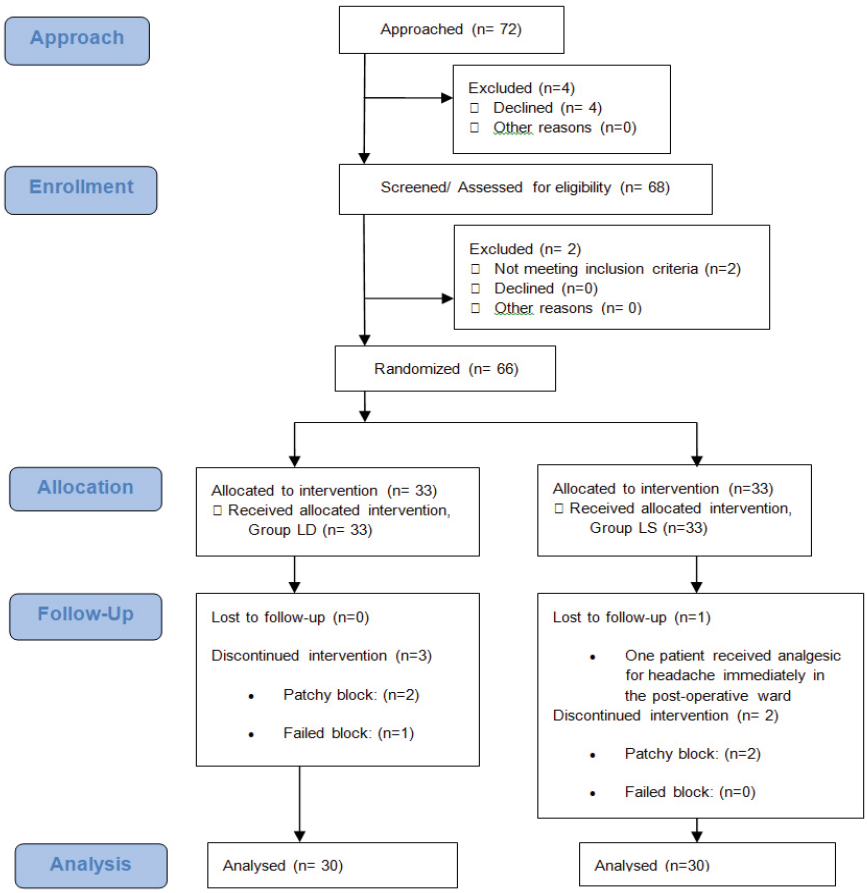

Figure 2. Flowchart showing the flow of participants (n= numbers)

less than or equal to 90%) were recorded and managed accordingly.

Post-operative pain was assessed by a non-researcher anaesthesiologist using a numerical rating scale (NRS), which was explained to the patient pre-operatively. Pain was graded on a scale of 0-10 with 0 being no pain and 10 being the worst possible pain. Inj. Diclofenac 75 mg was provided when NRS corresponded to 4 or more and the time to first analgesic request was noted. The duration of analgesia was considered as the time from completion of injection of study drug till the time when the patient's NRS became four or more or when the patient demanded analgesics.

Statistical analysis was done using SPSS software 20.0 (SPSS, Inc., Chicago, IL). Chi-square test was used to compute qualitative data and expressed in numbers. Continuous data was analyzed using student's t-test. P-value less than 0.05 were considered statistically significant.

Results

The total number of patients studied was 66. The demographic and surgical characteristics of the study population are shown in **Table 1** and it shows no significant difference between the two groups. There were, however, more males than females in each group. Four patients with patchy block and one patient with failed block along with one patient who received analgesic in the post-operative ward for other reasons were excluded from analysis as shown in **Figure 2**. Hence, 60 patients were taken for analysis.

Table 1. Comparison of demographic variables between two groups

Variable	Group LD (n=30)	Group LS (n=30)	p- value*
Age (years)	34.63±13.69	36.43±16.55	0.648[a]
Gender (n)			
Male: Female	22:8	20:10	0.573 (chi-square value = 0.317)[b]
Height (centimeters)	161.02±9.14	161.15±8.96	0.954[a]
Weight (kilograms)	62.17±9.51	60.2±8.18	0.394[a]
Amount of intravenous fluid infused intra-operatively (ml)	738.5±211.67	652.67±271.25	0.177[a]
Duration of surgery (minutes)	46.43±22.29	43.77±21.33	0.638[a]

[a] Based on Student's t-test, [b] Based on Chi-square test

The baseline hemodynamic parameters of the study population including the heart rate, mean arterial pressure, oxygen saturation and respiratory rates were comparable in the two groups (**Table 2**).

Table 2. Comparison of baseline hemodynamic parameters

Variable	Group LD (mean ±SD)	Group LS (mean ±SD)	p-value
Heart rate (/min)	77.97±15.89	77.6 ±12.02	0.920
Mean Arterial Pressure (mm Hg)	95.92±9.7	98.76 ±13.25	0.332
Oxygen saturation (%)	98.33 ±1.67	97.60 ±1.45	0.075
Respiratory rate (/min)	16.93 ±3.17	16.80 ±2.99	0.868

(Values expressed as mean±SD, p-value calculated using student's t-test)

The details of onset of sensory block and motor block and the duration of analgesia have been tabulated in **Table 3**. The onset of sensory block was significantly faster in the dexmedetomidine group while the onset of motor block among the two groups did not show any statistically significant difference. The duration of analgesia was also longer in the dexmedetomidine group and it was found to be statistically significant (p-value <0.05).

Table 3. Comparison of the characteristics of block and duration of analgesia between two groups

Variable	Group LD (mean ±SD)	Group LS (mean ±SD)	p-value
Onset of sensory block (min)	9.80±4.85 95% CI [7.99-11.61]	12.30±3.967 95% CI [10.82-13.78]	0.033
Onset of motor block (min)	13.00±5.849 95% CI [10.82-15.18]	16.10±6.408 95% CI [13.71-18.49]	0.055
Duration of analgesia (min)	286.73±55.38 95% CI [266.05-307.41]	226.53±41.19 95% CI [211.15-241.92]	<0.001

(Values expressed as mean±SD, 95% CI, p- value calculated using student's t-test))

The distribution of the patients according to the site of the surgery as categorized into elbow, forearm and hand has been demonstrated in **Figure 3**.

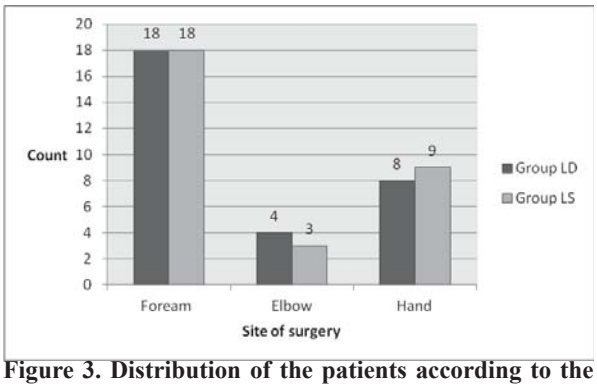

Figure 3. Distribution of the patients according to the site of surgery

There were no complications related to the procedure in any of the patients enrolled in the study. However, there were some adverse effects related to the study drug used which have been tabulated in **Table 4**.

Table 4. Intra-operative events and complications

Parameters	Group LD (n=30)	Group LS (n=30)
Bradycardia with need for Atropine administration	1 (3.33)	0
Oxygen desaturation with need for oxygen supplementation	1 (3.33)	0
Patchy block for which supplemental analgesics were needed	2 (6.67)	3 (10)
Failed block for which general anaesthesia had to be administered	1 (3.33)	0

[Values are expressed in number (percentage)]

Discussion

The results of our study show that the addition of 0.75 mcg/kg of Dexmedetomidine to 2% lignocaine with adrenaline significantly decreased the time to onset of sensory block and increased the duration of analgesia in comparison to the patients in the group which did not receive dexmedetomidine. However, facilitatory effect on the onset of motor block could not be demonstrated.

Dexmedetomidine is an α2 agonist with a α2:α1 selectivity of 1620:1 and hence has increased analgesic efficacy but with lesser side effects in comparison to its precursor, clonidine.[10] Systemic effects of dexmedetomidine are mediated through its action on alpha receptors. Dexmedetomidine has also been found to prolong the duration of analgesia when used intrathecally.[11] However, the effect of dexmedetomidine in peripheral nerve blocks is unrelated to its action on these receptors as α-2 receptors are not present in the axons of peripheral nerves.[12] When administered perineurally, dexmedetomidine blocks the hyperpolarization-activated cation currents and prolongs the hyperpolarized state of the neurons. This in turn, accentuates the inhibition of neuronal conduction and produces analgesia.[6,13] Andersen et al have also found that dexmedetomidine prolongs the duration of block by a peripheral mechanism.[14]

Dexmedetomidine has been used in various doses in conjunction with local anaesthestics ranging from 0.5-2 mcg/kg.[6,7] Most studies used either 1-2 mcg/kg or 50-100 mcg of the drug. Higher dose is associated with increased side effects, notably hypotension and bradycardia.[7] Sinha et al found no difference in the duration of analgesia between 50 and 100 mcg of dexmedetomidine when added to levobupivacaine in BPB, only the side effects were more.[15] Also, studies have been done comparing 0.5 mcg/kg with 1 mcg/kg of dexmedetomidine with lignocaine, but not with 0.75 mcg/kg.[16] Hence, we chose to use a slightly lower dose and aimed to evaluate its effects.

In our study, the time to onset of sensory block was significantly different in between the two groups. This finding is consistent with the result of various other studies.[17-19] Akhondzadeh et al have demonstrated significant improvement in the onset of sensory block with 3 mg/kg of 2% lignocaine and dexmedetomidine 1 mcg/kg. Most of the studies have used 1 mcg/kg of dexmedetomidine or higher doses like 100 mcg.[19-20] Thakur et al compared two doses of dexmedetomidine added to 2% lignocaine with adrenaline (0.5 mcg/kg and 1 mcg/kg) and found that addition of dexmedetomidine did not hasten the onset of sensory and motor block, in fact, the group in which no additive was added had the fastest onset. The reason might be the use of landmark technique for the performance of blocks. We used ultrasound for all our blocks, so precise deposition of local anesthetics might have led to the faster onset of blocks, even though only 0.75 mcg/kg of dexmedetomidine was used. Mirkhesti et al found that addition of dexmedetomidine had no significant effect on the onset of sensory block, though it hastened the onset of motor block and prolonged the duration of sensory and motor block and the time to first analgesic request.[20] The reason might be the low concentration of plain lignocaine they used in their study. The same explanation might also account for Esmaoglu et al having no effect in the onset of sensory and motor blocks in their study when they added 1 mcg/kg of dexmedetomidine to 3 mg/kg of lignocaine for Intravenous Regional Anaesthesia (IVRA).[21] The fact that 2% Lignocaine with Adrenaline (1:200,000) was used in our study while other studies used plain 2% Lignocaine might also have played a role in hastening the onset of sensory block. Adrenaline has been added to local anaesthetics since a long time to improve the onset of block and prolong the duration of analgesia. Adrenaline causes vasoconstriction due to the stimulation of α1 adrenoceptor stimulation, thereby, delaying the systemic uptake of LA.[12] The time to onset of motor block was not found to be enhanced by the use of 0.75 mcg/kg of dexmedetomidine in our study. Dexmedetomidine has been found to have greater inhibitory effect on Aδ and C nerve fibres relative to motor neurons.[12] Our finding is in accordance with study by Thakur et al who demonstrated that the time to onset of motor block was not hastened by addition of dexmedetomidine. Kaygusuz et al also had similar findings with dexmedetomidine added to levobupivacaine in axillary BPBs and have attributed the results to the use of lower dose of dexmedetomidine.[22] However, Sharma S et al have stated that addition of 0.75 mcg/kg dexmedetomidine significantly fastens the motor block when it was mixed to 0.5% ropivacaine in supraclavicular BPBs.[23]

The duration of analgesia (DOA) was shown to be prolonged by the addition of dexmedetomidine in our study. Vorobeichik et al have stated that dexmedetomidine prolonged the duration of analgesia by at least 39% in ICB and can effectively decrease the total opioid consumption.[6] Our findings coincide with the findings of other studies as

well.[17,20-21] Many explanations for the analgesic effect have been postulated; synergistic action of alpha-2 agonists with LAs, induction of vasoconstriction at injection site, release of anti-inflammatory cytokines and local release of enkephalin-like substances.[24] Dexmedetomidine leads to the activation of pre-synaptic alpha2 adrenoceptors in the central nervous system due to which the release of norepineprine is inhibited. This terminates the pain signals from being propagated. Hoo Soo Jung et al, on contrary, found that DOA was prolonged significantly only with 2 mcg/kg of perineural dexmedetomidine and not with lower doses.[7] The reason for this difference might be the fact that they evaluated the effect in shoulder arthroscopy but in our study, surgeries in elbow, forearm and hand were evaluated.

We did not encounter any procedure related side effects in our study. ICB in itself is a very safe peripheral nerve block to perform under USG. The main advantage of ICB over supraclavicular BPBs is the decreased incidence of pneumothorax and the ability to block the nerves without arm abduction in ICB is a huge relief for patients where positioning is often restricted as a result of limited abduction at the shoulder joint.[25] Furthermore, the depth of the plexus and the stability of the pectoral muscles make ICB a good technique for catheter placement for continuous local anaesthetic infusion techniques. A higher risk of hypotension and bradycardia may be seen in patients over 65 years of age and hence, dose reduction is suggested.[26] The use of low dose of dexmedetomidine might have been the cause for fewer incidences of side effects in our study. The maximum dexmedetomidine received in this study was 61.5 mcg. Our finding strengthens the statement by Vorobeichik et al and Desai et al that a 50-60 mcg dexmedetomidine led to maximum sensory block while minimizing hemodynamic side-effects.[6,12] Furthermore, Hussain et al have said that the incidence of bradycardia is dependent on the dose of dexmedetomidine used and is seen more frequently when dose more than 50 mcg is used.[13] Hypotension was not seen in any of our patients and findings from Hussain et al also reveal that there was no relation regarding intraoperative hypotension in patients receiving dexmedetomidine and again, it may be because of the low dose used in our study. Maximum recommended dose of lignocaine with adrenaline was used in order to balance the low dose of dexmedetomidine used. Even though such high dose was used, there is little risk of harm to the patient. That is because unless a significant amount of LA is injected intravascularly, even high plasma concentration does not usually lead to systemic toxicity.[27] Also, surgery leads to stimulation of hepatic alpha1-acid glycoprotein synthesis, which binds lignocaine, thus, decreasing toxicity.[27] One of the advantages of using dexmedetomidine in PNBs is that it has also been found to have neuroprotective effects. The combination of dexmedetomidine with bupivacaine was associated with significantly less perineural inflammation at 24 h when compared with bupivacaine alone.[28] The main limitation of our study is that we did not assess the study drug's effect on blood glucose levels, its cost effectiveness and long term outcomes like patient satisfaction. Further studies addressing these concerns might be warranted.

Conclusion

We conclude that the addition of 0.75 mcg/kg of dexmedetomidine to 2% Lignocaine with Adrenaline (1:200,000) in ultrasound and PNS guided infraclavicular brachial plexus blocks fastened the onset of sensory block and prolonged the duration of analgesia in upper limb surgeries.

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