

## Comparative evaluation of dexmedetomidine and tramadol as an adjunct to lignocaine for distal intravenous regional anaesthesia in buffalo calves

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*This study evaluated a novel distal intravenous regional anaesthesia (DIVRA) technique in buffalo calves using lignocaine combined with either dexmedetomidine or tramadol. Twelve buffalo calves of either sex, affected with various surgical hoof ailments, were randomly divided into two groups. Group I received lignocaine (2 mg/kg body weight) with dexmedetomidine (2.5 µg/kg), while group II received lignocaine (2 mg/kg) with tramadol (1 mg/kg) through the common axial digital vein.*

*In group I, heart rate decreased for up to 50 min, whereas in group II the decrease persisted for 10 min. Pulse rate declined at 10 min in both groups. Respiratory rate decreased for 30 min in group I and for 50 min in group II. SpO<sub>2</sub> values showed a reduction up to 50 min in both groups. Systolic blood pressure fluctuated during the observation period, showing an initial decline in group I and increases at specific time intervals in group II. The onset of sensory and motor blockade was faster in group I, while recovery time was longer in group II.*

*Overall, the findings indicated that lignocaine combined with dexmedetomidine provided more effective DIVRA compared to lignocaine combined with tramadol.*

**Keywords:** Dexmedetomidine, Intravenous regional anaesthesia, Lignocaine, Tramadol

**H**oof injuries are common in bullocks and dairy animals, causing pain, reduced productivity, and significant economic losses for farmers. Claw surgeries are often necessary to treat these conditions, but they can be highly painful and therefore require effective pain management. In large animals, general anaesthesia carries considerable risks, including bloat and regurgitation; consequently, local anaesthesia is preferred as a safer and more effective method of pain control during such procedures.

Intravenous regional anaesthesia (IVRA), also known as Bier's block, involves the injection of a local anaesthetic into a vein of a limb while circulation is occluded using a tourniquet, thereby producing rapid analgesia and muscle relaxation in the distal part of the limb (Holmes, 1963; Hassanein, 2016; Yadav *et al.*, 2021). Following its reintroduction with lignocaine,

IVRA has emerged as a safer alternative to general anaesthesia, particularly in high-risk patients (Mohr, 2006), and is widely employed for minor surgical procedures of the limbs. Lignocaine is commonly preferred for IVRA because of its rapid onset of action, simplicity, reliability, and cost-effectiveness (Fazili *et al.*, 2024). However, the technique has certain limitations, including a short duration of postoperative analgesia, inadequate muscle relaxation, tourniquet-associated pain, and the potential risk of local anaesthetic toxicity. These limitations can be reduced by the addition of adjunct drugs to the local anaesthetic solution, which may enhance anaesthetic efficacy and prolong analgesia (Bansal *et al.*, 2011).

Local anaesthetics alone are unable to induce analgesia and muscle relaxation during Bier's block, hence an adjunct drug should be used. Several local anaesthetic adjuncts that have been used are opioids (fentanyl, pethidine, tramadol etc.), NSAIDs (ketorolac, acetylsalicylate, lornoxicam etc.) and analgesics. Addition of dexmedetomidine to local anaesthetic solution in IVRA improved the quality of anaesthesia and decreased analgesic requirement but had no effect on the sensory and motor blocks onset and regression times (Esmoğlu *et al.*, 2005).

Dexmedetomidine has been shown to be as safe and effective as medetomidine when administered at equipotent dose (Kuusela *et al.*, 2001). Dexmedetomidine reduces the dose requirements of opioids and anaesthetic agents and attenuates the haemodynamic responses to surgical stimuli (Chandramohan *et al.*, 2024). In intensive care patients, dexmedetomidine has been used to achieve sedation without respiratory depression, and cardiac patients may benefit from the perioperative cardiovascular stability (Martin *et al.*, 2003; Venn *et al.*, 2003). Dexmedetomidine shows the highest affinity for alpha-2 adrenergic receptors compared with other similar compounds such as xylazine and medetomidine, and has gained interest in veterinary anaesthesiology over medetomidine (Kuusela *et al.*, 2000).

Tramadol is a synthetic opioid that has central analgesic effects as the result of its monoaminergic and

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mu-receptor agonistic activity, releases serotonin and in addition it interferes with neurotransmitter reuptake. Several studies showed that tramadol is beneficial as an additive to local anaesthetics in different regional nerve blocks including infiltration, caudal block, brachial plexus block and IVRA (Hall *et al.*, 2000).

The present study was designed to compare the analgesic efficacy of dexmedetomidine and tramadol as an adjunct to lignocaine hydrochloride in distal intravenous regional anaesthesia (DIVRA) technique for the management of hooves/claws diseases in buffalo calves.

### Materials and Methods

In the present study, distal intravenous regional anaesthesia (DIVRA) was induced in 12 buffalo calves of either sex having surgical hoof ailments like hoof avulsion, hoof necrosis and complications of FMD. Based on the drug combination, the calves were allotted randomly into two groups, each consisting of six animals. The age range of the animals included in both groups was 3-5 months; and the range of body weight of the animals in group I and II was 58-65 kg and 56-65 kg, respectively. In group I animals a mixed solution of lidocaine (2 mg/kg body weight) and dexmedetomidine (2.5 µg/kg), and in group II animals lidocaine (2 mg/kg) and tramadol (1 mg/kg) were infused in axial digital vein.

The blood and faecal samples of these animals were examined prior the study to eliminate possible systemic disease conditions and worm infestation. The animals were prepared as per routine surgical procedure. The affected animals were off fed overnight, and limbs were shaved below the pastern joint for distal IVRA. The animals were cast and restrained in lateral recumbency with affected limb upper most. The site was prepared aseptically, and the area was painted with povidone iodine. For DIVRA, an elastic tourniquet was applied just below the fetlock joint and distal to dew claws. Then the axial digital vein was catheterized at the bifurcation point using butterfly cannula No. 22 and under gentle flexion of the fetlock joint, blood was drained through the needle until the pressure dropped as indicated by slow dripping rather than blood running out of the hub (Fig. 1). Anaesthesia in different group of animals was induced as mentioned before.

The local anaesthetic effect was monitored by observing the following parameters:

Heart rate was taken preoperatively and at 5 min, 10 min, 15 min, 20 min, 30 min, 40 min and 60 min or till the anaesthetic recovery and after the removal of the tourniquet.

Pulse rate was recorded at the coccygeal artery as beats/min (bpm). Pulse rate of animals was taken preoperatively and at 5 min, 10 min, 15 min, 20 min, 30 min, 40 min and 60 min or till the recovery after the

administration of anaesthesia and after the removal of the tourniquet.

Respiratory rate was recorded preoperatively and at 5 min, 10 min, 15 min, 20 min, 30 min, 40 min and 60 min or till the recovery after the administration of anaesthesia and after the removal of the tourniquet.

Peripheral oxygen saturation (SPO<sub>2</sub>) readings were recorded using the sensor probe of the pulse oximeter placed on the ear pinna preoperatively and at 5 min, 10 min, 15 min, 20 min, 30 min, 40 min and 60 min or till the recovery after the administration of anaesthesia and after the removal of the tourniquet.

Systolic and diastolic pressure was measured by non-invasive blood pressure monitoring unit (Romsons BPX automatic BP monitor) in mmHg. The cuff was placed on the forelimb just above the carpus (median artery). The readings were noted preoperatively and at 5 min, 10 min, 15 min, 20 min, 30 min, 40 min and 60 min or till the recovery after the administration of anaesthesia and after the removal of the tourniquet. Mean arterial pressure was calculated as per the formula suggested by Tien *et al.* (2023).

$$\text{MAP} = \frac{\text{DP}+1}{3(\text{SP}-\text{DP})}$$

Where DP- Diastolic Pressure; SP- Systolic pressure

Sensory block onset time (the interval between drug administration and the achievement of sensory blockade in all dermatomes) was noted preoperatively and at 5 min, 10 min, 15 min, 20 min, 30 min, 40 min and 60 min or till the recovery after the administration of anaesthesia and after the removal of the tourniquet using pin pricks method. A 22G hypodermic needle was used to gently apply pinpricks along the cutaneous regions innervated by radial, ulnar, median, and musculocutaneous nerves. The response to the stimulus was observed. Absence of withdrawal, muscle twitching, or behavioural signs of discomfort (such as tail flicking or head turning) was considered indicative of effective sensory block.

Motor block (the impairment or loss of motor function, muscle movement, due to anaesthesia or other factors) was recorded preoperatively and at 5 min, 10 min, 15 min, 20 min, 30 min, 40 min and 60 min or till the recovery after the administration of anaesthesia and after the removal of the tourniquet. Motor function was assessed by observing the voluntary movement of part below the fetlock. A complete absence of voluntary movement or inability to resist passive manipulation was recorded as a full motor block.

Sensory block recovery time was measured after 30 min of administration of anaesthesia at every 10 min interval till the recovery from anaesthesia. The intervals selected (starting at 30 min post-administration) were based on preliminary observations and existing literature, ensuring the block had time to

establish before assessing recovery trends. The 10-min interval is broad enough to avoid over-handling the animal but frequent enough to provide a meaningful resolution for clinical or research evaluation. It facilitates comparison between groups or treatments, allowing for detection of significant differences in recovery speed.

Motor block recovery time was measured after 30 min of administration of anaesthesia at every 10 min interval till the recovery from anaesthesia. Motor function was assessed by observing the voluntary movement of the part distal to fetlock.

All the animals were vigilantly monitored for any signs of complication such as local anaesthetic toxicity, including regurgitation, skin rashes, muscle tremors, or convulsions, throughout the procedure and recovery period.

The data were analysed using one way ANOVA (Analysis of Variance) by comparing the mean values at different intervals with their base values. Independent "t" test was used to compare the mean values between groups at different intervals.

## Results and Discussion

Intravenous regional anaesthesia (IVRA) is a simple and valuable technique for surgical procedures on the limbs below knee and hock of large animal patients. Although IVRA is simple to perform but some studies highlighted adverse effects and disadvantages of this anaesthesia's strategy. For instance, the occasional haematoma at the site of injection and some complications such as severe lameness, local anaesthetic toxicity due to high dose and pain, if the tourniquet is left in the place longer than two hours, could be some disadvantages of IVRA (Muir *et al.*, 2007). DIVRA may be advantageous over conventional IVRA technique because it requires low dose of anaesthesia and subsequently less chances of toxicity as compared to conventional IVRA.

Lignocaine is a local anaesthetic agent characterized by rapid onset of action, excellent diffusion capacity, and effective surface anaesthesia; however, when used alone, it does not provide adequate postoperative analgesia (Yadav *et al.*, 2023). Therefore, in the present study dexmedetomidine and tramadol were used in combination with lignocaine for DIVRA in buffalo calves.

Heart rate (HR) decreased significantly at different time intervals in group I, however, in group II no significant change was observed at different time intervals (Table 1). A significant difference between the two groups was observed up to the 40 min interval. A decrease in HR was reported after the administration of dexmedetomidine as an analgesic additive to lignocaine in intravenous regional anaesthesia (Elramely *et al.*, 2016). Yavari *et al.* (2017) also reported a significant reduction in heart rate over time during IVRA following tourniquet removal with the use of 2%

procaine. Gerlach *et al.* (2007) reported that dexmedetomidine administration was associated with a higher incidence of bradycardia, moderate hypotension at the time of tourniquet release, and sedation during the subsequent 30 minutes.

Pulse rate decreased significantly ( $P < 0.05$ ) at the 5- and 10-min intervals in group I, whereas in group II animals, a significant decrease was observed only at the 10-min interval (Table 1). The initial decrease in pulse rate in both groups was probably attributable to the administration of dexmedetomidine (Gerlach *et al.*, 2007). Similarly, in human subjects, the combination of lignocaine and dexmedetomidine has been reported to cause a significant reduction in mean pulse rate (Bhaumik *et al.*, 2016). Following tourniquet removal, no significant alterations in pulse rate were observed in animals of either group, and the values gradually returned to near-normal levels.

Respiratory rate (RR) decreased significantly ( $P < 0.05$ ) at the 5- and 10-min intervals in group I and at the 30-min interval in group II (Table 1). The initial decrease in RR in both groups was probably attributable to lateral recumbency, which is known to reduce respiratory rate; however, the rate tends to increase subsequently due to tourniquet-associated pain (Yadav *et al.*, 2021). In the present study, no significant change in respiratory rate was observed following tourniquet release, which is in agreement with the findings of Acalovschi *et al.* (2001).

Peripheral oxygen saturation ( $SpO_2$ ) decreased significantly in both groups up to the 50-min interval (Table 1). This reduction in  $SpO_2$  may be attributed to the decrease in respiratory rate resulting from respiratory depression at anaesthetic dosages (Beths *et al.*, 2001). The significantly lower peripheral oxygen saturation could also be associated with lateral recumbency, in which the rumen exerts pressure on the lungs and diaphragm. In cows, lateral recumbency is known to impair respiration, leading to a moderate increase in arterial  $pCO_2$  and a decrease in  $pO_2$  (Yadav *et al.*, 2021). Following tourniquet removal, peripheral oxygen saturation decreased significantly only in group I, whereas no significant change was observed in group II animals. Nevertheless,  $SpO_2$  values remained within the clinically acceptable range throughout the study period (Flacke *et al.*, 1993).

Systolic blood pressure decreased at 5 min and subsequently increased significantly at the 15, 20, 30, and 40 min intervals in group I. In contrast, group II animals exhibited a significant increase in systolic pressure at the 5, 10, 15, and 20 min intervals. Diastolic pressure decreased at the 5 and 10 min intervals in group I, whereas in group II, a significant decrease was observed only at the 5 min interval. Following tourniquet removal, no significant changes in either systolic or diastolic pressure were observed in animals of either group (Table 1). The initial decrease in systolic and diastolic pressures may be attributed to the depressant effects of dexmedetomidine on cardiac

**Table 1:** Mean±SE of heart rate, pulse rate, respiration rate, peripheral oxygen saturation, systolic pressure, diastolic pressure and mean arterial pressure of animals of different groups at different time intervals.

Time interval	Heart rate (per minute)		Respiratory rate (per minute)		Pulse rate (per minute)		Peripheral oxygen saturation (%)		Systolic pressure (mm Hg)		Diastolic pressure (mm Hg)		MAP (mm Hg)	
	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II
0	72.50 ±1.96 <sup>a</sup>	64.67 ±1.40 <sup>b</sup>	23.00 ±1.29	25.50 ±1.26	71.50 ±0.85 <sup>a</sup>	52.50 ±3.39 <sup>b</sup>	91.67 ±0.76	93.00 ±1.21	124.00 ±1.53 <sup>a</sup>	131.34 ±1.98 <sup>b</sup>	91.67 ±0.67	93.34 ±0.85	102.44 ±0.59	106.00 ±0.77
5	44.67 ±4.87 <sup>a</sup>	63.84 ±1.79 <sup>b</sup>	16.17 ±0.60 <sup>a</sup>	23.67 ±1.34 <sup>b</sup>	68.17 ±0.30 <sup>a</sup>	51.50 ±2.92 <sup>b</sup>	86.34 ±0.80 <sup>a</sup>	91.00 ±1.59 <sup>b</sup>	120.00 ±1.87 <sup>a</sup>	132.84 ±1.54 <sup>b</sup>	82.00 ±1.24 <sup>a</sup>	91.34 ±1.23 <sup>b</sup>	94.67 ±0.61 <sup>a</sup>	105.16 ±1.05 <sup>b</sup>
10	39.17 ±1.07 <sup>a</sup>	63.17 ±2.15 <sup>b</sup>	18.34 ±1.40 <sup>a</sup>	23.00 ±1.64 <sup>b</sup>	68.34 ±0.67 <sup>a</sup>	49.00 ±3.47 <sup>b</sup>	81.50 ±0.76	85.84 ±3.06	123.50 ±1.48 <sup>a</sup>	134.00 ±1.79 <sup>b</sup>	85.34 ±0.67 <sup>a</sup>	91.84 ±2.46 <sup>b</sup>	98.07 ±0.36 <sup>a</sup>	105.89 ±1.97 <sup>b</sup>
15	47.67 ±0.72 <sup>a</sup>	61.50 ±2.03 <sup>b</sup>	19.17 ±1.45 <sup>a</sup>	20.84 ±1.45	72.17 ±0.70 <sup>a</sup>	49.34 ±3.47 <sup>b</sup>	81.84 ±0.70	84.17 ±2.69	132.50 ±2.05 <sup>a</sup>	135.84 ±1.47 <sup>b</sup>	91.50 ±1.77	94.67 ±1.89	105.17 ±1.52	108.39 ±1.17
20	50.67 ±1.35 <sup>a</sup>	60.17 ±2.15 <sup>b</sup>	21.17 ±1.45	20.00 ±1.18	74.17 ±0.47 <sup>a</sup>	50.50 ±3.78 <sup>b</sup>	84.17 ±0.79	84.67 ±2.53	144.84 ±4.39 <sup>a</sup>	136.67 ±1.03 <sup>b</sup>	94.50 ±1.77	94.50 ±1.19	111.28 ±1.31 <sup>a</sup>	108.99 ±1.00
30	51.67 ±1.76 <sup>a</sup>	61.17 ±2.84 <sup>b</sup>	21.34 ±1.76	18.34 ±0.95	74.00 ±0.52 <sup>a</sup>	50.67 ±4.34 <sup>b</sup>	86.00 ±0.68	85.50 ±2.18	139.00 ±3.3	134.50 ±1.75	90.84 ±2.49	94.50 ±1.19	106.89 ±1.42	107.84 ±0.98
40	52.84 ±2.03 <sup>a</sup>	63.84 ±1.76 <sup>b</sup>	23.67 ±1.31	20.50 ±0.50	72.34 ±0.42 <sup>a</sup>	52.00 ±3.93 <sup>b</sup>	87.34 ±0.76	86.00 ±1.21	135.00 ±2.27	133.00 ±1.98	91.67 ±0.85	91.50 ±1.55	106.12 ±0.93 <sup>a</sup>	105.34 ±1.42
50	56.67 ±3.42	63.67 ±1.61	25.00 ±0.86	22.84 ±0.75	73.17 ±0.47 <sup>a</sup>	53.00 ±3.87 <sup>b</sup>	87.67 ±0.80	88.17 ±1.17	115.67 ±16.33	131.67 ±1.89	89.50 ±2.22	90.50 ±2.39	98.23 ±6.29	104.23 ±2.07
After removal of tourniquet	61.33 ±3.49 <sup>a</sup>	63.00 ±0.96	25.50 ±1.12	26.00 ±0.68	71.84 ±0.54 <sup>a</sup>	53.84 ±3.84 <sup>b</sup>	88.84 ±0.79	91.00 ±0.68	127.84 ±2.97	131.67 ±1.53	86.67 ±2.80	90.34 ±2.54	100.39 ±1.48	104.12 ±2.06

\* Indicates a significant difference (P < 0.05) from day 0 value a,b Indicate significant differences (P < 0.05) at different time intervals between groups MAP: Mean Arterial Pressure; SpO<sub>2</sub>: Peripheral Oxygen Saturation; mm Hg: millimeter of mercury.

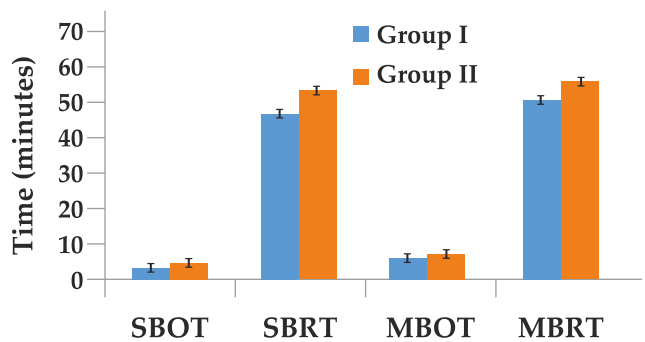
systolic and diastolic function. The subsequent increase observed after 5 min was probably associated with tourniquet-induced pain. A combination of lignocaine and dexmedetomidine has also been reported to cause a significant reduction in systolic blood pressure (Flacke *et al.*, 1993). In group II, the increase in systolic pressure at the 5, 15, and 20 min intervals, along with the rise in diastolic pressure after 5 min, may be attributed to the cardiovascular effects of tramadol. Tramadol has been reported to significantly increase systolic and diastolic blood pressure in patients, with no marked clinico-physiological alterations observed following tourniquet release (Gupta *et al.*, 2014).

Mean arterial pressure (MAP) decreased significantly (P<0.05) at the 5 and 10 min intervals in group I

animals; thereafter, the values increased significantly at the 20, 30, and 40 min intervals (Table 1). At low plasma concentrations, dexmedetomidine lowers MAP and heart rate through activation of presynaptic α<sub>2</sub>-adrenoceptors in the central nervous system and α<sub>2</sub>-adrenoceptors present in vascular endothelial cells. The initial reduction in MAP observed in group I was therefore likely attributable to the pharmacological effects of dexmedetomidine. The subsequent increase in MAP at the 20 and 40 min intervals may have resulted from stress and tourniquet-induced pain. Administration of dexmedetomidine has been reported to decrease MAP, whereas tramadol tends to cause a slight increase in MAP (Kalema-Zikusoka *et al.*, 2003). In group II, MAP increased significantly (P<0.05) at the 20 min interval and subsequently.



**Fig.1:** Placement of scalp vein catheter for distal intravenous regional anaesthesia in buffalo



**Fig. 2:** Mean±SE of sensory block onset time, sensory block recovery time, motor block onset time and motor block recovery time (in minutes) of animals of different groups.

declined toward baseline values. The significantly elevated MAP may indicate a stress response associated with tourniquet pain (Yadav *et al.*, 2023). Haider and Mahdi reported no significant alterations in blood pressure following IVRA using lidocaine alone or in combination with ketamine. Similarly, Yadav *et al.* (2021) observed a significant increase in MAP after IVRA, followed by a gradual decrease over time after tourniquet removal. Kalema-Zikusoka *et al.* (2003) also documented an initial increase in MAP following dexmedetomidine administration, which subsequently declined toward baseline values. In the present study, no significant change in MAP was observed in either group after tourniquet removal.

Sensory block onset time (SBOT) was shorter in group I ( $3.08 \pm 0.42$  min) compared to group II ( $4.17 \pm 0.67$  min) (Fig. 2). Dexmedetomidine has been shown to enhance the local anaesthetic effect of lignocaine via  $\alpha_2A$ -adrenoceptor-mediated mechanisms (Sheth *et al.*, 2016). The improved intraoperative conditions and faster onset of sensory block in group I may therefore be attributed to the addition of dexmedetomidine to lignocaine, which also likely contributed to reduced intraoperative pain. A significantly shorter SBOT has similarly been reported when lignocaine was used as an adjunct to tramadol and dexmedetomidine (Nasr and Waly, 2012).

Motor block onset time (MBOT) was also earlier in group I ( $6.00 \pm 1.04$  min) compared to group II ( $7.00 \pm 1.10$  min). A shorter MBOT with the combination of lignocaine and dexmedetomidine has also been observed in clinical studies (Bhaumik *et al.*, 2016). Dexmedetomidine is a potent  $\alpha_2$ -adrenoceptor agonist and the active enantiomer of medetomidine (Aantaa, 1991). In contrast, tramadol is a centrally acting synthetic 4-phenylpiperidine analogue of codeine, exerting its analgesic effect through weak  $\mu$ -opioid receptor agonism along with inhibition of serotonin and noradrenaline reuptake, thereby activating descending inhibitory pain pathways.

Sensory block recovery time (SBRT) was longer in group II ( $53.67 \pm 0.88$  min) compared to group I ( $47.34 \pm 0.71$  min) (Fig. 2). The use of a mixture of local anaesthetic agents for IVRA has been reported to provide more profound analgesia, a more successful block, and a lower incidence of complications compared to the use of individual agents alone (Kognole *et al.*, 2004). Motor block recovery time (MBRT) was also longer in group II ( $56.50 \pm 0.85$  min) than in group I ( $50.83 \pm 1.14$  min). Previous studies have similarly reported prolonged MBRT when lignocaine was used as an adjunct to dexmedetomidine and tramadol (Nasr and Waly, 2012).

Following tourniquet release after administration of lignocaine HCl alone and in combination with dexmedetomidine or tramadol, none of the animals exhibited any signs of local or systemic cardiovascular or central nervous system toxicity.

Based on the present study, it may be concluded that the combination of lignocaine and dexmedetomidine for distal intravenous regional anaesthesia (DIVRA) is more effective and suitable than the combination of lignocaine with tramadol.

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