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Continuous regional analgesia by intraneural block: Effect on postoperative opioid requirements and phantom limb pain following amputation

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Abstract—The objective of this study was to assess the effectiveness of a previously described technique of regional analgesia (continuous infusion of local anesthetic through a catheter placed at the time of amputation within the exposed sciatic or posterior tibial nerve) on relieving the postoperative pain in a heterogeneous group of patients who underwent lower extremity amputations. A second objective was to determine the effect of such treatment on the incidence and characteristics of phantom limb pain 6 months or more after surgery in the same patients. The study design was retrospective, unblinded, controlled (postoperative pain), and unblinded questionnaire and interview (phantom pain) were utilized. Subjects were inpatients at Harborview Medical Center, University of Washington, Seattle, WA. Nineteen bupivacaine-treated and 40 nonbupivacaine-treated patients who underwent lower extremity amputation subsequent to trauma, infection, long-standing injury (poor or no function), congenital deformity, or burns were evaluated in the postoperative pain management assessment. Nine treated and 12 untreated patients were interviewed in the phantom pain assessment. Bupivacaine 0.5% 2–6 ml/h was infused through a polyamide 20-gauge catheter inserted into the sciatic or posterior tibial nerve sheath under direct vision at the time of surgery. All patients, treated and control, received opioid analgesics systemically during the 72-hour period of study. The postoperative opioid analgesic requirement of treated patients was compared with that of control patients who received opioid analgesics alone. A questionnaire was administered to assess presence, severity, and character of phantom pain. The opioid analgesic requirement of treated patients was comparable to that of controls (132.7 ml of morphine equivalents/72 h treated; 151.3 ml morphine equivalents/72 h control), as were the incidences of all opioid related side effects. The follow-up questionnaire revealed a similar incidence (77% treated; 50% controls) and profile of phantom pain in both groups. In this study, continuous regional analgesia by intraneural infusion of local anesthetic failed to decrease systemic analgesic requirements or reduce the incidence of phantom pain compared with standard opioid analgesia. Since two previously published reports have found this technique effective, several possible reasons for the different results of this study are suggested.

Key words: *amputation, bupivacaine, narcotic analgesics, opioid analgesics, postoperative pain, phantom limb, regional anesthesia.*

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INTRODUCTION

Continuous regional analgesia by local anesthetic administration into a nerve sheath is a

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technique that has been used for postoperative pain control in patients who have undergone surgical procedures on an extremity, during which major peripheral nerves are easily accessible. A catheter can be placed within a peripheral nerve sheath at the time of surgery, and continuous local anesthetic infusion may result in excellent postoperative pain control. Although data on this technique are sparse, two studies have reported on its efficacy, safety, and advantages over parenteral opioids in controlling both acute and phantom post-amputation pain in a group of pediatric oncology patients (1) and in a group of adult vascular insufficiency patients (2), both of whom had lower extremity amputations. Investigators in both studies found that the consumption of supplemental opioids was reduced by 80–92 percent in the immediate postoperative period for patients so treated. No complications directly related to the use of intraneural catheters, including delayed wound healing, local or systemic infections, or signs of local anesthetic toxicity were reported. Blood bupivacaine levels, when they were measured, remained well below the toxic threshold (1). Additionally, treated patients complained of fewer side effects such as nausea, constipation, urinary difficulties, and clouding of sensorium than patients who received opioid analgesics alone (1).

None of the patients receiving continuous regional analgesia in either study complained of phantom pain in the immediate postoperative period. One of the studies reported that none of these patients had developed phantom pain even after one year (2). It was suggested that prolonged local anesthetic blockade of afferent nociceptive impulses may suppress the formation of a "nociceptive engram" in cortical somatosensory association areas which may be associated with phantom pain.

We undertook a similar study in a heterogeneous patient population (trauma, infection, chronic deformity, and vascular insufficiency) undergoing lower extremity amputations. We attempted to assess the two hypotheses: 1) that continuous regional analgesia is effective in the management of postoperative pain and 2) that continuous regional analgesia prevents phantom pain in a group of patients with diverse pathology requiring lower extremity amputation.

METHODS

With approval from the Human Subjects Review Committee of the University of Washington and with informed consent of study subjects, we reviewed a cohort of patients who had undergone lower extremity amputation above the level of the ankle at Harborview Medical Center between July 1989 and August 1991. The study groups consisted of those treated postoperatively with both continuous regional analgesia and supplemental opioid analgesics ("treated group") and a control group who received opioid analgesics only. The decision to place an intraneural catheter at operation depended primarily on familiarity of the operating surgeon with the technique. Among patients treated by the two surgeons trained in the technique, only those who had grossly contaminated wounds were deemed unsuitable candidates for intraneural catheter placement. No other surgeons used the technique during this time period.

Intraneural Catheter Placement

Following the procedure of Malawer, et al. (1) at the time of amputation, a 20-gauge polyamide catheter (Burron Medical Inc., Bethlehem, PA) was inserted through a small incision in the nerve sheath made several centimeters above the level of ligation and transection of either the exposed sciatic or posterior tibial nerve, depending on the level of amputation. The catheter was then advanced cephalad 5–15 cm. The catheter was externalized through a skin stab wound and secured. A bolus of 10–20 ml of 0.5 percent bupivacaine was injected into the catheter before wound closure to confirm catheter placement and to provide regional analgesia. Typically the injection was given 30–60min. before conclusion of the procedure. Bupivacaine (0.5 percent) was subsequently delivered at a rate of 2–6 ml/h by either a constant infusion or frequent intermittent boluses for 3–7 days. The two delivery methods have been shown to achieve essentially the same degree of analgesia (1).

The medical record of each patient was reviewed for age on admission, birth date, gender, date of amputation, indications for amputation, duration of pain before amputation, level of amputation, type of operative anesthesia, and method of delivery of postoperative opioid analgesia. We re-

corded opioids consumed only during the first 72 hours following surgery and converted these totals to morphine equivalents (3). The presence of diabetes or significant renal impairment as well as any history of opioid abuse was also noted. The length of hospital stay, and occurrence of complications directly related to the method of postoperative analgesia used, including nausea and vomiting, constipation, pruritis, drowsiness, confusion, hallucinations, excess sedation, respiratory depression, urinary retention, rash, intraneural catheter infection, and signs of bupivacaine toxicity were also noted.

Each patient was contacted by telephone at least 6 months post-amputation to gather data about phantom pain. The purpose of the study and the format of the questionnaire were explained, and informed consent was obtained before we administered the questionnaire.

The patients were questioned about phantom pain using questions designed to identify the spatial distribution, onset, temporal properties, and any changes in overall phantom pain severity that occurred since amputation. Each patient was asked about the presence and duration of pain in the injured limb before amputation, the similarity of phantom pain to the pain the patient had before amputation, the current impact of phantom pain on daily activity and sleep, the patient's use of a prosthesis, factors that make the pain better or worse, and pain treatments the patient had in the past. To this was added a short-form McGill Pain Questionnaire (4).

Statistical analyses were performed using the two-tailed Student's *t*-test for parametric data and the Fisher's exact test or the Mann-Whitney "U" test for nonparametric data. Data were summarized as mean/standard deviation. Differences were considered statistically significant when $p<0.05$.

RESULTS

Patient Characteristics

Patient characteristics are summarized in **Table 1**. The study groups were comparable with respect to age, sex, and indications for amputation. The proportion of patients who had amputations for trauma, peripheral vascular disease (nonhealing ulcers and gangrene), infection (osteomyelitis and cellulitis), and long-standing injuries previously treated with multiple orthopaedic procedures was similar in the two groups. Notable differences between the study groups included two patients in the treated group who underwent amputation for congenitally deformed limbs (none in the control group) and four patients in the control group who had amputations for burns (two thermal, two electrical; none in the treated group). Nearly one-third of control group patients had diabetes mellitus, while none of the treated patients had diabetes. The groups were similar regarding the presence of renal insufficiency and history of opioid abuse.

We also divided all patients into three subgroups according to the duration of the pain experienced before amputation: "acute" (no pain or pain for less than 24 hours), "intermediate" (duration longer than 24 hours and less than 6 months), or "chronic" (duration 6 months or longer). If these data were not available, pain duration was called "indeterminate." Duration of pre-amputation pain was verified by telephone interview whenever possible. Patients with chronic pain generally had pain for much longer than 6 months: five of six patients in the treated group and four of five patients in the control group classified as chronic pain patients had experienced pain for over one year. There was no difference in the distribution of pre-amputation pain duration between study groups.

The groups were similar with respect to the anatomic level of amputation. However, nearly one-third of the amputations performed in the treated group were revision procedures in which previous amputations were raised to new levels (e.g., revision of a transtibial to an transfemoral level). None of the control patients had undergone revisions.

In both study groups, general anesthesia was used more frequently than either regional anesthesia or the combination of regional and general techniques. There was a trend toward more frequent use of general anesthesia among controls.

Opioid Analgesic Requirements

Patients in both groups typically received parenteral opioids by patient-controlled analgesia (PCA). Parenteral or oral administration of opioid

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Table 1.
Patient characteristics.

Variable	Bupivacaine-Treated Group	Control Group	P*
n	19	40	
Sex (males:females)	17:2	36:4	0.347
Age (yr.)	42.4 ± 20.3	48.2 ± 20.1	0.310
Age Range (yr.)	18 – 83	20 – 91	
Indications for Amputation:			
Trauma	5 (26%)	16 (40%)	0.141
Peripheral Vascular Disease	6 (32%)	15 (38%)	0.210
Osteomyelitis/Infection	3 (16%)	3 (8%)	0.212
Long-Standing Injury	3 (16%)	2 (8%)	0.151
Congenital Deformity	2 (11%)	0 (0%)	0.099
Burns	0 (0%)	4 (10%)	0.201
Other Diagnoses:			
Diabetes Mellitus	0 (0%)	12 (30%)	0.005
Renal Insufficiency	1 (5%)	2 (5%)	0.456
Opioid Abuse	2 (11%)	3 (8%)	0.337
Duration of Prior Pain:			
Acute (<24 h)	5 (26%)	16 (40%)	0.141
Intermediate (24 h to 6 mo.)	7 (37%)	18 (45%)	0.189
Chronic (>6 mo.)	6 (32%)	5 (13%)	0.064
Indeterminate	1 (5%)	1 (3%)	0.444
Level of Amputation:			
Transtibial	11 (58%)	26 (65%)	0.196
Knee Disarticulation	3 (16%)	5 (13%)	0.288
Transfemoral	4 (21%)	8 (20%)	0.266
Hip Disarticulation	1 (5%)	1 (3%)	0.444
Revision	6 (32%)	0 (0%)	0.006
Type of Operative Anesthesia:			
General	10 (53%)	28 (70%)	0.099
Regional	6 (32%)	9 (23%)	0.186
General + Regional	3 (16%)	3 (8%)	0.212

*Student's *t*-test or Fisher's exact test. Values are ± S.D.

on demand by nursing staff occurred less frequently. The study groups were similar with respect to the various methods of postoperative opioid analgesia used.

The amount of opioid analgesics each patient received during the first 72 postoperative hours was recorded and converted to morphine equivalents (4). There was no significant difference in opioid consumption in the two groups during any of the three 24-hour postoperative periods or during the entire 72-hour postoperative period (**Table 2**). Similarly, only small differences were found between study groups in the incidence of complications commonly associated with opioid use. Pruritis tended to occur more frequently in patients treated with intraneural catheters. The incidence of drowsiness was also significantly greater in the treated group. However, neither of these observations reached statistical significance.

Table 2.
Mean opioid analgesic requirements during the first 72 postoperative hours expressed as morphine equivalents (mg) in bupivacaine-treated patients versus controls. Values are ± S.D.

Postoperative Period	Bupivacaine-Treated Group Morphine Eq (mg)	Control Group Morphine Eq (mg)	P*
0-24 h	49.0 ± 42.4	60.1 ± 45.5	0.374
24-48 h	50.2 ± 41.9	47.6 ± 46.9	0.841
48-72 h	33.5 ± 24.1	43.6 ± 51.3	0.421
Total 72 h	132.7 ± 92.8	151.3 ± 124.3	0.564

*Student's *t*-test.

Variation of Mean Opioid Analgesic Requirements

Both groups were divided into subgroup pairs according to duration of pre-amputation pain, level of amputation, type of operative anesthesia, and method of delivery of postoperative opioids (**Table 3**). The mean opioid requirement of each subgroup of the treated group was comparable to that of the corresponding control subgroup. When the two subgroups of each pair within the same study group were compared, it was found that mean opioid consumption did not differ significantly between different lengths of pre-amputation pain, levels of amputation, types of operative anesthesia, or methods of postoperative analgesia. A trend (statistically not significant) toward greater opioid consumption was present in both the treated and control groups in patients who suffered chronic pre-amputation pain and in those who received opioids by PCA postoperatively. Within the control group, the mean opioid requirement for patients with diabetes did not differ significantly from the requirement of those without diabetes.

Use of Intraneural Catheters

Intraneural catheters remained in use an average of 4.1 ± 1.5 days (range 1.3–7.0 d). No complications related to the use of intraneural catheters, including wound infection or delayed wound healing, were observed.

Length of Convalescence

The mean length of hospital stay was not significantly different between groups (20.2 ± 17.2 d treated; 27.5 ± 21.2 d control, $p = 0.197$). The duration of postoperative course, measured from the day of surgery until the patient was discharged to home, a nursing facility, or the rehabilitation service tended to be longer in controls (15.4 ± 12.5 d treated; 24.0 ± 9.4 d control, $p = 0.085$).

Questionnaire Results: Incidence and Characteristics of Phantom Pain

Nine patients (47 percent) in the intraneural catheter group completed the questionnaire, one patient (5 percent) was excluded due to dementia, and the remainder (47 percent) were not available for interview. Among the controls, 12 patients (30 percent) completed the questionnaire. Thirteen (32.5 percent) of the original controls were excluded due to deafness, aphasia, dementia, or inability to speak English, and the remaining (37.5 percent) were not available for interview. The interval between the date of amputation and the interview ranged from 6–32 months and tended to be longer in the treated group (**Table 4**). There were no differences between treated patients and controls in the incidence of

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Table 3.
Mean opioid analgesic requirements expressed as morphine equivalents in subgroups of bupivacaine-treated and control study groups. Values are ± S.D.

Subgroup	Bupivacaine-Treated Group Morphine Eq (mg)	Control Group Morphine Eq (mg)	P*
Duration of Prior Pain			
Acute	101.6 ± 24.6	134.1 ± 72.1	0.342
Chronic	145.8 ± 103.2	244.3 ± 245.8	0.392
Level of Amputation #			
TT	135.4 ± 90.7	159.6 ± 127.8	0.657
KD, TF, HD	124.6 ± 106.3	136.0 ± 120.6	0.826
Type of Operative Anesthesia			
General	138.3 ± 97.1	164.8 ± 125.9	0.550
Regional or Combined	126.6 ± 93.3	120 ± 119.7	0.893
Method of Postop. Analgesia			
PCA	152.9 ± 97.0	162.2 ± 103.2	0.794
Nurse-administered Opioids	63.7 ± 70.2	104.2 ± 76.8	0.418

*Student's *t*-test, bupivacaine-treated group compared to control group.
TT = transtibial amputation; KD = knee disarticulation; TF = tranfemoral amputation; HD = hip disarticulation.
Differences between the two subgroups in each subgroup pair within the bupivacaine-treated and control groups are not significant.

Table 4.
Pain questionnaire results.

Variable	Bupivacaine-Treated Group	Control Group	P*
n	9	12	
Follow-up interval (months)	20.2 ± 8.1	13.8 ± 7.8	0.080
Phantom Limb Sensations	7 (77%)	12 (100%)	0.171
Phantom pain:			
Currently	7 (77%)	6 (50%)	0.163
Previously	0 (0%)	3 (25%)	0.165
Never	2 (22%)	3 (25%)	0.389
Somatosensory Memories	3 (33%)	2 (17%)	0.272
Stump Pain	4 (44%)	7 (58%)	0.283

*Student's *t*-test or Fisher's exact test.

phantom limb sensations, phantom pain, residual limb pain, or "somatosensory memories" (defined as a pain or sensation referred to the missing part that is similar in both quality and location to a pain or sensation experienced in the limb before amputation) (5). Three controls developed phantom pain immediately after surgery, but the pain had completely resolved 1, 3, and 6 months postoperatively. The incidence of chronic phantom pain in both groups (treated group = 77 percent, controls = 50 percent) was similar to that reported in other studies (6–8).

The differences between study groups in the descriptor profiles and descriptor intensity ratings from the short form MPQ were not statistically significant (**Table 5**), nor were pain intensity ratings different. The onset of phantom pain, temporal properties, change since amputation, impact on daily activity and sleep, use of prostheses, and variety of pain treatments used were also comparable between groups.

In both groups, the occurrence of phantom pain had no relationship to the presence of pre-amputation limb pain, duration of pre-amputation pain, level of amputation, performance of a revision procedure, type of operative anesthesia, or presence of residual limb pain.

DISCUSSION

Continuous perineural local anesthetic infusions have been reported to be successful in providing effective postoperative analgesia. (9,10) A double-blind, randomized, controlled clinical trial by Dahl et al. (11) established the efficacy and safety of a continuous lumbar plexus block achieved through an intraneural catheter in decreasing morphine requirements and pain scores during the first 16 hours following exploratory knee surgery, although they found no advantage to the technique in decreasing the incidence of nausea and vomiting or urinary retention when compared with opioid analgesia alone. In a recent study, Edwards and Wright found that the 3-in-1 block performed with a continuous infusion of bupivacaine lowered postoperative pain scores and opioid analgesic requirements in patients undergoing total knee arthroplasty (12), but they did not investigate the ability of this method to decrease the incidence of side effects associated with opioid analgesia. The 3-in-1 block is performed by infusion of bupivacaine up the femoral canal to block the femoral nerve, the obturator nerve, and the lateral cutaneous nerve of the thigh. The sciatic nerve is not blocked in the 3-in-1 technique. Intuitively, the 3-in-1 technique might

Table 5.
Comparison of mean pain intensity scores in the bupivacaine-treated group and control group.

Pain Scale	Bupivacaine-Treated Group	Control Group	P*
n	7	6	
Sensory Descriptors	9.3 ± 5.2	9.3 ± 8.9	0.484
Affective Descriptors	2.1 ± 3.2	1.5 ± 2.1	0.485
Total Descriptors	11.4 ± 7.7	10.8 ± 10.7	0.484
Present Pain Intensity (0-10)	3.7 ± 2.7	2.3 ± 2.5	0.439
Pain at its Worst (0-10)	7.9 ± 2.3	7.3 ± 3.2	0.484
Pain at its Least (0-10)	1.0 ± 1.3	1.7 ± 2.0	0.436

*Mann-Whitney "U" test. Values are ± S.D.

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provide better analgesia for lower extremity amputation surgery than placement of a catheter in the tibial nerve or sciatic nerve.

An extension of the perineural infusion is the continuous intraneural injection of local anesthetics that would theoretically provide superior analgesia and could decrease opioid use and its associated side effects. The data presented here demonstrate that, although continuous regional analgesia by nerve sheath block did not introduce complications, it also did not reduce mean postoperative opioid requirements in this heterogeneous study population of patients recovering from lower extremity amputations. The incidence of unpleasant side effects associated with parenteral opioid administration likewise was not reduced, and the incidence, quality, and severity of phantom pain 6–32 months following amputation was similar in treated and untreated patients. These results differ from those in two previous studies.

Malawer et al. (1) investigated the use of the continuous block in 23 pediatric patients following amputations and limb salvage resection operations for primary musculoskeletal neoplasms. Fisher and Meller (2) investigated intraneural infusion analgesia in 11 patients who had undergone lower-extremity amputations for septic gangrene secondary to peripheral vascular disease. Both studies found that patients treated with intraneural local anesthetic infusion required considerably less supplemental opioid for pain control than did matched historical controls (mean opioid requirements: 25 mg morphine equivalents/72 h treated, 123 mg morphine equivalents/72 h controls in Malawer et al.; 1.4 mg morphine/72 h treated, 18.4 mg morphine/72 h controls in Fisher and Meller).

A number of possible explanations may account for the differences between our results and those of the other studies:

Patient Selection. Continuous regional analgesia may be effective, but unequal patient selection may have exaggerated characteristics that elevate opioid requirements in the treated group.

The inclusion of more chronic pain patients in the treated group may have elevated the incidence of phantom pain in this group. Among the factors identified by Jensen et al. (6,7) that were associated with a higher incidence of phantom pain 6 months after amputation were the presence of long-lasting (>1 month) pre-amputation pain and the presence of pain on the day of amputation. This relationship did not remain true 2 years after amputation, however. These investigators also found a trend toward a higher incidence of persistent phantom pain in patients with severe (opioid analgesic-dependent) pre-amputation pain than in those with less severe pre-amputation pain. Similarly, Katz and Melzack (5), in a retrospective study of 68 amputees, found that 57 percent of the amputees with phantom pain claimed that their pain resembled pain that existed in their limb before amputation in both quality and location. They used the term "somatosensory memory" to refer to these replicas of pre-amputation lesions and pains that are re-experienced after the loss of a limb as phantom pain (5).

In our patients, too, supplemental opioids tended to be delivered through PCA more frequently in treated patients than in control group patients. PCA users tended toward a higher consumption of opioid in both treated patients and controls, although this difference was not statistically significant.

Historical Controls. The use of historical controls in previous studies may have exaggerated differences between treated patients and controls.

The historical controls used by Malawer et al. and Fisher and Meller may not have been comparable to the patients they treated with continuous block, since more effective pain management protocols and improvements in surgical, anesthetic, and nursing practices could have occurred. The overall magnitude of opioid requirements for the 72-hour postoperative period also differs markedly between these two studies and may reflect differences in pain management practices between institutions. Since our study investigated a cohort that underwent amputation during a defined time period, significant differences between treated patients and controls in surgical, anesthetic, and nursing management are unlikely.

Study Design. Continuous regional analgesia may be effective, but this study design was not sensitive enough to detect a difference between treated patients and controls.

At a significance level of alpha = 0.05 and a power of 1-beta = 0.80, the sample size of our study was sufficiently large to find a difference of at least 81 percent between treated patients and controls in opioid requirements. An 81 percent difference is

comparable to that reported by Malawer et al., and Fisher and Meller (1,2).

Considering the normal wide variability of response to opioid analgesics, opioid consumption is a relatively insensitive gauge of pain in any patient population. However, opioid consumption has been used as an index to pain in other studies (1,2,11,12).

The inclusion of trauma patients, many of whom have concurrent painful injuries, is problematic, since they might require opioids for these other injuries. This would also make it difficult to find a difference in opioid use between groups, although there were more trauma patients in the control group than in the treatment group.

Study Technique. Continuous regional analgesia may be effective, but the particular technique used in this study may not have been used to its maximal effectiveness.

The technique employed was similar to that described by Malawer et al. (1), in which 0.5 percent bupivacaine at an infusion rate of 2–4 ml/h (10–20 mg/h) was used. In contrast, Fisher and Meller (2) used 0.25 percent bupivacaine infused at a rate of 10 ml/h (25 mg/h), a greater rate of bupivacaine administration in a larger volume. It is possible that the bupivacaine infusion was not consistently titrated to the optimal rate for maximal pain relief in patients in our study. The average rate of infusion over the 72-hour postoperative period delivered 7.8 mg/hr bupivacaine, a rate comparable to the baseline rate used by Malawer et al. but considerably less than that used by Fisher and Meller.

Single-nerve Block. Continuous intraneural analgesia may be ineffective as a method of postoperative pain control following lower extremity amputation.

The case reports by Rosenblatt and Smith et al. and the clinical trial reported by Dahl et al. attest to the value of the 3-in-1 block during knee and amputation surgery. Block of either the femoral nerve alone or of the sciatic nerve alone could be inadequate to provide adequate analgesia of the surgical wound.

CONCLUSIONS

Single-nerve intraneural infusion of local anesthetic seems ineffective in reducing postoperative opioid requirements in a heterogeneous population of patients undergoing lower extremity amputation. We were unable to detect a difference in the effectiveness of postoperative analgesia, incidence of side effects related to opioid use, incidence of phantom pain, or intensity of the pain experience in patients who developed phantom pain.

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