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Effect of multisensory exercise training on neuropathic pain, vibration threshold and sensorimotor function in patients with diabetic neuropathy: An interventional study

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Abstract
Background: Diabetic neuropathy is a common manifestation of peripheral nervous system in diabetes due to elevated glucose level. Symptoms include painful lower limbs, altered sensation, reduce reflexes and weakness of lower limb resulting in impairment in balance and gait. As a treatment various interventions are used such as balance training, strength training, aerobic exercise, sensory motor training. Multisensory exercise programmed, was considered as a new strategy to improve physical function in patients with diabetic neuropathy.
Objective: This study was to assess the effect of multisensory training on neuropathic pain, vibration threshold and sensorimotor function in patients with diabetic neuropathy.
Methods: This study was conducted in researcher's institute OPD and various diabetic centers of Surat. 28 diabetic neuropathic patients were randomly assigned in to 2 groups; 14 patients were allocated in group A (multisensory training & conventional) and 14 patients were allocated in group B (conventional therapy). Patients in both groups were treated for 3 days per week for 4 weeks. Conventional physiotherapy was given for 3 days in a week at home for 4 weeks. Neuropathic pain, vibration threshold, sensation, balance and gait were assessed by using DN4 questionnaire, Bioasthesiometer, Semmes-Weinstein monofilaments, berg balance scale and dynamic gait index respectively. Data were recorded at baseline and after 4 weeks of training.
Results: The present study included total 16 males and 12 females. Multisensory training and conventional therapy both showed significant improvement after intervention was administered ($p<0.05$). But the multisensory training showed more improvement than conventional therapy alone ($p<0.05$).
Conclusion: This study concluded that multisensory and control group showed improvement in patients with DN. The multisensory training showed more improvement than conventional therapy.

Keywords: Diabetic neuropathy, multisensory exercise training, neuropathic pain, sensorimotor function, vibration threshold

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by elevated blood glucose levels, leading to widespread disturbances in the metabolism of carbohydrates, fats, and proteins [1]. Its global prevalence presents a significant public health challenge, with an estimated 537 million adults affected in 2021. This number is projected to rise sharply to 643 million by 2030 and 783 million by 2045, underscoring the urgent need for effective management strategies [2]. Beyond hyperglycemia itself, diabetes predisposes individuals to a range of serious multi-system complications that develop over time, profoundly impacting quality of life and increasing healthcare burdens [3].

Among the most prevalent and debilitating of these complications is diabetic neuropathy (DN), a consequence of prolonged hyperglycemia. The American Diabetes Association (ADA) defines its most common form, diabetic peripheral neuropathy (DPN), as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes" [4]. DPN exhibits a highly variable prevalence, reported between 18.8% and 61.9%, and can manifest as either asymptomatic or with a range of distressing symptoms [5]. The pathogenesis of DN is multifactorial, involving several interconnected pathways including increased polyol pathway flux, protein kinase C (PKC) activation, accumulation of advanced glycation end-products (AGEs), and heightened oxidative stress [6]. These mechanisms collectively lead to reduced nerve conduction velocity, demyelination, and eventual axonal loss, primarily through impaired endoneurial blood flow and nerve hypoxia [6].

Clinically, DPN typically presents as a diffuse, distal, symmetric sensorimotor polyneuropathy that is often progressive and largely irreversible [7, 8]. The specific symptoms experienced by a patient depend on the type of nerve fibres affected. Large fibre involvement impairs proprioception and light touch, while small fibre damage leads to altered pain and temperature perception, often resulting in paraesthesia, dysesthesias, and neuropathic pain [5]. This neuropathic pain is a common and severe complaint, characterized by burning, tingling, or electric shock-like sensations that can significantly impair psychosocial and economic well-being [9]. Furthermore, the loss of vibratory sensation, mediated by mechanoreceptors, is a classic sign of large-fibre dysfunction and is a key clinical indicator of DPN [10].

The sensory deficits inherent in DPN have profound functional consequences. A primary concern is the detrimental impact on postural stability and balance. The somatosensory system, which includes tactile and proprioceptive feedback from the feet, is crucial for maintaining equilibrium. In DPN, the reduction in this sensory input disrupts postural control, substantially increasing the risk of falls, particularly in the elderly [11, 12]. This sensory loss also contributes to alterations in gait, as the integration of sensory information is essential for smooth and stable locomotion [13]. Numerous abnormalities, including sensory loss, decreased lower-extremity strength, and central nervous system changes, collectively contribute to an impaired and often unsteady gait pattern in this population [13].

Conventional management of DN and its symptoms primarily revolves around glycemic control through pharmacotherapy and lifestyle interventions, alongside medications specifically for neuropathic pain [9, 14]. Within rehabilitation, physiotherapy employs various sensory-specific modalities-such as transcutaneous electrical nerve stimulation (TENS) for pain, proprioceptive training for balance, and tactile stimulation with different textures to enhance touch perception-to retrain sensory pathways and help patients adapt to their changed capacities. Building on this principle, multisensory training has emerged as a novel strategy that integrates simultaneous stimulation of several sensory systems (somatosensory, visual, vestibular) to promote neuroplasticity and functional recovery [15].

While preliminary studies on multisensory training are promising, the existing literature has notable gaps. Research by Sowjanya Maruboyina *et al*. and Monireh Asadi Ghaleni *et al*. has demonstrated its benefits for improving balance in individuals with DN [16]. However, few studies have comprehensively investigated its effects on a broader range of critical outcomes, including vibration perception threshold, cutaneous sensation, neuropathic pain, and gait parameters within the same cohort. Furthermore, most existing research has been conducted in developed countries, and its generalizability to different healthcare contexts and patient populations, such as in India, remains uncertain.

Therefore, this study aims to investigate the effect of a structured multisensory exercise training program on neuropathic pain, vibration threshold, sensation, balance, and gait in Indian patients with diabetic neuropathy. The findings will contribute to the development of more effective and comprehensive rehabilitation protocols tailored to address the multifaceted deficits caused by this common and debilitating complication of diabetes.

Materials and Methods

This study employed an interventional design conducted over a period of 8 months. The sample size was determined a priori using G*Power software version 3.1.9.7. With an effect size set at 1.32 and an alpha error probability of 0.05, the calculation yielded a required sample size of 28, which was allocated as 14 subjects per group. A purposive sampling technique was used to recruit a total of 28 participants diagnosed with diabetic neuropathy, comprising both male and female genders.

Participants were selected based on predefined criteria. Inclusion required individuals aged 40-65 years with a confirmed diagnosis of diabetes mellitus for at least three years and electrophysiologically confirmed diabetic neuropathy with lower limb involvement via nerve conduction velocity (NCV) reports. Furthermore, participants had to be capable of walking for at least 6 minutes and score above 6 on the Modified Toronto Clinical Scoring System. Patients were excluded if they presented with any musculoskeletal disorder affecting the lower limb (e.g., fractures, tumors, infections, ligament injuries), peripheral vascular disease, common peroneal nerve injury, other neurological disorders that could influence gait (such as stroke or Parkinson's disease), or significant cardiovascular disease. The study setting included the Outpatient Department of the researcher’s institute and various diabetic centres in Surat, India. The ethical clearance was taken from institutional ethical committee. After getting ethical approval researcher contacted head of the department OPD and different diabetic centers of Surat to get the permission. Researcher contacted patients individually for permission. Subjects were screened on the basis of inclusion and exclusion criteria and the detailed procedure of study was explained to patients and signed consent form in language of their choice was taken from them before commencement of the study. The participants were allocated into two groups randomly using lottery method in which participants were allocated to Group A and Group B respectively. This same sequence was maintained throughout the study. Their demographic data was taken by an assessment Performa.

Total 33 patients were assessed for eligibility. Out of 33, 4 subjects did not meet the inclusion criteria. So total 29 subjects were enrolled in the study and allocated to two groups. Therefore, there were 15 participants in Group A (Interventional Group) received multisensory training along with conventional therapy and Group B (Control Group) received only conventional therapy. Outcome measures were assessed before starting the intervention of the study, and after 4 weeks of duration. In interventional group 1 patient was unable to complete 4 weeks protocol so, at the end of 4 weeks 28 patients were analysed. Group A: Multisensory exercise training + Conventional therapy

(Interventional group) and Group B: Conventional therapy (Control group)

In Multisensory exercise training protocol Special and focused exercises were given with emphasis on senses warm up and cool down which includes ankle plantar flexion and dorsiflexion (10 reps), inversion and eversion (10 reps), short walk (5 min), self stretching of calf and hamstring muscles. (3 reps with 30 sec hold). In touch walking on regular floor (5min), firm Mattress (5min) and foam rubber (5min). In proprioception and vestibular stimulation walk forwards, backwards, and sideways, with eyes both open and closed, at different speeds (starting with normal speed, in between ask patient to walk fast and slow) and for various distances. Also, bipedal support- unipedal stance, Eye open-firm surface, Eye open - soft surface, Eye closed- firm surface, Eye closed- soft surface (10 sec hold), double legged stance(10s), tandem stance(10s) and tandem walking(3min), obstacle walking (3min). Each exercise will be performed for 5 times [8, 17]. Intervention was given for 3 days per week for 4 weeks. 30 sec rest was given in between each exercise.

In conventional therapy patients received standard care given by physician for patients comprising of glycaemic control, diet advice (Offer the patient frequent sips of sugar-free fluids, and blood glucose is <15mmol/l) and palliative care for neuropathic pain. 25 min walking exercise prescription to be done 3 days in a week at home for 4 weeks [17]. Patient was informed to continue walking along with physician advice at home. Consent from the patient was taken for walking by telephone at every session. At 4th week, patient was called for post outcome measures of intervention. Conventional therapy was given for both the groups. The primary outcome measures assessed in this study were neuropathic pain [18, 19], vibration perception threshold [20, 21], and sensory-motor function [22]. Sensory motor function includes sensations [23] from sensory aspect and balance & gait [24] from motor aspect. Patients were assessed before and at 4th week of intervention.

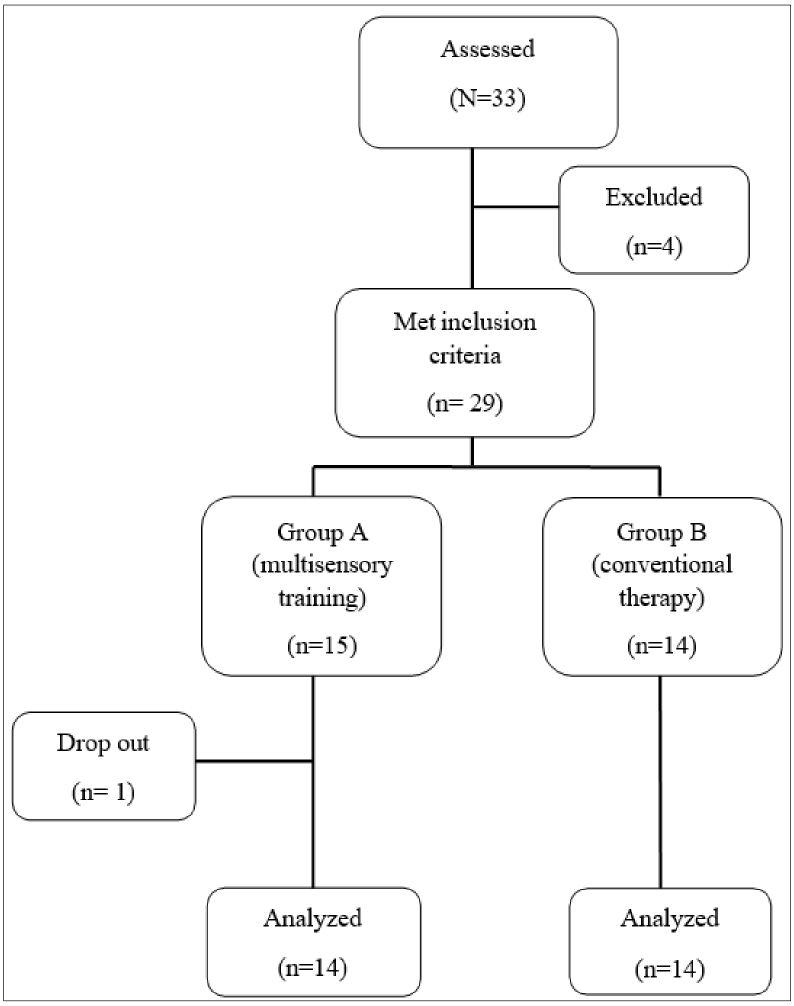


Fig 1: Consort flow chart

Statistical analysis and results

All statistical analyses were performed using SPSS software (Version 20.0). The study variables included quantitative measures-specifically, age, neuropathic pain, vibration threshold, sensation, balance, and gait-while gender was treated as a qualitative variable. The normality of the data distribution for all quantitative variables was confirmed using the Shapiro-Wilk test (*p*> 0.05), justifying the use of parametric tests for subsequent analyses. To ensure baseline comparability, the characteristics of the two intervention groups were assessed for homogeneity. For intragroup analysis, a paired sample t-test was used to evaluate the differences between pre- and post-intervention measurements. An independent t-test was employed to analyze the differences between the two groups. A 95% confidence interval was used, and the level of significance for all tests was set at *p*< 0.05. All 28 subjects who participated in the study were included in the final analysis.

Table 1: Descriptive analysis and pre treatment comparison

Variable	Group A (Multisensory training) Mean ± SD	Group B (Conventional) Mean ± SD	p - value
Age (in years)	60.00±4.61	57.21±7.78	0.256
Gender	1.29±0.47	1.57±0.51	-
Pre DN4	7.5±1.22	5.57±1.55	0.059
Pre VPT	28.32±4.85	21.61±2.83	0.169
Pre SWM	7.03±0.80	4.77±3.65	0.768
Pre BBS	37.21±5.27	45.71±5.55	0.220
Pre DGI	13.93±3.79	17.57±3.99	0.069

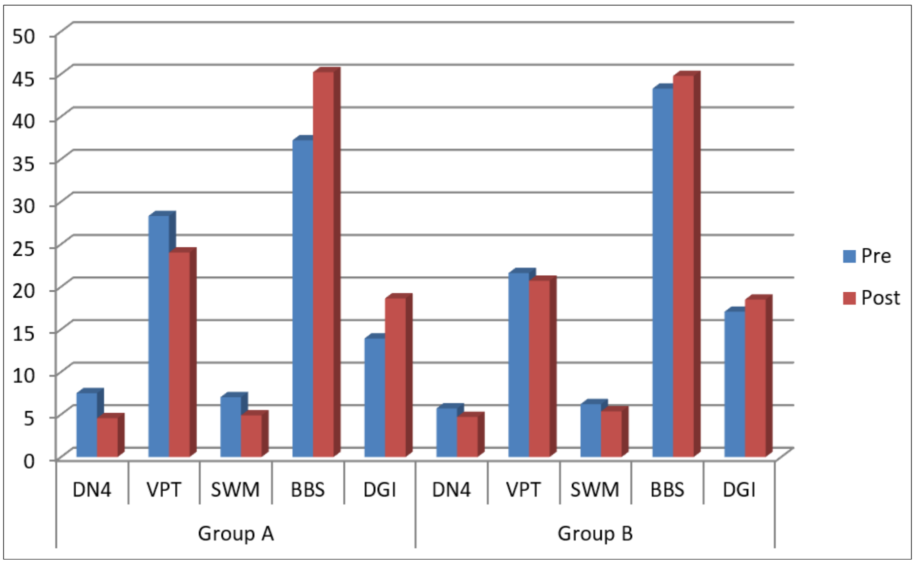
Table 1 shows mean and SD of baseline characteristics including age in years, gender, DN4 questioner, VPT, SWM, BBS, DGI of patients with DN. Mean age and SD for Group - A was 60.00±4.61 and for Group -B 57.21±7.78 years. Out of all participants, male was 16 (57.14%) and female was 12 (42.86%). It also shows pre treatment group comparison. The p value of the all the variables were $p>0.05$ which suggested that all the variables were normally distributed.

Intra group analysis was done by using Paired t-test was used to compare the value of the outcome measures namely, DN4, VPT, SWM, BBS and DGI within both the groups with Level of significance at $p<0.05$ with confidence interval 95%

Table 2: Intra group comparison of both the groups

Groups	Outcome Measures	Pre-value (1st - week)	Post-value (4th - week)	p-value
Group A	DN4	7.5±1.22	4.57±0.80	0.000
	VPT	28.32±4.85	24.03±4.47	0.000
	SWM	7.03±0.80	4.90±0.79	0.000
	BBS	37.21±5.26	45.21±4.81	0.000
	DGI	13.93±3.79	18.64±3.63	0.000
Group s	DN4	5.71±1.43	4.71±1.50	0.000
	VPT	21.61±2.83	20.71±2.75	0.000
	SWM	6.21±1.15	5.37±1.23	0.000
	BBS	43.28±6.71	44.78±6.52	0.000
	DGI	17.07±3.50	18.50±3.05	0.000

Table shows intra-group comparison of both the groups. The result shows significant difference ($p<0.05$) for DN4, VPT, SWM, BBS AND DGI in Group A and B both, which suggested that neuropathic pain was reduced and improved vibration threshold, sensation, balance and gait after 4 weeks of multisensory training along with conventional therapy.



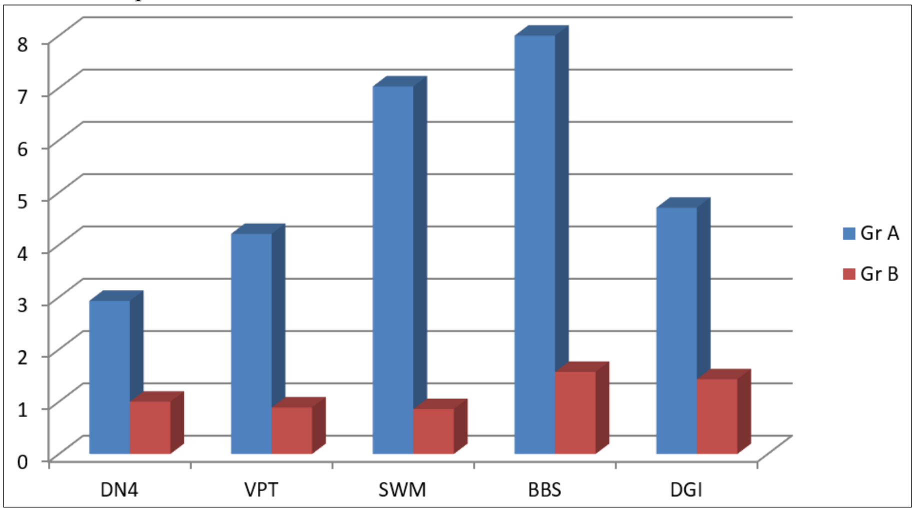
Inter-group analysis was done by independent t-test at level of significance $p<0.05$ with confidence interval 95%.

Table 3: Inter group comparison of both the groups

Outcome measures	Group-a	Group-b	P-value
DN4	2.93±0.73	1.00±0.68	0.000
VPT	4.21±2.13	0.89±0.49	0.000
SWM	7.03±0.80	0.86±0.42	0.000
BBS	8.00±4.00	1.57±0.51	0.000
DGI	4.71±1.63	1.43±0.65	0.000

Result shows significant difference ($p<0.05$) for DN4 which suggested that neuropathic pain was reduced in Group A than Group B after 4 weeks of intervention. It means multisensory training along with conventional therapy is more effective than conventional therapy alone which reducing DN4 score after 4 weeks of intervention.

There was significant difference(p<0.05) VPT, SWM, BBS and DGI which suggested that improved vibration threshold, sensation, balance and gait in Group A than Group B after 4 weeks of intervention.



Discussion

The present study investigated the efficacy of multisensory training on neuropathic pain, vibration threshold, sensation, balance, and gait in patients with diabetic neuropathy (DN). Conducted across various diabetic centres in Surat, the study employed a randomized design where participants were allocated into two groups. The intervention group (Group A) received multisensory training alongside conventional therapy, while the control group (Group B) received conventional therapy alone. Outcome measures, including the DN4 questionnaire, a Bioesthesiometer, Semmes-Weinstein Monofilaments (SWM), the Berg Balance Scale (BBS), and the Dynamic Gait Index (DGI), were assessed at baseline and after a 4-week intervention period.

The results demonstrated significant improvements in both groups following the 4-week intervention. Intragroup analysis, using a paired sample t-test, revealed that all outcome measures showed statistically significant improvement (p< 0.05) within each group. However, intergroup analysis using an independent t-test indicated that the magnitude of improvement was significantly greater in Group A (multisensory training) compared to Group B (conventional therapy alone). The mean values for all outcome measures were higher in Group A, with the intergroup comparisons also yielding p-values of less than 0.05, confirming the superior efficacy of the combined intervention.

The outcomes improved in the following order of magnitude, from greatest to least: balance, followed by sensation, vibration threshold, gait, and neuropathic pain. This hierarchy suggests that multisensory training may have a more pronounced effect on proprioceptive and integrative functions critical for balance before impacting pain perception.

The findings of this study affirm that a structured multisensory training regimen can significantly enhance sensory and motor functions in individuals with DN. The superior outcomes observed in the intervention group align with the physiological premise that targeted, multifaceted stimulation can promote neurological adaptation and recovery.

Neuropathic Pain and Vibration Threshold

The significant reduction in neuropathic pain in Group A can be attributed to several exercise-induced mechanisms. Physical activity is known to promote microvascular function and fat oxidation while reducing oxidative stress. Furthermore, exercise increases the expression of neurotrophic factors, which can enhance nerve conduction velocity and alleviate pain. This finding is supported by the work of Sukartini *et al*. (2019), who also demonstrated that diabetic foot exercise reduces neuropathic pain after a 4-week intervention [25].

Similarly, the improvement in vibration perception, a function of large myelinated fibers, can be explained by exercise improving intraneural circulation and axoplasmic flow. This process helps normalize the function of damaged nerves and reduces the hyperexcitability of abnormal impulse-generating sites. Enhanced peripheral blood circulation and better glycemic control further contribute to the restoration of sensory function. Our results corroborate the findings of Pankaj Preet Singh *et al*. (2012), who concluded that a 21-day exercise protocol including nerve mobilization significantly improves vibration threshold in DN patients [26].

Sensation, Balance, and Gait

The improvement in cutaneous sensation is critical, as abnormal sensory perception in the soles of the feet is a primary source of postural instability in diabetics. Multisensory training is postulated to improve sensation by enhancing local blood flow. During exercise, increased oxygen consumption by muscles triggers the release of vasodilators, opening capillaries and improving perfusion. This delivers essential oxygen and nutrients to peripheral nerves, helping to maintain sensory function.

This enhanced sensory input directly translates to improved balance. The cerebellum, which integrates somatosensory, visual, and vestibular information, relies on accurate proprioceptive feedback for postural control. Multisensory training, particularly on varied surfaces, provides rich proprioceptive input through the spinocerebellar tracts, increasing receptor sensitivity and improving the cerebellum's ability to modulate balance. Our findings are consistent with Sowjanya Maruboyina *et al*. (2019), who reported that 4 weeks of multisensory stimulation led to significant balance improvements in individuals with type 2 diabetic neuropathy [27].

Finally, the observed gait improvements can be linked to the cerebellum's role in modulating the step cycle. The automatic aspects of gait are regulated by the medial cerebellum, which integrates multisensory inputs to fine-tune motor output. By enhancing the quality of these inputs, multisensory training facilitates more stable and efficient gait patterns. This is supported by Nizar Abdul Majeed Kutty *et al*. (2013), who found that a 6-week multisensory exercise program significantly improved gait in DN patients [28]. Furthermore, the efficacy of multisensory integration approaches is well-established in other neurological populations, such as children with cerebral palsy, as evidenced by studies from Patel *et al*. (2015) and others, reinforcing the validity of this therapeutic model [29].

Limitations and Future Recommendations

This study has several limitations. The primary constraint was the small sample size (n=28), which may affect the generalizability of the findings. Secondly, the lack of a post-intervention follow-up assessment means the long-term benefits of the multisensory training remain unknown.

Based on these limitations, future research is recommended to employ larger sample sizes and include longer-term follow-ups to evaluate the sustainability of the improvements. It would also be valuable to compare multisensory training directly with other emerging interventions within the same population or to explore its efficacy in other patient groups with sensory deficits.

Conclusion

Both multisensory along with conventional therapy and conventional therapy showed significant improvement in neuropathic pain, vibration threshold and sensorimotor function but multisensory training showed better improvement than conventional therapy alone. Balance and sensation showed more improvement in multisensory training group than other outcomes.

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