

Pilot Trial of Osteopathic Manipulative Therapy for Patients With Frequent Episodic Tension-Type Headache

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Context: Osteopathic manipulative therapy (OMTh; manipulative care provided by foreign-trained osteopaths) may be used for managing headache pain and related disability, but there is a need for high-quality randomized controlled trials to assess the effectiveness of this intervention.

Objective: To explore the efficacy of OMTh for pain management in frequent episodic tension-type headache (TTH).

Design: Single-blind randomized placebo-controlled pilot study.

Setting: Patients were recruited from 5 primary care settings.

Patients: Forty-four patients who were affected by frequent episodic TTH and not taking any drugs for prophylactic management of episodic TTH were recruited.

Interventions: Patients were randomly allocated to an experimental or control group. The experimental group received corrective OMTh techniques, tailored for each patient; the control group received assessment of the cranial rhythmic impulse (sham therapy). The study included a 1-month baseline period, a 1-month treatment period, and a 3-month follow-up period.

Main Outcome Measures: The primary outcome was the change in patient-reported headache frequency, and secondary outcomes included changes in headache pain intensity (discrete score, 1 [lowest perceived pain] to 5 [worst perceived pain]), over-the-counter medication use, and Headache Disability Inventory score.

Results: Forty patients completed the study (OMTh, $n = 21$; control, $n = 19$). The OMTh group had a significant reduction in headache frequency over time that persisted 1 month (approximate reduction, 40%; $P < .001$) and 3 months (approximate reduction, 50%; $P < .001$) after the end of treatment. Moreover, there was an absolute difference between the 2 treatment groups at the end of the study, with a 33% lower frequency of headache in the OMTh group ($P < .001$).

Conclusion: This feasibility study demonstrated the efficacy of OMTh in the management of frequent episodic TTH, compared with sham therapy in a control group. Osteopathic manipulative therapy may be preferred over other treatment modalities and may benefit patients who have adverse effects to medications or who have difficulty complying with pharmacologic regimens. This protocol may serve as a model for future studies.

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Tension-type headache (TTH) is a prevalent condition with substantial socioeconomic impact, and the prevalence of frequent episodic TTH may be as high as 24% to 38.3%.¹⁻³ Tension-type headache has been defined as a multifactorial disorder, conceivably implying the need for diversified treatment strategies.⁴ Headache-related disability can usually be reduced by identifying and avoiding triggers combined with nonpharmacologic and pharmacologic treatments, but effective treatment modalities are still lacking.⁴

Patients are turning to complementary or alternative therapies for headaches, including osteopathic manipulative therapy (OMTh; manipulative care provided by foreign-trained osteopaths). In particular, our anecdotal clinical observations suggest that OMTh may have a prophylactic effect in patients with TTH. An important difference between conventional prophylactic management and OMTh is that the latter is not administered according to defined protocols but rather is usually personalized, with techniques tailored to the needs of each patient. Perhaps partly for these reasons, many reviewers have found no rigorously tested evidence that manual therapies in general have a positive effect on TTH.⁵⁻⁹

Some studies, however, have demonstrated positive effects of manipulative therapy. For example, Jull et al¹⁰ found that nonosteopathic manipulative therapy reduced the symptoms of cervicogenic headache. A systematic review by Bronfort et al¹¹ found spinal manipulative therapy to be as effective as commonly used first-line prophylactic medications for both TTH and migraine headaches, but the authors emphasized that their conclusions were based on only a few trials, raising the question of whether their analysis was methodologically adequate. Authors of a more recent systematic review¹² concluded that spinal manipulation might alleviate TTH but that the small quantity of available data prevented any definitive conclusions.

On the other hand, to our knowledge, OMTh has rarely been rigorously tested for the care of patients with

headache, although results of some published studies suggest positive effects.¹³⁻¹⁶ Thus, there is a need for further research with high-quality randomized controlled trials to rigorously assess the effectiveness of OMTh vs placebo in headache disorders, including TTH.^{5,10,17} Considering the costs of TTH management,^{18,19} the impact of OMTh on management cost could also be tested in future studies.

Our objective for the present study was to perform a methodologically rigorous pilot randomized controlled trial evaluating the efficacy of OMTh for pain management in frequent episodic TTH. If its effectiveness could be demonstrated, we believed that OMTh, being potentially characterized by fewer contraindications and adverse effects than conventional treatment, might be a good alternative treatment option, especially in patients not compliant with medication regimens and those with contraindications to prophylactic medications. We focused on frequent episodic TTH because it is the most common diagnostic category with indications for prophylactic drug management.

Methods

Study Design and Treatment Allocation

The present study was a single-blind randomized placebo-controlled pilot study using an experimental design. Patients with headache were screened and recruited from 5 primary care settings (general practitioners), as indicated in the guidelines for controlled trials of drugs in tension-type headache.²⁰ After protocol approval, participants received written explanations regarding the objective of the study and gave their consent regarding sensible data use. General practitioners received written explanation of the study aims. Inclusion criterion was a diagnosis of frequent episodic TTH (we used the episodic TTH diagnostic criteria of the International Classification of Headache Disorders).²¹ The exclusion criteria were age younger than 18 or older than 65 years; use of drugs for acute headache on 10 or more days per

month during the previous 3 months; duration of disease less than 1 year; presence of major psychiatric diseases; presence of headache as a result of another disorder (ie, secondary headache), including cognitive disorders and chronic pain; or any kind of ongoing prophylactic management during the study period.

The study included a 1-month baseline period, a 1-month treatment period, and a 3-month follow-up period (Figure 1). At the end of the baseline period, patients were randomly assigned to either a control or an experimental group, based on a coin toss by the treating physician (G.R.).

During the 4 weekly treatment sessions, patients in the OMTh group received corrective OMTh techniques. Patients in the control group received assessment of their cranial rhythmic impulse (sham therapy), considered as placebo; manual techniques were used, but observed osteopathic disorders were not corrected. Both OMTh and sham therapy were provided by the same physician (G.R.). To minimize the perceived differences between treatments, patients in both groups first provided their medical history, underwent postural evaluation and osteopathic structural examination, and were given advice about physical activity and lifestyle, with similar amounts of time spent in both groups.

At the end of the active treatment period, patients in both groups were followed up and evaluated after 1 and

3 months. Recruitment started in October 2009 and finished in April 2010, and the follow-up of the last recruited patients was completed in August 2010. Because this study was exploratory (ie, a pilot study), no power analysis was performed.

The guidelines recommend double-blind trials,²⁰ but manual techniques cannot be administered without the operator's awareness, so the treating physician cannot be blinded.²² Patients were blinded, however; in the preliminary document for informed consent, recruited patients were told that they would be randomly assigned to 1 of 2 groups in which 2 different manual treatments would be administered.

The corrective techniques applied in the OMTh group were not protocol based²² but rather were individually tailored for each patient, according to Greenman's descriptions.²³ Briefly, the OMTh techniques were focused on correcting osteopathic dysfunctions found during the initial evaluation; structural (including myofascial release and high-velocity, low-amplitude), visceral, and craniosacral techniques were performed as appropriate. For the sham therapy, the operator was restricted to assessing the patient's cranial rhythmic impulse, spending a similar amount of time as used for OMTh techniques in the treatment group.

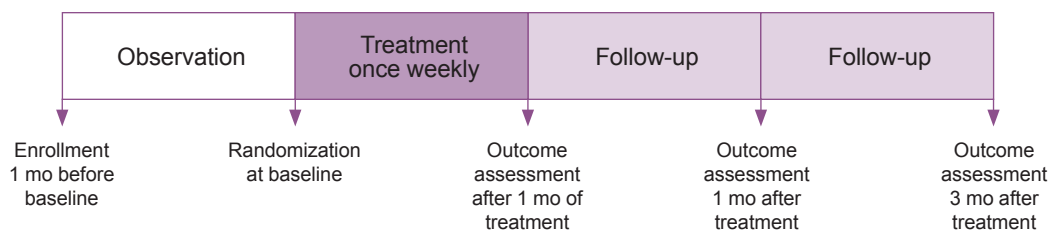


Figure 1. Gantt chart of study of patients with episodic tension-type headache.

Table
Baseline Values in Patients Receiving OMTh vs Sham Therapy
for Frequent Episodic Tension-Type Headache (N=40)

Variable	Baseline Value, Mean (SE)	
	OMTh Group (n=21)	Control Group (n=19)
Frequency, headaches/mo ^a	11.48 (1.36)	9.58 (0.77)
Over-the-counter medication use, medications/mo	8.09 (1.77)	6.63 (1.52)
Pain intensity score ^b	2.77 (0.18)	2.44 (0.13)
HDI score ^c	36.6 (2.94)	25.9 (2.57)

^a Baseline values were obtained at the end of the 1-month baseline period and represent values for that month.

^b Pain intensity was scored by patients on a scale from 1 (lowest perceived pain) to 5 (worst perceived pain).

^c Total possible Headache Disability Inventory (HDI) score ranged from 0 (no disability) to 100 (worst disability).

Abbreviation: OMTh, osteopathic manipulative therapy.

Outcome Measures

Patients were asked to keep headache diaries, which were used to evaluate efficacy of treatment. These diaries included changes in patient-reported headache frequency (number of episodes during the period considered), headache pain intensity (for each episode during the period, rated from 1 [lowest perceived pain] to 5 [worst perceived pain]), and over-the-counter medication use (total number of medications used during the period). We also assessed headache-correlated disability according to the Headache Disability Inventory (HDI),²⁴ a 25-item survey in which patients respond to questions related to disability as “no” (0 points), “sometimes” (2 points), or “yes” (4 points). The total possible score for the HDI ranged from 0 (no disability) to 100 (worst disability). Headache frequency was chosen as the primary outcome. All the other measures were considered as secondary outcomes. To increase sensitivity to patient-reported headache pain intensity, we use a scale from 1 to 5 instead of the suggested 0 to 3 scale.¹⁷ The HDI was self-reported by patients at the end of the baseline period, at the end of the 30-day treatment period, and at the first and third follow-up month (ie, 1 month and 3 months

after treatment). The headache diary referring to each previous period was obtained at the same time points.

Statistical Analysis

All hypotheses were verified by using the SPSS (version 18) statistic package. All significance tests were set at $P < .05$. The statistical tests were chosen following verification of the normality distribution of our samples using the Kolmogorov Smirnov test. Changes over time and the presence of a significant difference between the 2 study groups were assessed by the 2-way analysis of variance followed by multiple comparison Tukey test. Each difference vs baseline for each patient (delta) was assessed by the 2-tailed unpaired t test.

Results

Sixty-seven patients were screened, of whom 58 were enrolled (*Figure 2*). Fourteen dropped out because of deviation from the protocol—10 owing to poor compliance with the study procedures (ie, refusal to adhere to the treatment protocol at the baseline visit) and the other 4 owing to use of prophylactic drugs during the study

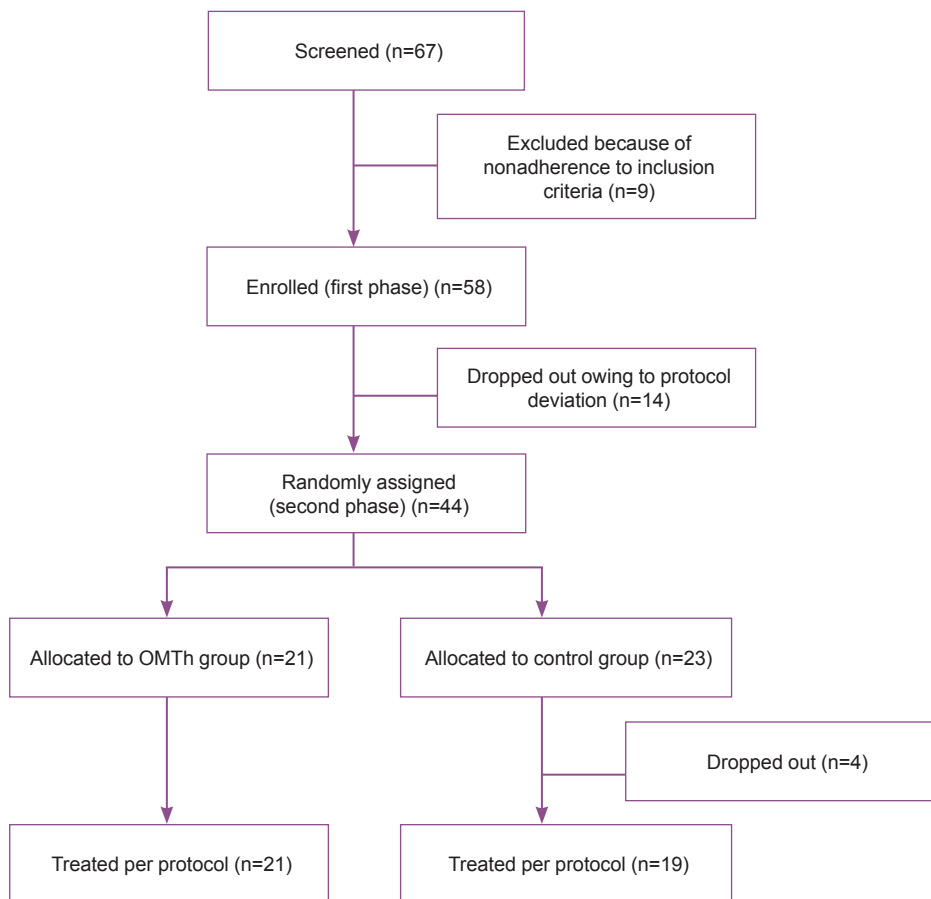


Figure 2.

Flowchart of enrollment and allocation of patients with episodic tension-type headache. *Abbreviation:* OMTh, osteopathic manipulative therapy.

period. Twenty-one patients were randomly assigned to the OMTh group and 23 to the control group. Four patients in the control group were eventually excluded from the study (per-protocol analysis): 2 specifically asked to interrupt the protocol during active treatment, and the other 2 used prophylactic drugs during follow-up; all patients in the OMTh group completed the study. Therefore, a total of 40 patients completed the study: 21 in the OMTh group and 19 in the control group (see baseline characteristics in the *Table*). The OMTh group included 4 male and 17 female patients, with a mean (SD) age of 32.7 (10.8) years, and the control group included 2 male and 17 female patients, with a mean age of 36.3 (13.2) years. No adverse events were recorded throughout the entire study for either group.

We found a significant change in headache frequency over time in the OMTh group (an approximately 50%

reduction vs baseline after 3 months of follow-up; $P < .001$) (*Figure 3*). We also found an absolute difference between the 2 groups at 3 months ($P < .001$), with a 33% lower frequency of headache in the OMTh group.

Regarding secondary outcomes, over-the-counter medication use was reduced only in the OMTh group, at all time points after baseline, compared with the baseline mean (resulting in an approximately 45% reduction vs baseline after 3 months of follow-up; $P < .001$) (*Figure 4*). Pain intensity was also modestly reduced over time in the OMTh group (resulting in an approximately 20% reduction vs baseline after 3 months of follow-up; $P < .001$). Finally, the HDI score showed no significant improvement; however, a change in the total score of at least 29 points from test to retest is required before the variation can be attributed to treatment effects,²² and the low baseline HDI score in our samples might help explain the

apparent lack of effect. Therefore, the comparison between the HDI score changes in the 2 groups highlighted a difference over time in the OMTh group (resulting in an approximately 40% reduction vs baseline after 3 months of follow-up; $P < .001$).

Discussion

Frequent episodic TTH was chosen for this trial because it is one of the most common indications for prophylactic management, for which we hypothesized that OMTh might represent an alternative. The drug treatments available for this condition are often unsatisfactory, and the social and health system costs can be high.³ The results of our feasibility study suggest that OMTh may be effective in the management of frequent episodic TTH. Headache frequency in the OMTh group, the primary outcome, was significantly reduced (by approximately 33%) compared with the control group at the end of the study. Secondary outcomes were also partially achieved, in particular a reduction in use over time of over-the-counter medications, implying a possible reduction in adverse effects and costs. No adverse effects were reported in this trial, although OMTh is not completely free of such effects.²⁵

The positive effects of OMTh on headache pain control could be a result of specific neurochemical effects, including an increase in the concentration of circulating opioids and serotonin with the involvement of serotonergic and noradrenergic descending tracts.²⁶ However, the molecular bases of OMTh clinical results are mostly unknown, and further studies are needed to investigate this issue.

Trials of OMTh, in part because OMTh techniques are individually tailored to each patient's needs, often fail to meet the strict evidence-based medicine requirements. In this study, therefore, we tried to plan a preliminary randomized controlled trial that was methodologically rigorous enough to be used as a model for planning future clinical trials in patients with episodic TTH. There is a need for future trials with sufficient power analysis; the present pilot study may offer a methodologic reference for designing such trials.

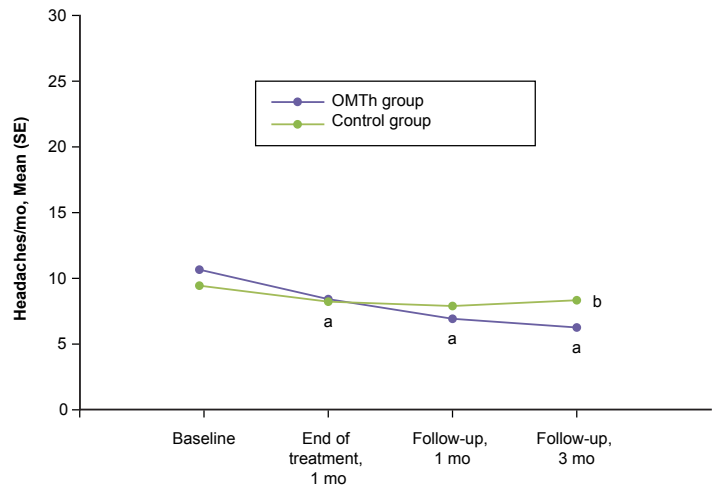


Figure 3.

Mean headache frequency of patients with episodic tension-type headache in the osteopathic manipulative therapy (OMTh) and control groups. ^a $P < .001$ for difference vs baseline; ^b $P < .001$ for difference between groups. Both values based on 2-way analysis of variance followed by Tukey post hoc analysis.

In planning the study we encountered other methodologic issues. The first concerns the double-blind condition. Unfortunately, OMTh and other manual therapies cannot be administered without the operator's awareness, thereby making it impossible to perform double-blind trials. Thus, all types of manual interventions may have an intrinsic limit.²² In the current study, sham therapy was used in the control group, allowing a manual approach that specifically excluded the correction of osteopathic dysfunctions. The lack of double blinding was clearly our study's greatest limitation along with the per-protocol analysis, which we preferred because it is intrinsically suited to preliminary and pilot studies, even though it is an obvious source of attrition bias.

The second limitation concerns possible differences between groups in patient confidence. Patients may perceive OMTh as a more credible treatment than many control procedures, and the study should be designed to equalize patient perceptions among interventions.²²

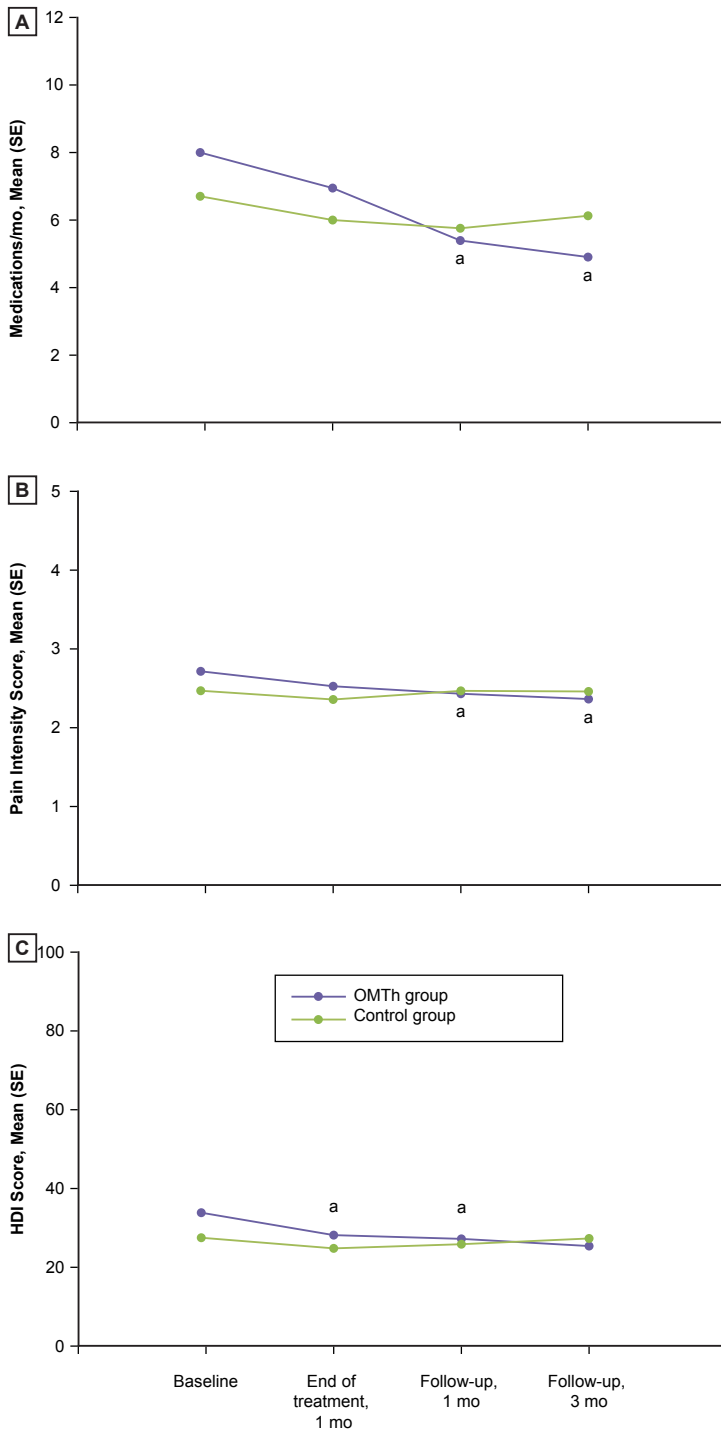


Figure 4. (A) Over-the-counter medication usage, (B) headache pain intensity scores (scale, 1 [lowest perceived pain] to 5 [worst perceived pain]), and (C) Headache Disability Inventory (HDI) scores (scale, 0-100) of patients with episodic tension-type headache in the osteopathic manipulative therapy (OMTh) and control groups. ^a*P*<.001 for difference vs baseline (based on 2-way analysis of variance followed by Tukey post hoc analysis).

We therefore tried to make the control and treatment interventions and settings as similar as possible to minimize perceived differences; patients in both groups provided their medical history, underwent postural evaluation and osteopathic structural examination, and were given advice about physical activity and lifestyle, with similar amounts of time being spent in both groups. The question of what should be considered an adequate placebo for OMTh is both relevant and complex, and previous studies, conducted with reasonably robust designs, have given different answers. For example, in a single-blind randomized experimental study,¹⁶ OMTh was offered to patients with TTH as an add-on therapy supplementing progressive muscular relaxation performed alone at home. To minimize bias, we decided that our control group should be attended to by the operator for the same amount of time as our OMTh group and that the procedures performed in the 2 groups should be as similar as possible.

The third limitation of our trial involves the lack of comparison between the novel intervention (in this case OMTh) and the therapeutic criterion standard (eg, amitriptyline or other drugs) to ensure sensitivity of the model; such comparison is requested in drug trials of episodic TTH prophylaxis.²⁰ This important limitation clearly needs to be addressed further in subsequent studies with sufficient power. However, prophylactic drug management often implies less contact (physical and over time) between patients and physicians, and our aim was specifically to distinguish any therapeutic effect of OMTh from the simple placebo effect of more frequent manual contact.

The last methodologic question concerns OMTh techniques per se. Treatments were individually tailored for each patient, as is usually done in osteopathic clinical practice, with corrective techniques applied to any noted dysfunctions. Because clinical observations in the field suggest that standardized osteopathic treatments are less effective than tailored ones, we decided that a preestablished protocol of techniques could limit the efficacy of OMTh; this option might be adopted in future trials, perhaps with mixed (partially structured) protocols.

Conclusion

Considering the results of our feasibility pilot trial, OMTh may be an interesting option for managing episodic TTH—one characterized by few contraindications and adverse effects and particularly indicated for patients not compliant with drug regimens and those at increased risk of adverse drug effects.

Author Contributions

Drs Rolle and Tremolizzo provided substantial contributions to conception and design and acquisition of data and drafted the article and revised it for submission; Dr Somalvico provided substantial contribution to analysis and interpretation of data; and Drs Ferrarese and Bressan gave final approval of the version of the article to be published.

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