



Brief report

Dietary correlates of chronic widespread pain in Meru, Kenya

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ABSTRACT

Objective: To gather preliminary data examining whether dehydration and/or exposure to monosodium glutamate (MSG) may influence pain in Meru, Kenya.**Methods:** Two small pilot studies were conducted in Meru, Kenya after community report of high chronic pain in the region. First, a prevalence estimate was conducted among 89 participants from random households. Second, widespread chronic pain participants, recruited from the community, completed a demographic questionnaire, pain impact questionnaire, and 1-wk food/symptom diary. Those who returned the food/symptom diary 1 wk later were assigned to a treatment group based on their report of water/tea intake per day (<2 L versus ≥2 L) and reported use of mixed spices with MSG (yes/no). Groups received 1) water, 2) alternative spices without MSG, 3) water and alternative spices, or 4) acetaminophen (1000 mg twice daily) for those with neither exposure. Improvement was defined as ≥30% reduction in pain impact score.**Results:** Prevalence of chronic pain among 89 participants surveyed was 60%. Thirty participants were recruited for the intervention (90% female; average age 56 [±18] y). The water and alternative spices and acetaminophen groups both experienced significant reductions in pain after 2 wk, with the greatest percentage of participants improving in the water and alternative spices group.**Conclusion:** This pilot data suggests an abnormally high prevalence of pain in Meru, Kenya, and that MSG intake, combined with dehydration, may be contributing to chronic widespread pain in this region. Future research should include a formal pain prevalence estimate and a randomized controlled trial to further test this dietary intervention.

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Introduction

Chronic pain is one of the most common and disabling medical conditions worldwide [1]. Data from the World Health Organization suggest that across 17 developed and developing countries, the population attributable risk for “yearly days out of role” was significantly higher for chronic pain than that of 19 other health conditions assessed [2]. Low- and middle-income countries (LMICs) could be disproportionately affected by chronic pain because of differences in exposures and treatment options available. Chronic pain may also have an impact on affected individuals in developing countries to a greater extent than in

the developed world because of the need for more physical labor.

Chronic widespread pain has been linked to central sensitization, which is a self-propagating upregulation of excitatory neurotransmission in the central nervous system [3]. This not only causes widespread pain but also negatively affects sleep, cognition, and mood as well [4]. This type of pain often presents with an unknown etiology, and individuals with central sensitization in LMICs may suffer disproportionately because of a lack of treatment options [5].

Most developing countries lack access to pain specialists, sophisticated imaging studies, expensive medications, and surgeons, limiting their ability to evaluate and treat pain adequately. One underexplored treatment option for chronic pain is dietary modification, especially for pain conditions that are more diffuse or systemic in nature, such as fibromyalgia. Dietary factors may play more prominent roles in developing countries because communities often lack adequate access to clean water and appropriate amounts of healthy food, increasing susceptibility to dehydration

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and malnutrition, which may affect neurotransmission and pain response. They may also be at higher risk for certain food-based exposures.

To date, most research suggests that the prevalence of pain in developing countries is similar to the United States and other developed nations. Studies on pain in various countries indicate that the overall pain prevalence is similar in developed (37% overall) and developing (41% overall) countries [6–8]. In a recent review article, chronic pain prevalence in LMICs was estimated to be around 33%, with a 4% prevalence rate for fibromyalgia [9]. This closely resembles prevalence estimates for overall pain (30%) [10] and for fibromyalgia (5%) [11] in the United States.

Community members in Meru, Kenya, have been concerned that they are experiencing abnormally high rates of chronic pain in the community and asked our research group to conduct a preliminary assessment of pain in the region. We used community-based sampling methods to assess local households in random areas of the Kithoka region of Meru, Kenya, to gain a very preliminary look at the potential prevalence of pain in the region, as well as the identification of shared dietary exposures, as one area of potential intervention. Of 89 individuals surveyed, 54 (61%) reported chronic pain lasting 3 mo or longer, with 30% of those surveyed meeting the criteria for fibromyalgia [12]. The prevalence rate identified in this very small sample was significantly higher than the chronic pain rates of 33% reported in other developing countries [9] and double the estimates of 30% from the United States [10], and self-report of fibromyalgia symptoms was six times higher than the US population estimate of 5% [11].

Common dietary exposures among those reporting pain in the surveyed group were found to be frequent use of mixed seasoning spices called Mchuzi mix and very low intake of water. Mchuzi mix contains added monosodium glutamate (MSG), which is used as a flavor enhancer in foods. Glutamate is well known in the field of nutrition as a negatively charged amino acid; however, glutamate is also the most common neurotransmitter in mammalian nervous systems [13]. Increased dietary consumption of free glutamate (in the form of additives) has the potential to enhance glutamatergic neurotransmission [14], which plays a pivotal role in central sensitization [3] and widespread chronic pain [15]. Dehydration has also been linked to increased brain activity related to painful stimuli [16]. Thus, there is good biological plausibility for how dietary exposure to MSG and inadequate water intake may be able to affect chronic pain.

Herein, we report the results of a quasi-experimental pilot study that tested the effects of removal of dietary MSG, increased water intake, or a combination of both, relative to acetaminophen (as the main treatment option available in Meru, Kenya), to determine the percentage of people with self-reported improvement in pain. Biological hypotheses and future directions based on this work are also discussed.

Methods

The research study was reviewed and approved by both University of Michigan and American University institutional review boards in the United States and was approved in Kenya by the Kenya Methodist University Scientific and Ethics Review Committee. All participants gave written informed consent; in the case of illiteracy, verbal consent was witnessed and formally recorded. English is the primary language of Kenya; however, some participants only spoke Swahili or the local dialect of Kimeru. Thus, translators were used to help individuals who did not speak English. In the case of illiteracy of a participant, research assistants filled out all questionnaires while interviewing the participants.

Individuals with chronic widespread pain were recruited from the community over 2 d using word-of-mouth advertising via clan elders and health workers in the local clinic. All interested parties were screened for widespread chronic pain; physical examinations were completed by two physicians; and height, weight,

and blood pressure were measured. Consent was obtained from those who were eligible for the study, and then they were asked to complete questionnaires including information on demographic characteristics, water intake, and frequency of mixed spice consumption (as the main source of MSG in the diet) and an assessment of pain impact. Participants were asked to rank their worst pain, least pain, average pain, and current pain. They were also asked how their pain affected their general activity, ability to walk, and ability to work, as well as their mood, sleep, relationships, and enjoyment of life. Lastly, participants were asked about the presence of fibromyalgia-like symptoms such as fatigue, trouble thinking, unrefreshing sleep, lower abdominal pain, depression, and headache. The pain impact score was scored as a summation of pain rankings, impact of pain on daily life questions (0–10), and presence or absence of fibromyalgia-like symptoms.

Much of the water intake in Meru is from tea consumption, so the combined intake of water and tea was measured. Participants were sent home with a food/symptom diary and were asked to record everything they ate and drank over the next week, in addition to recording daily symptoms. Participants who returned the food/symptom diary 1 wk later were assigned to intervention groups based on their reported exposures of inadequate water intake (defined as <8 cups/d or <2 L/d) and/or consumption of Mchuzi mixed spices, or lack of exposure to either one. The intervention groups were 1) “water only” (where those with low water intake were given bottled water and instructed to increase consumption to ≥ 2 L/d); 2) “spices only” (where those consuming Mchuzi mix were given MSG-free spices as a replacement); 3) “spices and water” (where those with both exposures were given MSG-free spices and bottled water with instruction to increase water intake to ≥ 2 L/d); and 4) “acetaminophen” (where participants with neither exposure were told to take 1000 mg of acetaminophen twice daily). The alternative spice mix contained the same spices as the Mchuzi mix, minus the MSG. This included cinnamon, coriander, cumin, fennel, fenugreek, garlic, ginger, salt, sugar, and turmeric. Participants were instructed to follow their prescribed intervention for 2 wk and then return to the clinic for reassessment of pain using the pain impact questionnaire. All participants were asked about consumption of foods that commonly contain MSG (including the Mchuzi mix), water and tea intake, and medication usage to assess adherence. Improvement was defined as a $\geq 30\%$ improvement in the pain impact score. A global impression of change was also assessed using a scale of 0 to 10 with 0 = “no relief from the intervention” and 10 = “complete remission of all symptoms from intervention.”

Statistical analyses

Data collected during the study were analyzed using SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA). Information from the food diaries was entered into Nutrition Data Systems for Research to obtain average nutrient intake values. Improvement from the intervention was defined *a priori* as a $\geq 30\%$ improvement in the pain impact score. Continuous data were determined to be non-parametric, so comparisons were made across treatment groups using Kruskal-Wallis tests (the non-parametric equivalent of a one-way analysis of variance). Pre-improvement versus post-improvement comparisons (within groups) were made using Wilcoxon signed rank tests, and categorical data comparisons were made using χ^2 tests.

Results

Table 1 describes the study population. The majority of participants were women (90%), and the average age was 56 (± 18) years. Age appeared to marginally differ across groups ($P = 0.07$), with older individuals being more likely to be in the acetaminophen or water only groups. Marginal differences were also noted for body mass index (BMI), with the acetaminophen group having the lowest BMI of 18 kg/m² ($P = 0.09$). Education significantly differed across groups, with the acetaminophen group also having the lowest reported education of 2 y ($P = 0.01$). As would be expected because group assignment was based on exposure history, average water/tea consumption at baseline significantly differed between intervention groups. The spice-only and acetaminophen groups had adequate water intake of 2.4 and 2.1 L/d respectively, whereas the spice and water and water only groups had inadequate intake of 1.12 and 1.06 L/d, respectively ($P < 0.0001$). Approximately half of the sample reported consuming Mchuzi mixed spices, with 20% of those reporting that they used the spice mix multiple times per day.

Table 1 also includes median nutrient intake by group assignment. The spice and water group had the lowest identified median caloric intake and correspondingly lower intake of all

Table 1
Demographic characteristics of chronic pain study participants in Meru, Kenya

<i>n</i> = 30	Intervention Group				<i>P</i> *
	Spices <i>n</i> = 6	Spices & water <i>n</i> = 8	Acetaminophen <i>n</i> = 10	Water <i>n</i> = 6	
	Median (IQR)				
Age (yr)	47.5 (24)	52.5 (28)	58.5 (20)	62.0 (16)	0.07
Education (y)	11.5 (7)	9 (6)	2 (7)	5 (8)	0.01
Weight (kg)	63 (15)	59.5 (21)	49 (17)	67.5 (11)	0.12
Height (cm)	163 (4)	163 (10)	165 (9)	164 (6)	0.76
BMI (kg/m ²)	24 (9)	24 (8)	18 (4.5)	26 (4)	0.09
Blood pressure (mm Hg)					
Systolic	118 (28)	135 (29)	137 (37)	139 (75)	0.40
Diastolic	81 (26)	86 (8)	80 (18)	75 (4)	0.23
Water consumption (L/d)	1.60 (1.42)	0.35 (0.53)	0.59 (0.59)	0.12 (0.47)	0.004
Water & tea consumption (L/d)	2.37 (0.71)	1.12 (0.59)	2.13 (0.47)	1.06 (0.59)	<0.0001
Energy intake (kcal)	2006 (691)	1542 (445)	1953 (933)	1892 (853)	0.82
Thiamin (g)	1.73 (0.75)	1.51 (1.10)	1.96 (0.74)	1.77 (0.47)	0.76
Riboflavin (g)	1.43 (0.73)	1.28 (0.38)	1.30 (0.76)	1.32 (0.66)	0.72
Niacin (g)	14.77 (7.42)	13.50 (10.01)	15.76 (5.11)	17.37 (8.99)	0.99
Vitamin B6 (mg)	1.79 (0.48)	1.64 (0.96)	1.86 (0.84)	2.01 (1.43)	0.97
Folate (μg)	581 (369)	411 (125)	562 (242)	533 (136)	0.20
Vitamin B12 (μg)	0.73 (1.2)	0.39 (0.30)	0.83 (0.90)	1.84 (2.37)	0.22
Vitamin A (IU)	21 697 (21 238)	14 607 (9971)	13 287 (17 705)	8584 (8172)	0.18
Vitamin C (mg)	90 (84)	72 (36)	74 (76)	87 (56)	0.50
Vitamin D (mcg)	1.95 (0.84)	1.11 (0.84)	2.21 (1.95)	1.79 (1.44)	0.32
Vitamin E (mg)	5.71 (3.22)	3.76 (3.24)	3.35 (2.23)	2.97 (2.50)	0.12
Vitamin K (mcg)	794 (511)	556 (427)	376 (600)	198 (429)	0.11
Iron (mg)	14.85 (7.91)	13.73 (7.87)	15.20 (7.11)	15.52 (7.40)	0.98
Magnesium (mg)	422 (281)	318 (85)	437 (281)	421 (73)	0.63
Phosphorus (mg)	1062 (608)	829 (306)	1027 (743)	1013 (346)	0.50
Potassium (mg)	3705 (1492)	2923 (1237)	3714 (1767)	3414 (1235)	0.68
Sodium (mg)	2215 (256)	2493 (590)	2908 (1200)	2353 (1020)	0.49
Zinc (mg)	8.92 (5.42)	7.14 (2.69)	7.34 (5.13)	9.43 (5.44)	0.52
	Number (%)				<i>P</i> [†]
Sex (% male)	0 (0%)	1 (13%)	1 (10%)	1 (17%)	N/A
Hypertension	3 (50%)	8 (100%)	6 (60%)	3 (50%)	0.09
Mchuzi mix Consumption	6 (100%)	8 (100%)	0 (0%)	0 (0%)	N/A

BMI, body mass index; IQR, interquartile range; N/A, not applicable.

* Kruskal-Wallis comparison across groups for nonparametric data, except for categorical data, where χ^2 was used.

[†] χ^2 .

nutrients except vitamins A, E, K, and sodium, though nutrient intake did not significantly differ among groups. Dietary energy intake (kcal) was found to be adequate in all groups, though median intakes of many micronutrients were less than the US recommended dietary allowance (RDA) or adequate intake (AI). Specific nutrients of concern included vitamins E and D, for which no participant met the RDA; choline and calcium, for which <5% met the RDA/AI; and vitamin B12 and potassium, for which <15% and <20%, respectively, met the RDA/AI. Zinc, iron, selenium, and vitamin C were also of concern, with 50% or less of the population consuming adequate amounts (Fig. 1).

Table 2 and Figure 2 demonstrate the pre- versus post-intervention change in pain impact score for each group. As illustrated in the figure, at baseline, the median pain impact score was highest in the spice and water group (93). This was followed by the spice-only group (83), then the acetaminophen group (78.5), with the lowest baseline score for the water-only group (54.5). Improvement after 2 wk on the intervention differed between groups, with statistically significant improvement being noted in the spice and water and acetaminophen groups (Fig. 2). The spice and water group had the highest number of participants (75%) who improved after 2 wk, followed by the spices and acetaminophen groups (50% each), and then the water-only group (33%).

Discussion

The results of this very preliminary pilot study suggest that a dietary intervention is feasible in the rural Kithoka region of Meru, Kenya. If the results presented here hold in a larger clinical trial, it would suggest that a low-glutamate diet combined with adequate water intake may be an effective low-cost treatment option for chronic pain. Future research should recruit widespread chronic pain participants with exposure to MSG and test the effects of this dietary intervention against acetaminophen (the main available treatment option in the region) as an active placebo, using a double-blind placebo-controlled design.

We hypothesize that dietary modulation of glutamate intake as a free amino acid (as opposed to being bound to other amino acids in forms such as meat) may be able to enhance central sensitization [3] occurring in widespread chronic pain [15]. Glutamate plays a key role in pain neurotransmission [17]. Injection of MSG into tissues can induce a peripheral pain response [18], with the response being more common in women (as is noted, with chronic pain being more common in women than men) [19,20], and glutamate levels in pain processing regions of the brain have also been associated with individual pain reports [21]. Both fibromyalgia and migraine patients have been found to have elevated cerebrospinal fluid glutamate levels [22], and emerging

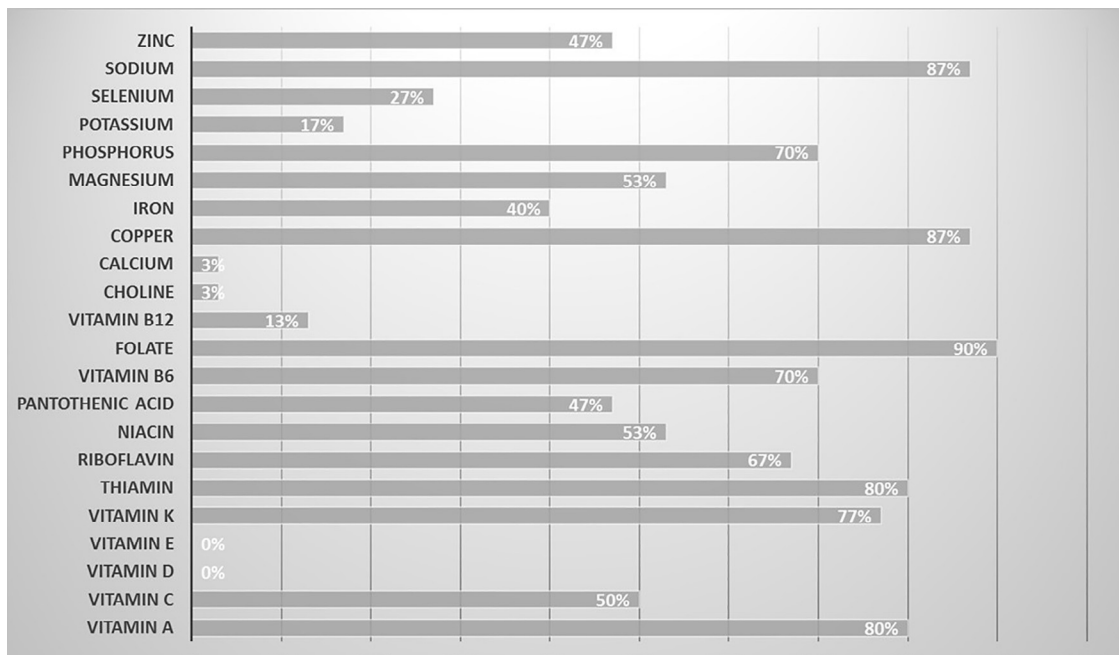


Fig. 1. Percentage of widespread chronic pain participants who met the US recommended dietary intake (RDA) or adequate intake (AI) for each micronutrient.

data support the idea that dietary modulation of glutamate (and aspartate, which has the ability to activate one glutamate receptor [NMDA]) can reduce or eliminate symptoms in fibromyalgia [23,24]. One study by Vellisca and Latorre [25] contradicts these findings by reporting no improvement after a 3-mo exclusion of MSG and aspartame. However, on closer examination, the authors actually report significant improvement after 1 mo on the diet. No details were given on dietary compliance; therefore, reduced dietary compliance over time, in addition to inadequate removal of all sources of free glutamate in the diet, may have led to a non-significant finding after 3 mo.

In the United States, a large number of foods contain free glutamate. Kenya is different in that it only has a few food items that constitute the major exposure to MSG in the region, with the largest exposure attributed to Mchuzi mixed spices. This spice mix is widely regarded as the “flavor of Kenya,” commonly being used in multiple dishes per day. In this pilot research, we

successfully recreated this mixed seasoning without MSG. Participants reported that they liked the flavor of the mixed seasoning and sought out ways to get more of the spices after the study. This suggests that this recipe (with and without MSG) can be used in future double-blind placebo-controlled research studies.

Low micronutrient intake was also identified over the week of recorded dietary intake in this study, as is common in many developing nations. It is possible that poor nutrient intake could be contributing to the high rates of chronic pain in this region. Specific micronutrients play important roles in preventing the excitotoxicity caused by excess glutamate [26], including magnesium [27], zinc [28], vitamin B6 [29], vitamin B12 [30], and vitamin D [31]. Vitamin D is of particular interest to the pain community because musculoskeletal pain has been linked to vitamin D deficiency in prior research [32]. However, because of Meru's location very near to the equator and because the participants in this study spend a good amount of time outside each day, we

Table 2

Pain impact score measures of chronic pain study participants in Meru, Kenya, by intervention group

n = 30	Intervention group				P *
	Spices n = 6	Spices and water n = 8	Acetaminophen n = 10	Water n = 6	
	Median (IQR)				
Pain impact scores					
Preintervention	83 (84)	93 (43.5)	78.5 (32)	54.5 (81)	0.58
Postintervention	39 (43)	44.5 (62.5)	29 (34)	48 (39)	0.85
Change scores	24 (66)	36 (53.5)	28 (66)	12.5 (30)	0.74
Global impression of change (scale 1–10)	7 (4)	7 (5)	6.5 (6)	5 (5)	0.68
	Number (%)				P†
Improved‡	3 (50%)	6 (75%)	5 (50%)	2 (33%)	0.50

IQR, interquartile range.

* Kruskal-Wallis used to compare across groups for non-parametric data, except for categorical data where χ^2 was used.

† χ^2 .

‡ Improvement defined as $\geq 30\%$ improvement on pain impact score after 2 wk of intervention.

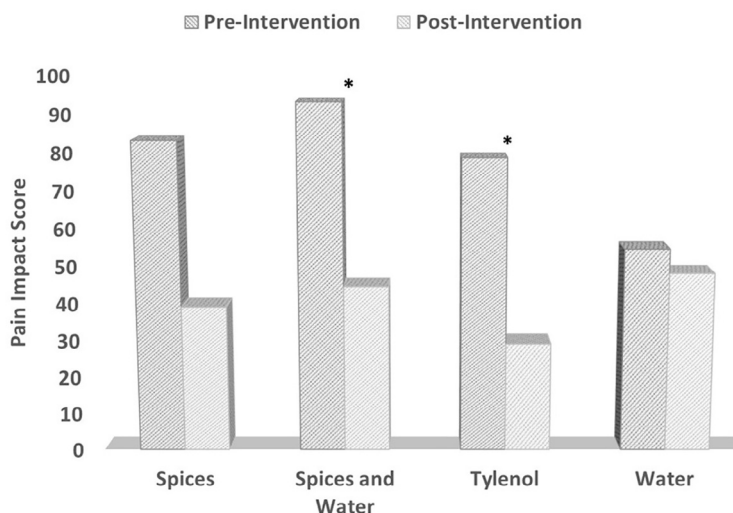


Fig. 2. Change in pain impact score after 2 wk intervention by group. *Significant improvement based on comparison of pre- versus postintervention scores, Wilcoxon signed rank, $P < 0.05$.

believe that it is unlikely that the pain being reported in this population is caused by vitamin D deficiency. Nonetheless, it will be very important for future research to further evaluate dietary intake and nutritional biomarkers in this population.

By itself, water was not found to effectively mitigate pain; however, the group receiving spices and water experienced slightly more improvement than the group that only received spices. Thus, additional benefits may be realized from adequate hydration, in addition to reduced exposure to MSG.

The results presented herein are very limited by the small sample size and lack of blinding in this pilot study. However, these preliminary findings support the hypothesis that MSG may be able to modulate pain response and suggest that a future larger study is feasible and warranted in this population. The participants in this study were recruited in only 2 d via word-of-mouth advertising. This quick recruitment likely reflects the inadequate treatment options currently available for pain in this area. Furthermore, as mentioned earlier, the recipe used to create the alternative spice mix was found to be an appropriate substitute for the Mchuzi mixed spices, suggesting that this recipe could be used for adequate blinding of spices (in addition to blinding of acetaminophen) for a future double-blind placebo-controlled clinical trial.

Conclusions

The results of this preliminary research suggest that dietary contributions to widespread chronic pain should be studied in more depth in Meru, Kenya. Ideally, future research would include a formal prevalence estimate in a large random sample of the community, detailed evaluation of common exposures (including dietary exposures), and further work to conduct a large-scale blinded intervention testing the effects of removing MSG and increasing water intake relative to acetaminophen. Using acetaminophen as a comparison group will elucidate the expected benefit of a low-cost dietary treatment approach relative to what is currently available. If these results hold in a larger research study, this could provide a low-cost dietary treatment option, which could be implemented throughout Kenya, as well as in other developing nations with similar exposures.

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