Rapid Resolution of Chronic Back Pain with Magnesium Glycinate in a Pediatric Patient

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Abstract
A 10-year-old male presented to a pediatric complex chronic pain clinic with debilitating back pain associated with vertebral compression fractures secondary to corticosteroid-induced osteoporosis. The pain failed to respond to routine analgesics and zoledronic acid. Oral magnesium glycinate and topical magnesium/guaifenesin cream were initiated upon presentation to the clinic, and resulted in a rapid and sustained reduction in pain, increased flexibility and improved quality of life. Magnesium is a known N-methyl-D-aspartate receptor antagonist, and should be considered in the management of chronic pain. The roles of glycine and guaifenesin in the management of chronic pain are not well-understood, but may warrant further examination in the context of chronic pain.

Keywords: Chronic pain; Magnesium glycinate; NMDA receptor; Pediatric

Introduction
Chronic pain has been defined as continuous or recurrent pain of sufficient duration and intensity to adversely affect a patient’s level of function or quality of life [1]. There are a number of possible approaches to the pharmacological management of chronic pain, one approach involving the targeted inhibition of the N-methyl-D-aspartate (NMDA) receptor [2]. When activated by repeated or sustained noxious stimuli, NMDA receptors facilitate neuronal influx of calcium, leading to a state of hyper excitation, which then leads to increased response to subsequent stimuli; a phenomenon known as ‘NMDA wind-up’. One feature of NMDA receptors is a magnesium binding site that, when occupied, blocks neuronal influx of calcium, and prevents potentiation of pain signalling [3]. The role of magnesium in the treatment of chronic pain is that of NMDA receptor antagonism like ketamine and dextromethorphan [4], though it exhibits a unique mechanism of action.

The following case report presents a patient who experienced a rapid reduction in pain and sustained improvements in flexibility and functionality upon starting magnesium glycinate therapy.

Case Report
The patient is a 10-year-old male with a complex medical history of uncontrolled asthma with frequent severe exacerbations leading to steroid-induced osteoporosis with vertebral compression fractures of T5-7. He also suffered from gastritis, allergic rhinitis and sinusitis with seasonal exacerbations. Although the patient reported sporadic reports of mild back pain in the spring of 2010, his first significantly painful episode occurred later that summer, after he and his family had spent six continuous hours in the car, during which time he experienced continuously escalating back pain. Once at home, the patient could not sit or lie down without severe pain in his back. Soon after this episode, investigations were done to assess his bone mineral density (BMD), which was determined to be myofascial in origin. His spine MRI was read for two years. After assessment by the chronic pain specialist, his pain illness and zoledronic acid infusions 0.025 mg/kg every six months were prescribed for fear of exacerbating his severe asthma. The patient continued physiotherapy throughout the fall, although his back pain remained debilitating. His sleep also became affected, as he was waking most nights crying in pain. Heat pads and transcutaneous electrical nerve stimulation provided only mild, temporary relief.

After four months of unsuccessful treatments and worsening back pain the patient was referred to the chronic pain clinic as his pain was having a significant impact on his quality of life. At this time his medication regimen consisted of calcium carbonate 750 mg (elemental calcium 300 mg) po twice daily, vitamin D 800 international units po daily, salbutamol 100 mcg 2 puffs as required for asthmatic symptoms, montelukast 5 mg po daily, omalizumab subcutaneous injection twice weekly, hydrocortisone 10 mg po as a stress dose for use during acute illness and zoledronic acid infusions 0.025 mg/kg every six months for two years. After assessment by the chronic pain specialist, his pain was determined to be myofascial in origin. His spine MRI was read...
as normal with no evidence of nerve compression and maintenance of intervertebral disc spaces in the thoracic spine. He was prescribed oral magnesium glycinate 1300 mg/day (elemental magnesium 260 mg/day, glycine 1040 mg/day) in two divided doses (to be increased to the maximum non-cathartic dose), topical magnesium/guaifenesin cream (magnesium chloride (H₂O), 12%, guaifenesin 8%, thiamin HCl 0.4%, pyridoxine HCl 0.4% and vitamin E 1%) to be applied to the painful area three times daily (TID), amitriptyline 10 mg po daily at bedtime, and gabapentin, to be increased up to 300 mg po TID. The patient’s parents felt uncomfortable with the potential adverse effects of amitriptyline and gabapentin, and decided to start only the magnesium glycinate and the topical magnesium/guaifenesin cream. Within 12 hours of his first dose of magnesium glycinate and topical magnesium/guaifenesin cream, the patient was visibly more flexible than he had been in months. The night after starting this regimen, the patient slept soundly for 12 hours, without waking once. His muscle spasms did not resolve immediately, but gradually began to decrease in frequency and severity.

One month later, the patient was taking oral magnesium glycinate 2600 mg/day in two divided doses (elemental magnesium 520 mg/day, glycine 2080 mg/day), applying the topical magnesium/guaifenesin cream TID and still taking no other medications for pain. The patient had significantly regained his flexibility and functionality, and no longer experienced muscle spasms. He was once again able to run up and down the stairs in his house, and wrestle with his brother. The patient’s mother reported that “things are now back to normal”.

Discussion

There is currently no evidence supporting the use of magnesium supplementation in myofascial chronic back pain. However, there is a small body of evidence demonstrating the efficacy of magnesium in the prophylaxis of migraine [5,6] and tension-type headaches [7], and in reducing pain scores in patients with complex regional pain syndrome (CRPS) type 1 [8].

Reduction in migraine headache frequency and severity was demonstrated in pediatric patients by Wang and colleagues [6]. In this placebo-controlled trial, 58 patients supplemented with oral magnesium oxide 9 mg/kg/day in three divided doses (elemental magnesium 5.4 mg/kg/day) for 16 weeks exhibited a significant downward trend in the frequency and severity of migraine headaches. Patients receiving placebo showed no difference in the frequency or severity of migraines. Serum magnesium levels were not monitored in this study. The dose of oral magnesium used in this study was comparable to that of our patient, though the onset of effect was much slower and gradual as compared to our patient’s rapid response.

Another placebo-controlled trial was conducted in 81 adult patients by Peikert and colleagues [5]. In this study, 53% of patients receiving oral tridiamagnesium dicitrate 600 mg/day in a single daily dose (elemental magnesium 590.4 mg/day) for 12 weeks exhibited a 50% reduction in the frequency of migraine headaches from baseline as compared to 34% of patients receiving placebo. In 39% of patients in the treatment group, they experienced greater than 50% reduction in the frequency of migraines from baseline as compared to 22% of patients in the placebo group. Baseline serum magnesium levels were 0.82 mmol/L and 0.86 mmol/L for patients in the treatment and placebo arms respectively, but no follow-up levels were taken at any point during or after the treatment period. The dose of magnesium used in this trial was higher and exhibited a much slower onset of effect than in our patient. Grazzi and colleagues [7] investigated the efficacy of magnesium supplementation in reducing the frequency of tension-type headaches in 45 pediatric patients. Supplementation with oral magnesium pidolate 4500 mg/day in two divided doses (elemental magnesium 366 mg/day) over three months reduced the number of headache days per month by almost 70% from baseline, while the use of adjuvant pain medications decreased 65% from baseline. Serum magnesium levels were not measured in this study. The dose used for magnesium supplementation in their study was comparable to that used by our patient. Again, the time to onset of effect was much slower than reported in our case.

Magnesium therapy has also been investigated for pain reduction in adult patients with CRPS type 1, as done by Collins and colleagues [8]. In that study, 8 patients received magnesium sulphate 70 mg/kg/day (elemental magnesium 710 mg/kg/day) intravenously for 5 days, while two patients received equal-volume of 0.9% NaCl to act as controls. Pain scores were significantly decreased in patients receiving magnesium upon follow-up at 1, 3, 6 and 12 weeks. Quality of life was reported to be significantly improved in patients receiving magnesium upon follow-up at 12 weeks. Serum magnesium levels were above the normal range (0.7-1.0 mmol/L) in 4 patients after the first day of treatment (mean level 1.25 mmol/L), but normalized over the course of the treatment period. The other 4 patients maintained magnesium levels in the normal range throughout the entire treatment period. Although the dose of magnesium used in this trial was much higher than that used in our patient, this study showed comparable time to onset of effect and the same sustained pain relief.

Serum magnesium levels have been correlated with pain levels in patients experiencing headaches. Dhorout Mees and colleagues observed that, in 108 patients with a history of subarachnoid haemorrhage, lower serum magnesium levels were associated with increased headache pain [9]. Lower serum magnesium levels have also been identified in adult and pediatric patients who regularly experience migraines as compared to individuals who do not [10].

The use of magnesium glycinate for supplementation was specifically chosen for our patient because it is absorbed faster, thus resulting in a steeper increase in plasma magnesium levels than magnesium oxide. The bioavailability of magnesium glycinate, however, is no different than that of magnesium oxide [11].

It is possible that the glycine content of magnesium glycinate contributed to our patient’s remarkable response to this therapy as well, although the role of glycine in pain transmission is not well-understood. Glycine receptors (known as glycineₐ receptors) reside directly on the NMDA receptor, that, when bound, activate the NMDA receptor [3]. Conversely, another subset of glycine receptors (known as glycineₐ receptors) have been identified in spinal cord dorsal horn synapses unrelated to NMDA signalling [12]. These glycineₐ have an inhibitory effect on neurotransmission [12], and function much like gamma-aminobutyric acid (GABA) receptors in dampening nociceptive transmission from the periphery to higher areas of the brain [13]. Dysfunction of these inhibitory actions on dorsal horn interneurons is another emerging theory for the pathogenesis of chronic pain [13]. Animal studies have revealed a role for glycine in pain transmission, as decreased glycnergic action has been associated with peripheral inflammation-induced central sensitization [14] and allodynia [15]. Evidence assessing oral glycine supplementation in patients with chronic pain is scarce. Oral glycine supplementation of 100 mg/kg/day for 4 to 5 weeks has been associated with improvements in pain for patients with trigeminal neuralgia [16]. The dose of oral...
glycine used in this study was much higher than that received by our patient. While intrathecal administration of glycine has been associated with decreasing or preventing hyperalgesia in rats, the same has not been effective in reducing pain in humans with chronic regional pain syndrome, type 1 [17]. In 19 adult patients with CRPS, glycine administered intrathecally at a dose of 32 mg/day did not improve pain scores or functionality after 4 weeks of treatment [17].

Our patient’s substantial improvement in pain, flexibility and functionality could also be related to the topical magnesium/guaifenesin cream he started with the magnesium glycinate. Guaifenesin may play a role in chronic pain management through its muscle relaxant action, though this role is not well-defined. Guaifenesin is the active metabolite of the muscle relaxant methocarbamol [18], and has demonstrated centrally-mediated skeletal muscle relaxation in humans [19], and is routinely used for skeletal muscle relaxation and anaesthesia in animals [20]. A double-blind, placebo controlled trial was carried out by Bennett and colleagues [21], which evaluated the effect of oral guaifenesin 1200 mg/day in two divided doses for one year in patients with fibromyalgia. Guaifenesin did not improve pain scores or quality of life indices. Guaifenesin also demonstrated no significant benefit when studied in female patients with dysmenorrhea. Patients receiving oral guaifenesin 2400 mg/day for two days during each cycle demonstrated some reduction in abdominal pain, severity of headaches and back pain, although none of these reductions were statistically significant from placebo.

Conclusion

After initiating oral magnesium glycinate and topical magnesium/guaifenesin cream, our patient experienced rapid reduction in his myofascial pain, with sustained improvements in flexibility and functionality without the use of any other pain medications. Targeting NMDA receptor blockade peripherally and centrally via oral and topical magnesium supplementation should be considered by clinicians for patients with chronic myofascial pain, as the risk of very mild side effects is undoubtedly offset by its enormous potential. However, due to the multitude of mechanisms of pain pathogenesis that may be at play, NMDA receptor blockade may not be sufficient as monotherapy in all patients. Larger scale studies are certainly needed to better define the role and guide dosing of systemic and topical magnesium in the treatment of various chronic pain syndromes. The role of glycinate and guaifenesin in the management of chronic pain states also needs to be evaluated further.

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References