

Adjuvant Acupuncture for Youth with Sickle Cell Pain: A Proof of Concept Study

Devika Bhushan, MD,¹ Kim Conner, RPh, MAc,² Jonathan M. Ellen, MD,³ and Erica M.S. Sibinga, MD, MHS¹

ABSTRACT

Background: Sickle cell disease (SCD) is a common hemoglobinopathy characterized by debilitating vaso-occlusive crises (VOCs) that can require hospitalization for treatment. Despite optimization of multimodal allopathic inpatient treatment, pain burden remains high. Narcotics, the mainstay of therapy, incur adverse side effects, tolerance, and the potential for addiction. Adjunctive treatments are sorely needed and patients' families have reported openness to complementary modalities to fill this need.

Objectives: The aim of this pilot study was to assess initial feasibility and acceptability of inpatient adjuvant acupuncture and its potential impact on pediatric VOC-related pain.

Materials and Methods: This prospective, single-center study at an urban children's center sought to recruit 13–17-year-old patients with either HbSS (2 mutated sickle hemoglobin copies, each denoted HbS, are inherited, one from each parent) or HbSC (1 sickle hemoglobin variant, or HbS, is inherited from one parent and another hemoglobin variant, HbC, from the other) disease being admitted for VOC management. The patients were recruited within 24 hours of admission. Upon enrollment, a trained acupuncturist evaluated and treated patients according to Worsley Classical Five-Element Acupuncture daily while they required patient-controlled analgesia pumps.

Results: Over a 9-month period in 2004, ~40 patients were identified for possible participation. Of 13 patients interested in the study and eligible, 2 (5% of total; 15% of eligible and interested) ultimately completed it. Both patients conveyed openness to acupuncture, achieved some pain reduction and/or relaxation through it, and indicated that they would want repeated treatments. Care providers were also impressed favorably with the pain attenuation and functional gains achieved.

Conclusions: In the total sample, there were some barriers to feasibility and acceptability. However, the 2 patients who received adjuvant acupuncture treatment, their families, and providers alike perceived clinical benefit. Adjuvant inpatient acupuncture for pediatric SCD VOC pain control merits further study.

Key Words: Acupuncture, Anemia, Sickle Cell Disease, Vaso-Occlusive Crisis, Acute Pain Management, Pediatric

INTRODUCTION

SICKLE CELL DISEASE (SCD) is a hemoglobinopathy affecting >50,000 Americans. It is caused by a recessively inherited single-base mutation in the beta-globin gene, which results in abnormal membrane properties and consequent periodic sickling of red blood cells, resulting in

chronic, ongoing hemolysis that can be accelerated under certain conditions. The combination of sickling, endothelial activation, and vasoconstriction sometimes occludes blood flow altogether, leading to downstream tissue hypoxia, damage, and possible infarction—a cascade that can be set into motion in any part of the body. Inherent to this process, known as a vaso-occlusive crisis (VOC), is debilitating acute

¹Department of Pediatrics, and ²Department of Pediatric Pharmacy, Johns Hopkins University School of Medicine, Baltimore, MD.

³Department of Pediatrics, All Children's Hospital, Johns Hopkins Medicine, St. Petersburg, FL.

pain, at times requiring inpatient management. Other potential sequelae of the disease include acute chest syndrome, cerebrovascular accidents, functional asplenia with susceptibility to serious bacterial infections, renal dysfunction, avascular necrosis, and premature death.^{1,2}

Recurrent VOC-related pain is a hallmark symptom of SCD, representing the single most common reason for emergency department visits and hospitalizations for patients with SCD.³ Increased frequency of such episodes correlated with earlier death in a prospective study examining pain-related outcomes in 3578 adult patients with SCD.⁴

Current pediatric VOC pain management relies on a multimodal approach—cognitive and mind–body techniques (such as biofeedback and child life interventions); intravenous (IV) fluids; other nonpharmacologic approaches (heat or ice application; electrostimulation, and physical therapy); and pharmacologic therapies, including nonsteroidal anti-inflammatory drugs and opioids, often using IV patient-controlled analgesia (PCA) pumps.^{5,6} Despite optimization of these methodologies, studies show that inpatient VOC pain control in pediatrics has been suboptimal. In one retrospective review, among 59 inpatients being treated for SCD VOCs at an urban pediatric hospital (mean age: 11.5 years), average pain scores remained in the moderate-to-severe range, defined as $>5/10$, throughout the majority of the hospitalization (mean length of stay [LOS]: 4.6 ± 2.7 days).⁶

Although they remain the most heavily relied on and potent conventional avenue for pain reduction, opioids have several common side effects, including itching, sedation, depressed respiratory effort, nausea, vomiting, and constipation. The suppression of respiratory drive is particularly problematic in the context of a VOC, because an opioid can predispose a patient toward developing the potentially life-threatening acute chest syndrome.⁵ In addition, the potential for tolerance, dependence, and addiction with frequent use often complicates and limits the future efficacy of this class of medications. Thus, particularly for patients who are the most ill, those “who remain in the hospital for longer periods of time and have persistently elevated pain scores, opiates may not be a sufficient analgesic option,” according to Zempsky et al.⁶ The long average LOS and persistently elevated pain scores from the Zempsky et al. study attest to these significant treatment challenges.⁶

Because the current treatment model is constrained in these ways, the study team became interested in exploring the adjunctive potential of acupuncture for inpatient treatment of pediatric VOC pain. In a survey of 227 adults with SCD, 92% (208) had used complementary and alternative medicine (CAM) therapies, led by prayer (61%), relaxation techniques (44%), and massage (35%).⁷ In a similar survey of 57 parents of pediatric SCD patients, 83% of respondents felt that CAM therapies could be beneficial for adjunctive management. More than half (54%) of families reported current use of CAM therapies, including bioenergetics (42%, consisting of prayer, spiritual, and energy healing),

lifestyle and mind–body techniques (28%, including relaxation techniques, exercise, imagery, and diet modification), biochemical interventions (12%, herbal, vitamin, and folk remedies), and massage or chiropractic manipulation (5%). Of note, severity of SCD, as indexed in part by VOC frequency and rates of hospitalization, was positively correlated with CAM use.⁸

Acupuncture has been used in China for thousands of years and, over the last several decades, has gained traction in Europe and the Americas. Many mechanisms have been posited for its effects, including stimulation of neurotransmitter release in key central nervous system regions, such as beta-endorphins, enkephalins, and serotonin; mediation of autonomic nervous system signals; and nitric oxide generation and increased local blood flow. According to classical theory, acupuncture is used to correct the perceived imbalances in energy or Qi that are believed to give rise to a patient’s disease symptoms; achieving energetic balance and harmony in the opposing life forces of Yin and Yang is thought to mediate a return to health.^{9,10}

Acupuncture has previously been found to be beneficial as an adjunct for addressing a number of chronic and acute pain conditions, and as a primary treatment for postoperative and chemotherapy-induced nausea and emesis in adults.¹¹ In pediatrics, a recent meta-analysis comprising 24 reviews showed that this modality also has promise for adjunctive treatment for aspects of cerebral palsy, nocturnal enuresis, tic disorders, amblyopia, and pain, although further studies are needed to establish this definitively.¹⁰ Very few significant adverse events (AEs) are routinely reported, and those that occur are thought to result from substandard practices, although AEs are thought to be inconsistently reported in the literature.¹² Minor AEs that have been reported include pain, bruising, bleeding, and worsening of symptoms, and, overall, occurred in studies at a rate of 11.8% (95% confidence interval: 10.1%–13.5%).¹²

There are only a few studies on acupuncture treatment for sickle cell VOC pain, and almost all have focused on adults. A retrospective review of 24 adults who received acupuncture for adjunctive VOC pain control showed a significant reduction in pain in the inpatient setting (on average, by 2.1 points) and 75% of the time in the outpatient cases.¹³ A 1979 study conducted on 10 adult inpatients with 16 VOC pain episodes used both standard and sham (5 cm from standard points) needling points simultaneously in all participants. Pain relief was achieved in 15 of 16 cases, regardless of the use of standard or sham needling technique. However, given that the effect of acupuncture is now thought to be systemic, this study design makes it difficult to interpret the etiology for the clinical benefit.¹⁴

On the pediatric front, a case series of 5 adolescent patients in Nigeria who received acupuncture as the sole treatment for VOCs had immediate improvements in pain control, in addition to mean higher hemoglobin values (by 21.1%, nonsignificant) after acupuncture in the acute setting

and had improved physical and mental well-being over a 1–2-year follow-up period.¹⁵

Based on this limited body of literature and the pressing need for additional strategies for VOC acute pain management in pediatric SCD, the study team pursued a pilot project examining the role of adjuvant acupuncture in the inpatient setting. This was a prospective, single-center study at an urban children's center. The research was intended to assess the initial feasibility and acceptability of this modality for patients, families, and providers, as well as to evaluate its potential impact on acute VOC pain.

MATERIALS AND METHODS

Participants were 13–17-year-old adolescents with SCD (either genotype HbSS or HbSC*) being admitted for VOC pain management to the inpatient pediatric hematology service at the Johns Hopkins Hospital's Children's Center in Baltimore, MD. The study was approved by the Johns Hopkins School of Medicine's institutional review board. Within 24 hours of admission, eligible patients were invited by the clinical team to learn about the study. Exclusion criteria included inability to contact a parent for consent, pregnancy, and pain unrelated to VOC.

Following parental consent and patient assent, the acupuncturist (K.C.) evaluated each patient and performed the initial treatment. Acupuncture evaluation and treatment was then repeated daily while each patient required a PCA pump (IV morphine or hydromorphone) as part of the pain management regimen.

Treatment was performed by an experienced acupuncturist who is licensed in the state of Maryland and trained in the principles of Worsley Classical Five-Element Acupuncture.¹⁶ The initial evaluation included a comprehensive medical and psychosocial history, including identification of symptom patterns, alleviating or aggravating lifestyle factors, and the individual's bioenergetic attributes. A physical examination included classical pulse reading at the bilateral radial pulse points, both prior to and after each session. Based on determination of the individual's bioenergetic identity, known as the Causative Factor, and any identified regions of imbalanced or blocked Qi (energy), the acupuncturist then selected precise anatomical locations along the appropriate meridians for needle placement. This was done in an attempt to rebalance the patient's Qi and thereby achieve diminution of the VOC pain. The points chosen did not necessarily correlate specifically with the VOC pain locations identified by the patients, but were determined by the energetic acupuncture diagnostic system.

*An HbSS genotype denotes that 2 identical sickle hemoglobin variants, or HbS, were inherited from each parent. HbSC signifies that 1 sickle hemoglobin variant, or HgS, is inherited from one parent and another abnormal hemoglobin variant, HbC, is inherited from the other.¹

Needles were inserted to the depth specified by classical teaching in *fen* (1/10 of distance between 1st and 2nd joint of middle finger on left hand for men and right for women) units for the selected points.

For both patients, initial treatment included needling of the back *Shu* points, believed to affect Yin organ energies, with the even technique (with no lateral or rotational motion on insertion). Needles were inserted fairly superficially at these points (~1 mm) and left in place for 10–25 minutes or as tolerated. Initial and subsequent treatments also targeted “command” points, which are the distal components along each of the 12 meridians, located in the regions between the elbows and fingertips and knees to toes. Treatment at these distal points is felt to affect the energy flowing along the entire meridian powerfully, including that associated with the meridian's corresponding internal organs, enabling improvement in the patient's overall energetic balance.

Each needling site could be accessed in one of two ways, to either achieve tonification (stimulation and strengthening of Qi) or sedation (dispersion or draining of overabundant Qi). Tonification technique is characterized by quick needle insertion, clockwise rotation, and needle removal, followed by covering the point. Sedation technique refers to slow needle insertion, counterclockwise rotation, leaving the needle in place for up to a few minutes, and needle removal without covering the point. In VOC pain, energetic deficits are anticipated, and, therefore, tonification is likely to be the technique needed in most cases.

Prior to needling, the acupuncturist would have ideally utilized moxibustion at the treatment points with *Artemisia vulgaris*, or mugwort, which is usually placed on top of the skin at the required points, lit, allowed to burn until perceived as heat by the patient, and then removed. This process transmits thermal energy to the site and is thought to activate or stimulate the bioenergy associated with these acupuncture points.¹⁶ However, because of hospital policy prohibiting lit objects indoors, this was not possible during this study.

Following each acupuncture session, the acupuncturist then reassessed each individual's bioenergetic state by reexamination of the pulses, given that a successful session should produce a harmonizing of the volume and other pulse qualities that were deemed to be previously imbalanced or lacking.

The acupuncture needles used were size 37, gauge, 15–30-mm long, sterile, individually wrapped, surgical stainless steel. They were disposed of in accordance with Johns Hopkins Hospital's (Baltimore, MD) sharps policy at the time of the study.

In addition, physicians, the patients who underwent the treatments, and parents completed a structured questionnaire regarding the impact of acupuncture on pain management, need for pain medications, perceived side effects of these medications, overall coping, and ease of integration of acupuncture into their care. These items were graded on a Likert-type scale, ranging from “better than expected” (1) to “as expected” (3) to “worse than expected” (5). They

were all also asked if conventional clinical activities or procedures were disrupted in any way by the study's protocol; and if they felt that their current hospitalizations were different from prior ones and, if so, how. Additional space was provided for any other comments they might have had.

RESULTS

Approximately 40 pediatric patients with SCD were hospitalized for treatment of VOC-related pain during the 9-month study recruitment period in 2004 and were deemed potentially eligible by the inpatient pediatric hematology team. In total, 15 patients were interested in learning about the study. Two of these 15 patients were excluded, 1 for active pregnancy and the other for not having SCD-related pain. Three others were unable to gain access to acupuncture treatment either because of being discharged earlier than anticipated or because the acupuncturist was unavailable. Of the 10 remaining patients, 3 were interested in hearing about the study, and 2 (5% of total screened; 15% of those both interested and eligible) ultimately provided parental consent and participant assent and were enrolled in the study.

T.B. was a 17-year-old African-American female with HbSS disease who typically had many hospitalizations per year for VOC-related pain, despite optimized allopathic therapy and outpatient follow-up. After being admitted for management of right-arm pain, she underwent acupuncture four times (on successive days), with initial treatment of the *Yin Shu* points, followed by treatment of the Command points along the Stomach and Spleen meridians.

"I really like what [the acupuncturist] did for my pain," she reported. "I think other people should try acupuncture for the sickle pain." Her mother commented that the acupuncture "was a start with help[ing] my child with pain," adding that "as a parent[,] I would really like for my child to keep receiving acupuncture." The attending hematologist, who knew T.B. well from her previous hospitalizations, commented that "her pain appeared to resolve more quickly" during this admission than during previous admissions. The attending physician recounted that T.B. communicated a "sense of calm or feeling 'free,'" especially after the initial treatment. He commented that she also "seemed less passive in her care, more positive" and reported to him a "loss of [her previous] 'bad attitude' towards [*sic*] pain." He also said: "She felt positively about the whole experience, would do it again on subsequent admissions, and recommend it to others." The pediatric intern caring for this patient commented that this exercise represented a "beneficial shift from a purely biomedical evaluation of pain."

D.B. was a 14-year-old African-American male with severely symptomatic HbSS disease also requiring many hospitalizations per year. He was admitted during the study period for back and chest pain. He received acupuncture three times—again, on successive days. He described the

experience of getting acupuncture as "relaxing"; he reported that the needles were not as painful as he had anticipated. He said that he would also recommend acupuncture to others with VOC pain. The third-year resident caring for him noted that, not only was D.B. "actually quite receptive [to] acupuncture," but he also seemed to experience "overall decrease[d] pain/more ambulation after [the] procedure." After acupuncture sessions, D.B. was noted to be able to rise from his usual recumbent position in the hospital bed and, in fact, could play pool for up to an hour after treatments.

Quantitative data on pain management, need for and side effects of medications, overall coping, and overall ease of integration of acupuncture were also collected, but interpretation of results was limited by the small sample size, so these data were not able to be analyzed meaningfully and are not presented here.

In speaking about the challenges posed by the inpatient setting and its incumbent procedures, the acupuncturist commented that the location of the peripheral IV and associated dressings (right arm initially and left arm on a subsequent encounter) interfered with his ability to perform pulse analysis adequately. There was also restricted space in the inpatient room that affected ease of manipulation, and the various alarms in the room disrupted the flow of treatment. Despite these limitations, treatments were completed successfully with some maneuvering.

DISCUSSION

Only a small proportion of patients (5% of all eligible; 15% of those interested and eligible) were willing and able to receive acupuncture treatments through the study. Acupuncture was, however, demonstrated to be an agreeable modality for the 2 patients who were enrolled. Although this was a small sampling, for these 2 patients, the series of acupuncture treatments were thought to be beneficial for pain management and in enabling functional gains during the hospitalizations. These benefits were not only noted by the patients and their families, but also by their medical care providers.

Limitations of this initial study included the small sample size; lack of geographic variability in sampling; the availability of only 1 acupuncturist; and limited data, including data on pain scores (before and after each treatment session) and posthospitalization follow-up metrics. Also, these data are now more than 10 years old; given the pilot nature of the study and the small number of participants, the results were initially assumed to be of limited interest. However, as more time passed, it has become clear that these findings are indeed a contribution to the scant literature on acupuncture integrated into pediatric care. Additional studies are needed to determine whether an overall improvement in pain treatment, reduction in hospital LOS, number/frequency of hospitalizations, and time to next VOC, could be affected meaningfully by the use

of acupuncture in the acute setting. In addition, the efficacy of ongoing acupuncture treatments in a longer-term fashion for maintenance and prevention of VOC recurrence was also outside the scope of this initial study. If any of these outcomes could be demonstrated, adjuvant acupuncture could be of substantial benefit for patients with VOC pain.

The role of the outpatient primary hematologist or pediatrician in discussing, coordinating, and assessing the efficacy of the integration of this modality in ongoing symptom management would be important to promote. Of note, the pediatric SCD survey on CAM modalities revealed that although 70%–74% of parents expressed a desire to discuss CAM modalities with their pediatricians or hematologists, only about a third perceived that their providers would be interested in these discussions. In addition, although no families had yet used acupuncture for their children with SCD, 41% of parents reported a willingness to try acupuncture if it were thought to be helpful, which attests to a wider potential acceptability pending further demonstrable results and provider-initiated discussion of these results with families.⁸ Future research should be performed to explore patient attitudes toward—and barriers to—acceptability of this modality for adjunctive pain control for VOCs.

While this pilot study demonstrated an ability to integrate this modality into a standard inpatient setting, some modifications might optimize treatment further. Conventional inpatient procedures, such as the common placement of peripheral IVs in the wrists, inability to administer moxibustion in many hospitals, and physical constraints of the inpatient room, including limited space and frequent alarms, could be better tailored to facilitate acupuncture, including enabling pulse diagnosis more reliably and providing a logistically viable physical space to access needling points with ease.

CONCLUSIONS

This study demonstrated both barriers to broad-based feasibility and acceptability of acupuncture as reflected in the general unwillingness to participate in the sample and simultaneously, among the 2 patients who participated, a receptiveness to and overall perceived benefit for adjunctive inpatient VOC pain management. Given the substantial need for additional treatment strategies in this population, further research into adjuvant acupuncture for the treatment of VOC pain is warranted.

ACKNOWLEDGMENTS

The authors would like to acknowledge the willing participation of the study participants and their families, as well as the encouragement and support of Drs. James F. Casella, MD (Rainey Professor and Chief, Pediatric

Hematology, Johns Hopkins School of Medicine) and George J. Dover, MD (Professor of Pediatrics, Johns Hopkins School of Medicine), and the rest of the Johns Hopkins Pediatric Hematology team.

AUTHOR DISCLOSURE STATEMENT

No author has any conflicts of interest relevant to the work discussed here. No outside funding was provided for this project.

REFERENCES

- Ashley-Koch A, Yang Q, Olney RS. Sickle hemoglobin (HbS) allele and sickle cell disease: A HuGE review. *Am J Epidemiol.* 2000;151(9):839–845.
- Wright J, Ahmedzai SH. The management of painful crisis in sickle cell disease. *Curr Opin Support Palliat Care.* 2010;4(2):97–106.
- Ellison AM, Shaw K. Management of vasoocclusive pain events in sickle cell disease. *Pediatr Emerg Care.* 2007;23(11):832–838;quiz:838–841.
- Platt OS, Thorington BD, Brambilla DJ, Milner PF, Rosse WF, Vichinsky E, Kinney TR. Pain in sickle cell disease: Rates and risk factors. *N Engl J Med.* 1991;325(1):11–16.
- Yaster M, Kost-Byerly S, Maxwell LG. The management of pain in sickle cell disease. *Pediatr Clin North Am.* 2000;47(3):699–710.
- Zempsky WT, Loiselle KA, McKay K, Blake GL, Hagstrom JN, Schechter NL, Kain ZN. Retrospective evaluation of pain assessment and treatment for acute vasoocclusive episodes in children with sickle cell disease. *Pediatr Blood Cancer.* 2008;51(2):265–268.
- Majumdar S, Thompson W, Ahmad N, Gordon C, Addison C. The use and effectiveness of complementary and alternative medicine for pain in sickle cell anemia. *Complement Ther Clin Pract.* 2013;19(4):184–187.
- Sibinga EM, Shindell DL, Casella JF, Duggan AK, Wilson MH. Pediatric patients with sickle cell disease: Use of complementary and alternative therapies. *J Altern Complement Med.* 2006;12(3):291–298.
- Jindal V, Ge A, Mansky PJ. Safety and efficacy of acupuncture in children: A review of the evidence. *J Pediatr Hematol Oncol.* 2008;30(6):431–442.
- Yang C, Hao Z, Zhang LL, Guo Q. Efficacy and safety of acupuncture in children: An overview of systematic reviews. *Pediatr Res.* 2015;78(2):112–119.
- National Institutes of Health (NIH). Acupuncture. *NIH Consensus Statement.* 1997;15(5):1–34.
- Adams D, Cheng F, Jou H, Aung S, Yasui Y, Vohra S. The safety of pediatric acupuncture: A systematic review. *Pediatrics.* 2011;128(6):e1575–e1587.
- Lu K, Cheng MC, Ge X, Berger A, Xu D, Kato GJ, Minniti CP. A retrospective review of acupuncture use for the treatment of pain in sickle cell disease patients: Descriptive analysis from a single institution. *Clin J Pain.* 2014;30(9):825–830.

14. Co LL, Schmitz TH, Havdala H, Reyes A, Westerman MP. Acupuncture: An evaluation in the painful crises of sickle cell anaemia. *Pain*. 1979;7(2):181–185.
15. Sodipo J. Acupuncture and blood studies in sickle-cell anaemia. *Am J Chin Med*. 1993;21(1):85–89.
16. Worsley Institute. Worsley Five Element Acupuncture. Online document at: <https://worsleyinstitute.com/worsley-five-element-acupuncture> Accessed June 15, 2015.

Address correspondence to:

Devika Bhushan, MD

Department of Pediatrics

Charlotte R. Bloomberg Children's Center

Johns Hopkins University School of Medicine

1800 Orleans Street

Baltimore, MD 21287

E-mail: dbhusha1@jhmi.edu