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BRIEF REPORT

Daily Associations between Child and Parent Psychological Factors and Home Opioid Use in Youth with Sickle Cell Disease

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Abstract

Background Opioid analgesics are frequently used in the home setting to manage episodic pain in youth with sickle cell disease (SCD). Given the risk of adverse side effects, including constipation and sedation, understanding factors associated with at-home opioid use is important for maximizing pain relief while minimizing negative side effects.

Purpose The present study aimed to evaluate the relationship between individual psychological factors (pain catastrophizing and negative affect), caregiver psychological factors (catastrophizing about child's pain and caregiver negative affect), and home opioid use in youth with SCD.

Methods Youth with SCD (n = 32) and a caregiver (n = 28) recruited during a routine outpatient hematology visit completed electronic 14 day diaries assessing pain, opioid use, and psychological factors.

Results Approximately 28% of youth (n = 9) reported pain ≥50% of diary days and a third of youth (n = 11, 34%) used opioid analgesics at least one of the diary days. The number of days opioid analgesics were used ranged from 0 to 7 (50% of diary days). Results from generalized linear mixed models indicated greater child negative affect accounted for increased odds of opioid use on a given day when accounting for pain intensity. Greater caregiver catastrophizing about children's pain was also associated with increased odds of children's opioid use.

Conclusions Child and parent psychological factors relate to child opioid use at home for SCD-related pain. Future research is warranted in larger samples to identify targets for interventions to enhance pain management while reducing opioid-related risk and side effects.

Keywords Pain • Opioid • Hematology • Sickle cell disease • Pediatrics • Psychology

Approximately half of youth with sickle cell disease (SCD) use opioid analgesics in the home setting to manage pain [1]. Although opioid analgesics are often indicated for severe acute pain management [2, 3], their appropriateness for managing frequent pain associated with pediatric SCD is less clear given the risk of adverse side effects, including constipation and sedation [4]. Understanding factors associated with at-home opioid use is important for maximizing pain relief while minimizing negative side effects.

Pain catastrophizing, which refers to the extent to which one magnifies or fixates on the threat of pain, is associated with greater use of opioids in the home setting for adults with SCD and predicts opioid use even on low pain days [5]. Based on the fear-avoidance model of pain [6], individuals who catastrophize more about pain are more likely to engage in frequent attempts to avoid painful experiences and engage in behaviors (e.g., sedentary behavior, long time in bed) that maintain pain. Consistent with the social communication model of pain, in the case of children, displaying significant pain

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behaviors and catastrophizing about pain could prompt caregivers to offer children opioid medication to reduce pain and associated pain behaviors [7]. In fact, parents' own catastrophizing about their child's pain is associated with greater child functional impairment and may influence decision-making regarding opioid medication use at home [8]. Thus, both child and parent catastrophizing about children's pain represent potentially modifiable factors that may influence the frequency of opioid use at home.

Child and parent negative affect may also contribute to home opioid use for SCD pain. Higher levels of negative affect have been associated with less pain relief for individuals using opioid analgesics [9]. High negative affect may further contribute to opioid "cravings" and increased risk for misuse [10, 11]. A daily diary of adolescents with SCD found increases in negative affect and decreases in positive affect predicted greater pain and health care utilization [12]. Similarly, daily diary studies in youth with SCD have found negative and positive affect to be important predictors of pain and pain-related outcomes such as sleep [12, 13]. Although prior diary studies have not evaluated parent negative affect, cross-sectional studies suggest that parent stress and negative affect relate to children's own negative affect and pain severity [14–16]. No studies to date have evaluated both child and caregiver psychological factors as predictors of home opioid use in youth with SCD.

The present study evaluated the relationship between child individual psychological factors (pain catastrophizing and negative affect), caregiver psychological factors (catastrophizing about child's pain and caregiver negative affect), and opioid use in youth with SCD using a child and caregiver electronic 14 day diary. We hypothesized that greater child pain catastrophizing and negative affect on a given day would be associated with higher odds of taking an opioid medication when accounting for child pain intensity. Further, we hypothesized that greater caregiver catastrophizing about child's pain and caregiver negative affect would be associated with higher odds of the child taking an opioid medication.

Methods

Sixty-five African-American youth with SCD (ages 10–18 years; hemoglobin SS, SC, and SB+ thalassemia) and a caregiver were approached regarding this study between February 2017 and December 2017 during a routine hematology visit. Of those approached, 40 dyads (61%) provided informed consent and assent and were enrolled in the study. Twelve (18%) dyads declined participation and 13 dyads (20%) indicated they were willing to participate but did not have time currently. Inclusion criteria included: age 10–18 years, diagnosis of SCD, ability to complete online diaries through mobile phone or computer, and a parent or guardian who was willing to participate in the study and able to complete questionnaires. Enrolled dyads received daily prompts via text message or email each evening at 7 PM for 14 days to complete a diary through REDCap [17]. All procedures were approved by the University of Mississippi Medical Center Institutional Review Board.

Upon enrollment, dyads completed a questionnaire battery that collected demographics, medical, and pain information. The Pain Questionnaire assessed average pain frequency and number of pain locations over the past 3 months [18]. Daily diary items for youth were rated on a 0–100 scale [1]: pain intensity—"Rate your average pain intensity today" [2], one aspect of pain catastrophizing (rumination)—"Today, I could not keep pain out of my mind," and [3] negative affect—"To what extent did you feel negative emotions today? (e.g., anger, sadness, anxiety)." Caregivers completed demographic forms and completed daily diaries with an identical negative affect item and modified pain catastrophizing item (i.e., "my child's pain"). The pain intensity item used the anchors "No Pain at All" to "Worst Pain Imaginable," while the other items used the anchors "Not at All" to "All the Time." The pain catastrophizing item was chosen from the Pain Catastrophizing Scale [19, 20], which had a 0.67-item total correlation in this sample of youth and parallels the rumination item used by Finan et al. [5]. Negative affect descriptors were based on common dimensions assessed by standardized measures. Daily diary items were transformed to a 0–10 scale for statistical analyses to aid in interpretation. Youth also indicated whether or not they took prescription opioids each day by choosing medication names from a list of common opioid medications.

Diary Completion and Analyses

Of the 40 dyads enrolled, 7 youth (17%) had >65% missing diary days and one child was hospitalized during the course of the daily diary period, and were excluded from analyses. Of these 32 youth, 4 had caregivers (12%) with >65% missing diary days and were excluded from caregiver analyses. Youth who completed the study and those excluded did not significantly differ on age, gender, or SCD type ($ps > .05$). Thus, data were considered missing at random and handled with maximum likelihood estimation [21]. The final sample included 32 youth and 28 caregivers.

To evaluate daily associations between psychological factors and opioid use over the 14 day diary, generalized linear mixed models (GLMM) fit by maximum

likelihood estimation with a binomial distribution were estimated with the lme4 package in R 3.4 [22]. The data met the core assumptions for GLMM analyses with a binomial distribution including binary nature of dependent variable and little multicollinearity between independent variables. GLMM analyses were modeled with 14 days nested within 32 child and 28 caregiver participants. Data were available for 373/448 diary assessments (83%) for the child model and 316/392 diary assessments (80%) for the caregiver model. On average, children completed 11.88 diary days [standard deviation (SD) = 2.37, range: 5–14] and parents completed 12.57 diary days (SD = 1.26, range: 9–14). Two GLMM models were estimated with opioid use today (no/yes) as the dependent variable. Models initially tested youth age as a potential covariate, which was excluded from final models due to lack of association with the dependent variables. The first model contained child-reported factors (pain intensity, pain catastrophizing, and negative affect). The equation for the first model is listed below.

$$\begin{aligned}\text{logit}(\text{child opioid use})_{ij} = {} & \beta_{0j} + \beta_{1j}(\text{child pain intensity})_{ij} \\ & + \beta_{2j}(\text{child negative affect})_{ij} \\ & + \beta_{3j}(\text{child pain catastrophizing})_{ij} \\ & + \beta_{4j}\,(\text{day})_{ij}\end{aligned}$$

The second model contained caregiver-reported factors (catastrophizing about children's pain and caregiver negative affect). The equation for the second model is listed below.

$$\begin{aligned}\text{logit}(\text{child opioid use})_{ij} = {} & \beta_{0j} + \beta_{1j}(\text{caregiver catastrophizing} \\ & \text{about childrens pain})_{ij} \\ & + \beta_{2j}(\text{caregiver negative affect})_{ij} \\ & + \beta_{3j}(\text{day})_{ij}\end{aligned}$$

Post-hoc power analyses using the two-sided ratio formula of true parameter value to standard error revealed that the available 373 study days provided greater than 0.80 power for the primary child multilevel modeling analyses, given the average 12 Level 1 observation days per child (17% missing diary days) and 3 Level 1 predictors.

Results

Youth were non-Hispanic Black (100%), 53% male, with a mean age of 13.96 years (SD = 2.19, range: 10.05–17.52; Table 1). Caregivers were predominately mothers (82%). Significant variability was observed in children's pain over the 14 day diary. Approximately 28% of youth (n = 9) reported pain ≥50% of diary days; 44% (n = 14) reported pain between 1 and 7 days; and 28% (n = 9) did not report pain over the diary period. Approximately a third of youth (n = 11, 34%) used opioid analgesics at least one of the diary days. The number of days opioid analgesics were used ranged from 0 to 7 (50% of diary days). The most commonly reported opioid analgesic was acetaminophen/hydrocodone (Norco, Vicodin).

Table 1 Demographic characteristics

Child characteristics	n = 32
Age, *M (SD)*	13.96 (2.19)
Male *n* (%)	17 (53)
SCD type	
Hemoglobin SS *n (%)*	26 (81)
Hemoglobin SC *n (%)*	5 (16)
Hemoglobin SB+ thalassemia *n (%)*	1 (3)
Hydroxyurea *n (%)*	17 (53)
Pain frequency (past 3 months) *n (%)*	
None	7 (21.88)
~1× per week	7 (21.88)
2–3× per week	10 (31.25)
3–6× per week	3 (9.38)
Daily	5 (15.63)
Number of pain locations, (0–7), *M (SD)*	1.64 (1.65)
Opioid use, no. of diary days, (0–14), *M (SD)*	1.32 (2.18)
Caregiver characteristics	n = 28
Relation to child, *n (%)*	
Mother	23 (82)
Father	3 (11)
Grandparent	2 (7)
Relationship status, *n (%)*	
Single	14 (50)
Married or partnered	10 (36)
Separated, divorced, or widowed	3 (11)
Annual income, *n* (%)	
< $10 000	9 (32)
$10 000–$19 000	3 (11)
$20 000–$29 000	4 (14)
$30 000–$39 000	4 (14)
$40 000–$49 000	5 (18)
>$50 000	2 (7)

M mean; *SCD* sickle cell disease; *SD* standard deviation.

Table 2 presents results from GLMM analyses. As hypothesized, controlling for daily pain intensity, daily child negative affect was associated with increased likelihood of taking an opioid. Specifically, a 1 unit increase in negative affect was associated with 21% increased likelihood of taking an opioid. Pain catastrophizing did not reach significance in the model. For the caregiver model, daily catastrophizing about children's pain was associated with increased odds of the child taking an opioid.

Table 2 Results from GLMM analyses modeling daily associations between home opioid use and psychological factors in youth with SCD

Variable	$\hat{\beta}$	*SE*	*z*	*p*	OR	95% CI
Model 1—child daily diary variables						
Intercept	−3.779	0.778	−4.856	<.001		
Day	−0.048	0.064	−0.760	.447		
Pain intensity	0.387	0.092	4.224	<.001	1.473	1.231–1.763
Pain catastrophizing	0.146	0.086	1.705	.088	1.157	0.978–1.369
Negative affect	0.193	0.096	2.001	.045	1.213	1.004–1.465
Model 2—caregiver daily diary variables						
Intercept	−3.863	0.766	−5.040	<.001		
Day	−0.048	0.057	−0.840	.401		
Catastrophizing about child's pain	0.120	0.095	2.003	.045	1.209	1.004–1.455
Caregiver negative affect	0.196	0.105	1.865	.062	1.216	0.990–1.493

Caregiver diary variables were run in separate models from child variables in order to reduce cross-informant bias. Analyses of the subset of youth (n = 11) who took an opioid at least 1 day during the diary period yielded similar results.

CI confidence interval; *GLMM* generalized linear mixed model; *OR* odds ratio; *SCD* sickle cell disease; *SE* standard error.

Specifically, a 1 unit increase in catastrophizing about their child's pain was associated with 21% increased likelihood of the child taking an opioid. Caregiver negative affect trended toward significance in the model (p = .062,). Follow-up analyses evaluated models among youth who took an opioid at least 1 day during the 14 day diary period (n = 11, 126/154 diary assessments) in order to examine whether results were influenced by base rate effects. Results remained similar for both models for the subset of youth who took an opioid at least 1 day during the diary period.

Discussion

Overall, home opioid use for pain management in the present sample of youth with SCD had a low base rate. This is consistent with literature suggesting that opioid analgesics are typically used to manage acute pain crises and misuse is rare in patients with SCD [23]. However, a small proportion of youth used opioids around half of the diary days, and routine use of opioids could result in adverse side effects such as sedation, cognitive impairment, and abdominal pain resulting from constipation, which could be particularly problematic for youth who are attending school [4, 24]. Thus, finding alternative therapies that could improve pain management and reduce the amount of opioid analgesics required for adequate pain management could improve functioning and quality of life.

In youth with SCD, higher negative affect accounted for variance in opioid use when accounting for pain intensity. This finding mirrors a recent larger study in adults with SCD and highlights the potential utility of psychological interventions for reducing opioid use in youth with SCD. In the adult chronic pain literature, higher levels of negative affect have been associated with decreased pain relief from opioid analgesics [9]. Individuals with higher levels of negative affect may consume greater quantities of opioid analgesics in order to receive the same level of analgesic effect as an individual with lower negative affect. Further, prior diary studies have found a significant association between negative affect and pain severity in youth with SCD [12, 13]. Thus, reducing negative affect could potentially reduce the quantity of opioids youth require to achieve adequate pain relief.

Psychological interventions have shown preliminary evidence for improving outcomes in youth with SCD and may be helpful in reducing negative affect in this population [25–27]. Further, psychological interventions for pain in youth often include a parent component [28, 29] focused on reducing parental reinforcement of a child's pain behaviors and reframing negative cognitions such as catastrophizing. Our finding that caregiver catastrophizing about their child's pain was associated with child opioid use supports a family-based approach.

Strengths of the present study include an electronic daily diary methodology that incorporated both child and caregiver report. Limitations include a small sample size, significant proportion of youth without pain or opioid use, 20% missing data for diary assessments, limited assessment of pain catastrophizing, and the reliance on child-report data for opioid use. Furthermore, timing and directionality of these effects cannot be inferred for this once-daily diary study as the relation between pain intensity, negative affect, and opioid use is potentially complex. Larger studies oversampling for youth who routinely use opioids for home pain management are needed to replicate our findings and test

temporal relations between child and caregiver psychological factors and opioid use. Future studies should also assess dose, number of times opioid analgesics are taken each day, and opioid-related side effects to better evaluate opioid use in the home setting. Based on child pain frequency reported over the past 3 months, our sample comprised both youth with chronic pain and youth with episodic acute pain [30]. It is plausible that the relation between psychosocial factors and opioid use may differ among individuals with acute, episodic, and chronic SCD pain. Future studies with larger sample sizes should examine pain frequency as a moderator of these relationships.

Our study found that a 1 unit change in pain intensity on a 0–10 scale corresponded with 47% increased odds of taking an opioid. For youth with SCD, pain reduction of 0.9 cm on a 0–10 visual analog scale has been found to represent minimal clinically significant improvements in pain [31]. Thus, a 1 unit change was likely clinically meaningful and associated with a perceived increase in pain. However, future research is warranted regarding the clinical utility of our findings.

In conclusion, youth with SCD on average demonstrated low-frequency use of at-home opioid prescriptions. However, a subset of youth demonstrated higher frequency of opioid use around 50% of dairy days. Home opioid use on a given day was significantly associated with youth-reported negative affect when accounting for pain intensity as well as caregiver catastrophizing about their child's pain. Multimodal pain interventions, including psychological interventions, could enhance current pain management for youth with SCD. Future research should evaluate whether family-based psychological interventions reduce pain and opioid use in youth with SCD.

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Compliance with Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards The authors have no conflicts of interest to disclose.

Authors' Contributions A. L. Stone secured the funding, designed the study, analyzed the data, and drafted the manuscript. Z. Williams collected data. M. McNaull, A. C. Wilson, and C. W. Karlson mentored the first author and contributed to the study design and formulation of research question. All authors provided revisions to the manuscript and approved of the final version.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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