

Pain, mood and opioid medication use in sickle cell disease

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Patients with sickle cell disease show wide variations in their experience of pain, and in the impact of pain on everyday functioning. This study examined relations between pain, mood, physical activity, and medication use in a longitudinal naturalistic self-monitoring study of 21 adult sickle cell patients over 12 months. Results suggest that opioid medication use is related to the impact of pain on daily life. Patients who use opioids more frequently for sickle cell pain show more disruption of their lives, with reduced activity levels and more pessimistic mood.

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Background

Pain associated with sickle cell disease is a persistent problem for affected individuals, and its management continues to pose a challenge to practitioners. Opioids are recommended for the treatment of severe sickle cell pain, and have been used successfully in the management of this pain in the community.¹ Sickle cell pain assessment is crucial, and accurate estimation is important for its effective management. Information obtained from patients is usually collected cross-sectionally by interview or questionnaire in a clinical situation. Diaries can give insight into patients' pain experience and coping strategies, especially when used in the natural environment, although some inherent difficulties remain.² Diaries can help practitioners assess sickle cell pain in the community, and related quality of life in patients.³ Nevertheless, pain measurements on multiple occasions increase the burden on the patient unnecessarily, and could result in unreliable data since patients may resort to retrospective recordings of pain. For this reason it has been difficult to carry out longitudinal studies of pain self-monitoring in sickle cell disease.

The main aim of this study was to determine the level and variability of sickle cell pain experienced in the community over 12 months, and to assess pain medication use, particularly opioid analgesia, in response to this pain. The second aim was to ascertain the associations of sickle cell pain with patients' moods and activity levels.

Methods

A sickle cell pain diary was constructed for use in a naturalistic self-monitoring study with the view to easing the burden of completion and providing reliable information. In all, 33 adults with sickle cell disease were invited opportunistically for routine follow-up from a cohort representing the spectrum of demographic and clinical characteristics attending St George's Hospital in London.⁴ All 33 patients consented to take part in the study. A total of 21 participants were included in the analyses (Table 1). Exclusions were: two nonparticipants in related study; one death; three dropouts; six nonrespondents (did not return any diaries). Patients completed diaries for any three consecutive days a month for 12 months, providing ratings of pain severity, mood (bad–good), and physical activity (low–high) on 10-point scales, together with information on medication use. Diaries were sent out monthly with a *Freepost* return envelope. Patients were telephoned each month to encourage them, emphasis was placed on the monthly return of each set of diaries. They were also instructed to complete the diaries only at home and not in hospital, and at the end of the day. Medical records were also examined for clinical information. The data were analysed, and overall patterns of pain associated with vaso-occlusive crises and medication use were determined for the 12-month period. Also, associations and analysis of covariance between pain, medication use, mood, and activity were examined allowing for both between- and within-subject effects.

Results

Demographic characteristics of patients are presented in Table 1, which also shows data on complications

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Table 1 Demographic and clinical characteristics of patients

Variable	N	Mean	s.d.	Range
Age		28.9	6.6	16–42
Complications (12 months)		0.9	0.9	0–3
Emergency visits (12 months)		2.5	2.4	0–10
Hospital admissions (12 months)		2.4	2.3	0–10
Duration of admissions (days)		9.0	8.8	0–33
General practitioner visits (12 months)		2.2	2.9	0–8
Gender				
Female	15 (71%)			
Male	6 (29%)			
Phenotype				
HbSS	15 (71%)			
HbSC	4 (19%)			
HbS β thalassaemia	2 (10%)			
Ethnic origin				
African	11 (52%)			
Caribbean	10 (48%)			

associated with sickle cell disease and health service utilization reported during the 12-month period preceding the study. The number of days on which patients reported pain ranged from 5 to 100%, with only one patient reporting pain 100% of the time. Average pain severity (0–10 scale) was 4.3, ranging from 2.0 to 7.7 across patients. Individual patients' experience of pain was highly variable: on the days that patients reported any pain, ratings varied between an average of 0.3–6.5. Within-person correlations across days between pain and mood averaged $r = -0.40$, but varied from -0.95 (more pain, bad mood), to $+0.81$ (more pain, good mood). Pain–activity correlations varied from -0.90 (more pain, reduced activity) to $+0.24$ (more pain, increased activity), and averaged $r = -0.34$. The strength of the relations between pain and mood or activity was not related to average pain severity, so patients who experienced more pain did not show more consistent associations between pain and everyday functioning.

All types of opioid medication used by patients were computed. Half the patients took opioid medication on at least 5% of days, while the remainder took less or no opioid medication. The more frequent users of opioid medication showed consistent negative associations between pain and mood (mean $r = -0.91$, 95% CI -0.48 to -0.86), while the remainder did not ($r = -0.06$, CI 0.36 to -0.46), after controlling for pain severity ($P = 0.009$, analyses carried out following Fisher's r to Z transformation). Similarly, pain and activity were negatively correlated in opioid users ($r = -0.55$, CI -0.33 to -0.70), but not in other patients ($r = -0.17$, CI 0.12 to -0.43 , $P = 0.032$). Analysis of covariance of the within-subject correlations in the more and less frequent opioid users performed, with average pain included as a covariate, is shown in Table 2. These findings indicate that opioid medication use is related to the impact of pain on daily functioning, independently of pain severity.

Opioid medication use was also positively associated with health service utilization (emergency visits, hospital admissions, days of hospitalizations) as a composite index after controlling for pain ($r = 0.59$, $P = 0.007$). Patients who tended to use opioid analgesia also had made more frequent contact with hospital services over the previous 12 months. It seems plausible that opioid medication use is a function of hospitalization. Opioid medication use was not associated with patient demographics and complications.

Discussion

This study has highlighted a number of interesting issues. First, patients with sickle cell disease experience frequent episodes and manage significant levels of pain in the community. They also show wide variations in their experience of pain. Second, sickle cell pain interferes with the day-to-day well-being of patients, but the significance of pain on quality of life varies greatly between them. Third, opioid medication use is related to the impact of pain on daily life. Patients who are frequent users of opioid medication in the community appear to have more disruption in their lives when they are in pain, with lower activity levels and more negative moods. Fourth, opioid medication use in the community may be a consequence of health service utilization. Patients who frequently utilize hospital services are also more likely to use opioids indepen-

Table 2 Analyses of the differences between more and less frequent users of opioid medication in the strength of correlations between pain and mood, and pain and activity

Variable	Opioid medication usage and average pain	N ^a	F	P
Z average pain versus mood	Less frequent users	9	6.23	0.023
	More frequent users	11		
Z average pain versus activity	Less frequent users	9	4.59	0.047
	More frequent users	11		

^aOne patient excluded because of nonreport of pain on any day. Average level of pain included as a covariate in both analyses.

dently of severe pain. Those who make frequent contact with hospital services may be perceived as having more severe disease and related pain, hence are also more likely to be prescribed opioids for use at home. Opioid medication reported in the diaries included dihydrocodeine, oral pethidine, and oral morphine. Taken together these findings may reflect different patterns of coping and has important implications for management.

The demographics of the patients in the study did not reflect that of the adult sickle cell patient population of about 55/45% females/males and 60/40% Africans/Caribbeans attending St George's Hospital. There was a female predominance consistent with other behavioural studies in the UK. This suggests better acceptance of or adherence to self-monitoring approaches to management among the female population of patients with sickle cell disease. The number of complications

averaged about one in the preceding 12 months indicating moderate disease, and did not appear to influence medication use. These included acute chest syndromes, leg ulcers, and infections.

We are cautious about generalizing the results given the small number of patients studied from just one hospital. Also, the patients were predominantly HbSS in phenotype who generally have more severe pain. Nonetheless, this emphasizes the need for further research in this interesting area.

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