

## The Relationship of Opioid Analgesia to Quality of Life in an Adult Sickle Cell Population

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### ABSTRACT

**BACKGROUND:** Pain is a limiting factor in the daily life activities of sickle cell disease (SCD) patients. Although opioid analgesics are widely used, to date there have been no studies on the relationship of daily opioid use to quality of life (QoL) measures in this population.

**OBJECTIVE:** To determine the relationship of opioid analgesia to QoL in adults with SCD.

**DESIGN:** There were 185 outpatients with various SCD genotypes evaluated. Data were collected by patient interviews as well as review of medical records. QoL as determined by the Medical Outcome Study 36-item Short Form Survey (SF-36) was the main outcome measured.

**RESULTS:** QoL outcomes were not lower in the classically more severe homozygous SS individuals when compared with the heterozygous SC patients. However, SF-36 scores were significantly lower in individuals using opioids daily compared with those who did not, in all age groups and for all diagnoses. When controlling for hydroxyurea use, the negative association between opioid use and QoL scores remained unchanged. QoL scores were significantly higher in those who were either on no medications or on hydroxyurea alone, as compared with those who were on opioids alone or on hydroxyurea and opioids concurrently. Disease severity scores were not different between medication groups.

**CONCLUSIONS:** SCD patients on daily opioids had poorer QoL scores than those who were not on opioids, independent of disease severity. Hydroxyurea had a positive impact on QoL, although that effect was not observed in patients also using chronic opioids. Prospective studies are needed to define the relationship of opioid use to QoL and the significance of the interaction of both drugs in SCD.

**KEYWORDS:** Opioid analgesia; Quality of life; Sickle cell disease

**Sickle** cell disease (SCD) is an inherited hemoglobin disorder that results from a single-point mutation in the hemoglobin gene, causing the production of an abnormally rigid hemoglobin S. The circulating sickle cells cause endothelial activation, inflammation, poor vascular flow and, ultimately, ischemia. The disease runs a life-long complicated clinical course characterized by chronic pain, punctuated with acute pain episodes. Over the past decade, very little progress has been made in the attempt to effectively manage SCD-related pain, despite the introduction of hydroxyurea. Hydroxyurea is the only approved medication for the prevention of SCD-related complications including pain episodes. It acts mainly by increasing intracellular hemoglobin F, which reduces red cell rigidity and ensures the delivery of more oxygen to the tissues. Furthermore, hydroxyurea reduces white blood cells, platelets, and reticulocytes, and downregulates endothelial adhesion, thus obliterating the main mechanisms of vasoocclusion. Unfortunately, hydroxyurea is still underutilized in SCD and many patients do not experience the benefits of this treatment.<sup>1</sup>

In practice, after the onset of the pain cycle, an analgesia ladder is used to break this cycle. More often than not, opioid analgesics are the only effective analgesics for SCD-related pain.

The use of opioids to manage chronic nonmalignant pain has been heavily debated due to the potential risks (ie, addiction, tolerance, persistent side effects, and decrease in physical and psychological functioning) and the questionable effectiveness of this type of therapy.<sup>2</sup> Despite its possible negative effects, opioid therapy can relieve pain and improve mood and functioning.<sup>3,4</sup> The importance of a standardized approach based on these findings has been emphasized through consensus statements that both support the use of opioid treatment and guide physicians in the prescription of these drugs.<sup>5,6</sup> Some investigators, however, remain skeptical and consider opioids to be only marginally useful in decreasing pain or even capable of worsening pain.<sup>7-9</sup>

Pain poses a continuous challenge for SCD patients and is a limiting factor in their daily life activities. More than 90% of hospital admissions of SCD patients are for acute pain management.<sup>10</sup> Sickle cell pain is unpredictable, recurrent, intense, and frequently persistent.<sup>11</sup> Recently, in the Pain in Sickle Cell Epidemiology Study,<sup>12</sup> more than half of all SCD patients completing up to 6 months of pain diaries reported experiencing SCD-related pain, crisis, or health care utilization on more than half of the days. Almost one-third (29%) reported experiencing pain every day.<sup>12</sup> Although guidelines for the treatment of sickle cell-related pain exist, physicians are mostly unaware of the treatment recommendations provided.<sup>13</sup> No studies have adequately prospectively evaluated the use of opioids in chronic pain management among patients with SCD.<sup>14</sup> Despite the lack of evidence supporting the effectiveness of opioids in this patient population, opioids are widely used in SCD.

In recent years, hydroxyurea has been found to ameliorate the clinical course of SCD, leading to less frequent painful crises and lower morbidity and mortality, with the benefit of few adverse side effects.<sup>15-17</sup> Patients on long-term opioid pain management also may be receiving hydroxyurea treatment. Therefore, the effect of opioid pain management cannot be fully evaluated without also considering the role of hydroxyurea as a concomitant medication.

The aim of the current study was to define the relationship between pain management with opioid analgesics and health-related quality of life among SCD patients. Hydroxyurea use, its interaction with opioids, and their combined effect on quality of life outcomes also were evaluated.

## METHODS

### Patients and Measurements

There were 185 adult SCD patients from the outpatient clinic at Duke University Medical Center included in the study. Patients were approached to participate in the study during routine clinic visits, between 2004 and 2005. One hundred seventeen patients had either homozygous sickle cell disease (SS) or S $\beta$ <sup>0</sup> thalassemia (S $\beta$ <sup>0</sup>), and 68 had doubly heterozygous genotypes, including S $\beta$ <sup>+</sup>, SC, S $\delta$  $\beta$  thalassemia,

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