

## Pain in $\beta$ -thalassemia major patients: an important yet neglected issue

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### LETTERS TO EDITOR

$\beta$ -thalassemia Major ( $\beta$ -TM) is the most commonly inherited hemolytic anemia. Patients with  $\beta$ -TM require life-long adherence to distressing treatment regimens, including regular blood transfusions and daily chelation therapy. Therefore, maintaining hemoglobin target levels as well as appropriate chelation therapy has been particularly emphasized in the care of patients with  $\beta$ -TM [1,2]. In keeping with improvement in life expectancy of  $\beta$ -TM patients, some previously unrecognized health issues have been identified in these patients that affect their quality of life as well as their overall ability to adhere to treatment [3].

Although, pain is not a symptom commonly associated with  $\beta$ -TM, it has been recently reported as an emerging complication and a major cause of morbidity in these patients [2,4]. A study by Haines et al. [2] demonstrated that 84% of  $\beta$ -TM patients experienced pain in the past month and 22% of patients reported pain on a daily basis. In addition, 81% and 31% of all patients experienced pain for one to five year or longer, respectively.

Moreover, it has been shown that age was an independent predictor of pain intensity and frequency in thalassemia patients, irrespective of transfusion status,

iron overload, gender, type or administration of iron chelator regimen, and bone density. In terms of pain perception, 39% of patients described their worst pain as severe, while 42% of them reported their worst pain as moderate.

The most frequent location of pain was the lower back (82%), followed by the leg (56%), head (48%), and mid-back (47%). As described by participants, the nature of pain was aching (79%), throbbing (61%), sharp (50%), and tiring (55%) [2].

The results of another study aiming to evaluate the pain intensity of thalassemia patients over a 9-month period revealed that 56% of patients experienced pain at least once over the study period, of whom 32% reported severe pain and 16% of patients experienced pain during the whole study period. Also, it has been shown that patients who were experiencing more frequent and higher intensity pain had a poorer physical quality of life, as well as more anxiety and depression [3].

Studies have shown that as the age rises, the incidence and duration of pain also increases. For example, Oliveros and colleagues showed that the incidence of pain in patients over 35-years-old is threefold of that in patients younger than 18-years-old. Seventy-nine percent of patients suffered from pain for at least one year and 34%

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for 5 years. In descending order, the most common locations of pain were the lower back, legs, middle back, and head. On average, patients experienced pain in at least four parts of their bodies [3].

In another study, 62% of  $\beta$ -TM patients undergoing iron chelation therapy reported a moderate level of pain [5]. Trachtenberg et al. [6] revealed that 69% of thalassaemia patients had bodily pain (28% of which was moderate or severe) and the frequency of pain episodes increased significantly with age, and was more frequent in patients older than 35 years.

The exact mechanism of pain in thalassaemia has not yet been fully elucidated; however, iron overload, low hemoglobin level, and low bone mass have been suggested as potential etiologies [4,7]. Nevertheless, the current evidence does not confirm these suggestions [2]. It is assumed that lower hemoglobin levels, which occur at the end of a transfusion cycle, are possibly associated with worsening of pain in  $\beta$ -TM patients [2,7]. In addition, due to skeletal changes and bone marrow expansion, the risk of developing pain increases in patients who delay the blood transfusion; however, these relationships still need to be clarified in future studies [7].

In summation, despite its devastating impact on patient outcomes, pain is a profoundly understudied symptom in  $\beta$ -TM patients. Therefore, further studies are required to further elucidate the different mechanisms of pain in  $\beta$ -TM patients. Thereafter, the effect of both pharmaco-

logical and non-pharmacological interventions, according to those possible underlying pathologic mechanisms, should be evaluated. It is worth mentioning that future trials must consider the influence of other relevant variables, such as anxiety and depression, which is frequent in these patients.

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