in the previous 12-month period before survey, were assessed. Patients were also asked to classify which level of pain would cause them to use strong analgesics (such as opiates), to seek the assistance of a medical professional, to miss work/school and to miss important social events in a scale ranging from 0 (not severe al all) to 10 (worst imaginable). Descriptive analyses and chi-square tests were performed. **Results:** A total of 260 Brazilian patients of all genotypes (self-reported) with diagnosis SCD were included, most of them female (58.5%; n = 152) with a mean age of 23.1 (SD: 14.0) years. The prevalence of at least one VOC in the previous year was 87.7% (n = 228) for total sample, 88.3% (n = 98) among those aged 6-16 years old and 87.2% (n = 130) among those >16 years. Patients had a mean of 4.0 (SD = 4.6) crises, 12.3% (n = 32) had only one episode, 44.6% (n = 116) 2-4, 25.4% (n = 66) 5-10 and 5.4% (n = 14) ≥11 episodes. A similar percentage distribution was observed when the subjects was stratified by age. No difference in the frequency and distribution of VOC was observed in patient with or without HU (HU 87.6% *vs* without HU 87.9%; p = 1.000) and the categories of frequency of episodes during the year (p = 0.799). Considering crisis management, 32.3% (n = 84) reported to deal with it at home, most frequently due to reasons such as a poor experience at the emergency room or hospital (n = 41; 48.8%). The patients with the worst imaginable level of pain (a pain score of 10) led patients to use analgesics, to seek for assistance, to miss work/school and social events for 24.9%, 24.1%, 23.1% and 21.3% of patients, respectively. **Discussion:** Almost all patients experience at least one VOC in a 12-month period, regardless the age and HU use. Furthermore, the frequency of crisis may be greater than five for about 30% of patients in all age groups. Data is consistent with those previously reported and reinforces the importance of VOC on SCD management. **Conclusion:** The vast majority of Brazilian SCD patients reported at least one episode of VOC in a 12-month period, regardless of age. Thus, VOC is still an important issue for Brazilian SCD patients and interventions able to decrease its occurrence are still needed.

https://doi.org/10.1016/j.htct.2020.10.098

HEMOSTASIA E PAREDE VASCULAR: DOENÇAS DA COAGULAÇÃO E FIBRINÓLISE

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A FIRST-IN-HUMAN FOUR-YEAR FOLLOW-UP STUDY OF DURABLE THERAPEUTIC EFFICACY AND SAFETY OF AAV GENE THERAPY WITH VALOCTOCOGENE ROXAPARVOVEC FOR SEVERE HEMOPHILIA A

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Background: Long-term clinical benefit has been demonstrated in people with hemophilia A following a single administration of the investigational gene therapy valoctocogene roxaparvovec (AAV5-hFVIII-SQ). Safety, clinical effectiveness, and mechanisms of episomal vector DNA persistence have been previously described, but outstanding questions pertain to the maintenance of these attributes over increasing durations of follow-up. **Aims:** The four-year safety, efficacy, and durability of valoctocogene roxaparvovec is evaluated in a Phase 1/2 clinical study for severe hemophilia A. **Methods:** Adult male study participants with severe hemophilia A were followed for up to four years after receiving a single intravenous dose of valoctocogene roxaparvovec at 6×10^{13} vg/kg (n = 7) or 4×10^{13} vg/kg (n = 6). **Results:** After four (6×10^{13} vg/kg) or three (4×10^{13} vg/kg) years, all study participants demonstrated clinically meaningful FVIII activity levels with reductions in bleeds and FVIII usage. Following withdrawal from prophylaxis, annualized bleeding rate declined from pre-treatment mean by 95% at year four in 6×10^{13} vg/kg participants, and 93% at year three in 4×10^{13} vg/kg participants. Despite FVIII activity levels continuing to decline at a shallow rate, all patients in both cohorts remained off prophylaxis. After four years, the safety profile of valoctocogene roxaparvovec remained favorable and unchanged, with no inhibitor development or treatment-related ALT elevations beyond year one. **Conclusions:** Four-year follow-up data demonstrate that gene transfer with valoctocogene roxaparvovec leads to substantial and sustained FVIII activity levels, clinically relevant reductions in self-reported bleeding episodes, and significant reductions in FVIII replacement infusions. These data from the first-in-human trial represent the most up-to-date, long term follow-up data currently available for the investigational use of AAV-mediated therapy for hemophilia A.

https://doi.org/10.1016/j.htct.2020.10.099