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Hepatitis B immunization in sickle cell disease patients

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Abstract

Introduction: Sickle cell disease, also known as sickle cell anaemia, is an inherited haemoglobinopathy resulting in the production of the abnormal haemoglobin of sickle cell disease: haemoglobin S. Sickle cell patients are exposed to frequent deglobulation crises, often requiring several blood transfusions and hospitalisations at risk of transmission of infectious diseases such as hepatitis B (HBV). The objective of our study is to describe the immunisation against hepatitis B of vaccinated sickle cell patients and then to propose a course of action for non-immunised patients in the Haematology Department of the Joseph Ravoahangy Andrianavalona University Hospital (JRAHU).

Material and Methods: The study was a prospective descriptive study investigating on the immunisation against hepatitis B of vaccinated sickle cell patient's patients in the Haematology Department of the Joseph Ravoahangy Andrianavalona University Hospital (JRAHU) from June 2019 to March 2020. The study population concerned all sickle cell disease children under 15 years of age, girls or boys, of any ethnic origin, with or without clinical or biological signs of hepatitis, vaccinated against hepatitis B according to expanded program of immunization with at least 3 injections of hepatitis B vaccine, transfused or not. The included patients were be tested for HBsAg and anti-HBsAb.

Results: During the study period, a total of 36 sickle cell patients were included. The average age was 8.2 years with an extreme of 2 and 13 years. Of the 36 sickle cell patients vaccinated, none had HBsAg and 28 patients (77.8%) were anti-HBsAb positive, protected against hepatitis B and 8 patients (22.2%) were serologically negative and at risk of contracting hepatitis B.

Conclusion: Sickle cell disease patients are exposed risk of transmission of infectious diseases, if their antibody level between 1 and 10 mIU mL-1 is considered a poor response, those affected should receive a booster.

Keywords: Sickle Cell Disease; Hepatitis B Vaccine; Immunization; Anti-Hbsab; Madagascar

1. Introduction

Sickle cell disease, also known as sickle cell anaemia, is an inherited haemoglobinopathycharacterised by the substitution of a glutamic acid for a valine at the 6th amino acid of the A segment of the beta globin chain (β6Glu --> Val) on chromosome 11, resulting in the production of the abnormal haemoglobin of sickle cell disease: haemoglobin S [1].

Currently, haemoglobinopathies are an increasingly important public health problem, especially in black Africa. Their prevalence is estimated at 7% of world population [1].

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Sickle cell disease is the most common haemoglobinopathy in Madagascar. Its prevalence is around 10%.

Sickle cell patients are exposed to frequent deglobulation crises, often requiring several blood transfusions and hospitalisations at risk of transmission of infectious diseases such as hepatitis B (HBV). Since 2002, vaccination against hepatitis B has been part of the extended vaccination program in Madagascar administrated in three doses from the 3rd month of life [2]. But at present, no data has been published on the effectiveness of the vaccination coverage in the general population and in particular among patients at risk such as sickle cell patients.

With this respect, we conducted a study to describe the immunisation against hepatitis B of vaccinated sickle cell patients and then to propose a course of action for non-immunised patients in the Haematology Department of the Joseph Ravoahangy Andrianavalona University Hospital (JRAHU).

2. Methods

We conducted a prospective descriptive analytical study from June 2019 to March 2020. The study population concerned all sickle cell children under 15 years of age, girls or boys, of any ethnic origin, with or without clinical or biological signs of hepatitis, vaccinated against hepatitis B according to Expanded Program of Immunization with at least 3 injections of hepatitis B vaccine, transfused or not, who came for a follow-up or a consultation at the Haematology Department of JRAHU during the study period

Persons not included in the study:

- All sickle cell subjects under 15 years of age who refused the study
- Sickle cell subjects positive for HBsAg.
- People who were excluded from the study:
- All sickle cell subjects who did not have EPI in Madagascar during childhood
- All sickle cell patients who did not receive the hepatitis B vaccine
- Children with less than 3 doses of vaccine

We conducted an exhaustive sampling of all sickle cell subjects under 15 years of age who came during the study period.

After informed consent from the patients, a questionnaire provided information on their age, marital status, ethnic origin and vaccination status.

The included patients were sampled on a 5ml dry tube to be tested for HBsAg (HBs Ag RAPIDS LABS® UK) and anti-HBsAb (HBsAb ELISA kit RAPIDS LABS® UK)

Data were collected on Microsoft office Excel 2013 and statistical analysis of the data was performed with R software, the p-value threshold is 5%. The Chi-square test was used to compare the observed percentages. The Student's t-test was used to compare the means. Measures were taken to ensure strict confidentiality in the preparation of the records. The study was conducted with the signed consent of the patient.

3. Results

During the study period, we recruited 500 children with sickle cell disease of whom 400 were excluded and 64 not included due to parental refusal to participate in the study. A total of 36 sickle cell patients were included.

Of the 36 sickle cell patients, 64% were male, with a sex ratio of 1.77. There was a clear predominance of patients aged between 10 and 15 years, with 15 cases (42%). The average age was 8.2 years with an extreme of 2 and 13 years. The 10-15 year old age group was the most represented.

Of the 36 subjects vaccinated, only 2 (5.56%) had received a booster

Of the 36 sickle cell patients vaccinated, none had HBsAg and 28 patients (77.8%) were HBsAb positive, protected against hepatitis B, and 8 patients (22.2%) were serologically negative and at risk of contracting hepatitis B (table 1).

Most of the children (63.89) had received less than 5 transfusions, 16.67 between 5 and 10 transfusions, and the rest 13.89 had more than 10 transfusions.

Table 1 Sickle cell disease trait and immunisation

	HbS Antibody negative	HbS Antibody positive	p
Heterozygous	0 (0. 00%)	1 (2.77%)	0.38
Homozygous	8 (22. 23%)	27 (75%)	

4. Discussion

Approximately 400 million people worldwide are currently infected with the hepatitis B virus, and approximately 500,000 to 700,000 die each year from this disease [3].

Madagascar is classified as an intermediate endemic country with a current HBsAg prevalence of 5.3% [4]. In sickle cell disease patients in our center the prevalence of HBsAg was 1.41% in 2018 [5], Higher in other African countries, in the Central African Republic, in 2008, was 14.3% [81], 10% in the Democratic Republic of Congo and 6.48% in Cameroon [6] [7]. Children with sickle cell disease are vulnerable to infections and must therefore be protected by vaccines.

In our study, the rate of immunisation against hepatitis B was 77.8%, similar to a study carried out in Africa, in Ivory Coast, this prevalence was 65.1%. Similar to a study done in Mali that all sickle cell children are correctly vaccinated according to EPI, next to a study done in Ouagadougou with the rate of vaccination coverage according to EPI in sickle cell patients was 97.5% [8].

Hepatitis B vaccine for infants had been introduced nationally in 189 Member States by the end of 2019. Global coverage with 3 doses of hepatitis B vaccine is estimated at 85%. In addition, 109 Member States have introduced one dose of hepatitis B vaccine for newborns within the first 24 hours of life. Global coverage is 43% and is as high as 84% in the WHO Western Pacific Region, while it is estimated at only 6% in the WHO African Region [9] [10]. At present in Madagascar, vaccination at birth is not yet available.

In our study, we found that the vaccination coverage rate of sickle cell disease patients is good, similar to the study done in Mali (97.5%) and another study done in Madagascar (78.7%). However, we found that 22% of sickle cell patients failed to receive the vaccine.

According to the literature, after a complete vaccination regimen, the percentage of non-responders, unprotected with anti-HBs, is low in immunocompetent adults, ranging from 5 to 7%. However, there are factors that contribute to a lower response: male sex, age (over 30 years), obesity, smoking and various situations that alter the immune system, such as AIDS, diabetes, haemodialysis and immunosuppressive treatments. The high rate of non-responders in our series could be explained by the immunosuppression of sickle cell patients partly due to functional asplenia following multiple splenic infarcts. All our patients were SS homozygotes [11].

An antibody level between 1 and 10 mIU mL-1 is considered a poor response, and those affected (poor responders) should receive a booster injection at that time, but do not need further serological testing [23]. In practice, if there is no response after a total of 6 injections, there is no need for an additional injection. Approximately 15-25% of people will respond to one additional dose, and 30-50% to three additional doses [12].

5. Conclusion

In conclusion, 77.8% sickle cell patients are protected against hepatitis B. Others patients need to receive a booster injection. Efforts to raise awareness and provide vaccines to at-risk individuals such as sickle cell disease patients must be undertaken.

Compliance with ethical standards

Disclosure of conflict of interest

All authors declare no competing interests.

Statement of informed consent

The study was carried out with the agreement signed by patients or their guardians.

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