RESEARCH ARTICLE

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Evaluation of Safety and Efficacy of Emicizumab Prophylaxis in Egyptian Pediatric Patients with Hemophilia A

Mısırlı Pediatrik Hemofili A Hastalarında Emisizumab Profilaksisinin Güvenlilik ve Etkililiğinin Değerlendirilmesi

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Abstract

Objective: Hemophilia A (HA) is a hereditary X-linked bleeding disorder secondary to deficiency of the clotting factor VIII (FVIII). Emicizumab is a monoclonal antibody that replaces the function of the activated FVIII and prevents bleeding in HA patients. Emicizumab is expected to ameliorate bleeding risk in those patients together with subsequent complications. However, there is a scarcity of data about its safety and efficacy in patients with HA. We aimed to evaluate the safety and efficacy of emicizumab prophylaxis in Egyptian pediatric patients with HA.

Materials and Methods: A prospective cohort study was carried out with 88 HA patients who received emicizumab prophylaxis. Breakthrough bleeding episodes and the annualized bleeding rate (ABR) were reported for all patients before and after emicizumab prophylaxis. Also, all adverse events during prophylaxis were documented to evaluate the safety of emicizumab.

Results: Joint bleeds occurred in 94% of the patients. Among those patients, 58% had one target joint, 36.4% had more than one target joint, and 5.6% had no target joints. Furthermore, 17% of patients were positive for FVIII inhibitors. The median annualized joint bleeding rate was reduced remarkably after emicizumab prophylaxis (36 before versus 0 after emicizumab). The median ABR was 48 before emicizumab versus 0 after emicizumab. Eight patients experienced mild breakthrough bleeding episodes. The most common adverse events were local reactions at injection sites, headache, arthralgia, fever, and diarrhea.

Conclusion: Prophylaxis using emicizumab was associated with a significantly lower bleeding rate in HA patients with and without inhibitors. The majority of patients had zero bleeds with emicizumab prophylaxis.

Keywords: Emicizumab, Safety, Efficacy, Hemophilia A

Öz

Amaç: Hemofili A (HA), X'e bağlı çekinik kalıtılan ve pıhtılaşma faktörlerinden faktör VIII'in (FVIII) eksikliği ile ortaya çıkan bir kanama hastalığıdır. Emisizumab, aktif FVIII'in işlevini yerine getirebilen bir monoklonal antikordur ve HA hastalarında kanamayı önlemektedir. Emisizumabın bu hastalarda kanama riskini ve kanama ilişkili komplikasyonları engellemesi beklenmektedir. Ancak, emisizumabın HA hastalarındaki güvenliliği ve etkililiği hakkında çok az veri bulunmaktadır. Bu çalışmanın amacı, Mısır'daki pediatrik HA hastalarında emisizumab profilaksisinin güvenliliği ve etkinliliğini değerlendirmektir.

Gereç ve Yöntemler: Emisizumab proflaksisi kullanan 88 HA hastasını içeren prospektif kohort çalışması yürütüldü. Tüm hastalar için emisizumab profilaksisi öncesi ve sonrası kanamaları ve yıllık kanama oranı (ABR) raporlandı. Ayrıca, emisizumab profilaksisi sırasında ortaya çıkan her türlü olumsuz etki kaydedilerek emisizumabın güvenliliği değerlendirildi.

Bulgular: Eklem kanamaları, hastaların %94'ünde görüldü. Bu hastaların %58'inin tek hedef eklemi, %36,4'ünün birden fazla hedef eklemi vardı, %5,6'sının ise hedef eklemi yoktu. Ayrıca, hastaların %17'sinde FVIII inhibitörleri pozitifti. Emisizumab profilaksisi sonrası medyan yıllık eklem kanama oranı, emisizumab öncesine kıyasla önemli ölçüde azalmıştı (öncesi 36, sonrası 0). Medyan ABR ise emisizumab öncesi 48, sonrası ise 0'dı. Sekiz hastada hafif düzeyde kanama yaşanmıştı. En yaygın olumsuz etkiler enjeksiyon bölgesinde lokal reaksiyonlar, baş ağrısı, eklem ağrısı, ateş ve ishaldi.

Sonuç: Emisizumab profilaksisi, inhibitörü olan ve olmayan HA hastalarında kanama oranlarında önemli bir azalma ile ilişkili bulundu. Çoğu hasta, emisizumab profilaksisi ile hiç kanama yaşamamıştı.

Anahtar Sözcükler: Emisizumab, Güvenlilik, Etkililik, Hemofili A

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Introduction

Hemophilia A (HA) is hereditary X-linked recessive disease secondary to low functional plasma clotting factor VIII (FVIII) level. Patients with HA usually present with prolonged and excessive bleeding either spontaneously or after trauma [1]. Patients with severe HA may have serious joint bleeding, soft tissue bleeding, muscle bleeding, and life-threatening bleeding manifestations such as intracranial hemorrhage [2]. About 25% to 30% of patients with severe HA can develop inhibitors to the infused FVIII that make FVIII replacement therapies ineffective and expose hemophilia patients to a higher risk of spontaneous and post traumatic bleeding episodes. There are limited treatment options for hemophilia patients with inhibitors like recombinant activated FVII (rFVIIa) and activated prothrombin complex concentrate (aPCC), which offer alternative treatment modalities but are associated with greater treatment burden and discordant bleeding control [3].

Replacement therapy is the main treatment for HA, either as in response to bleeding episodes (on demand treatment) or in the form of regular infusions of FVIII (prophylactic treatment) to avoid bleeding episodes [4]. Currently, regular prophylactic infusion of FVIII is the standard of care for patients with severe HA [5]. However, because of the short half-life of FVIII, a minimum of two infusions are needed per week to maintain safe trough levels, resulting in great treatment burden and insufficient level of care especially for patients unable to stick to treatment [6]. In spite of regular prophylaxis therapy, clinical and subclinical bleeding episodes may still arise. Thus, another treatment option with higher efficacy and less burden is still needed [7].

Emicizumab is the first commercially available non-factor replacement therapy for treatment of congenital HA. Emicizumab is a recombinant bispecific modified IgG4 monoclonal antibody that bridges activated factor IX and factor X to replace the missing function of activated FVIII, that way rebalancing the hemostasis [8]. Emicizumab is approved for bleeding prevention in patients with HA irrespective of their inhibitor status. The lower dosing frequency, subcutaneous administration, efficacy in bleeding prevention, and reduced annualized bleeding rates (ABRs) have encouraged many patients with HA to switch to emicizumab to limit their bleeding episodes [9].

Despite the fact that emicizumab's safety profile is largely favorable, the danger of thrombotic microangiopathy (TMA) remains a major cause for concern. TMA events have been reported only when high dosages of aPCC have been given alone or with rFVIIa [9]. We conducted the present study to evaluate the safety and efficacy of emicizumab prophylaxis in Egyptian patients with HA.

Materials and Methods

Study Population

This cohort study included 88 children diagnosed with congenital HA who were followed in the Hematology Clinic of the Pediatric Department in Zagazig University Hospitals from December 2020 to December 2021.

Patients were considered to be eligible for enrollment in the current work if they fulfilled the specified inclusion criteria: diagnosis of severe HA or moderate HA with severe bleeding profile and/or target joints; age of >1 year and <18 years; written informed consent granted by any of the parents or guardians.

All enrolled patients had complete history-taking with special emphasis on a detailed bleeding history; complete physical examination including vital signs and examinations of sites of bleeding and affected joints; calculation of the ABR before and after receiving emicizumab therapy; and recording of breakthrough bleeding episodes (numbers, severity, treatment given, and duration).

Treatment Protocols Before Emicizumab

All enrolled patients were previously treated with on-demand standard FVIII concentrate before starting emicizumab. The dose of FVIII was calculated in units/kg according to the site of bleeding. None of the patients had previously received standard FVIII replacement therapy as prophylaxis. The considered study period before patients were switched to emicizumab encompassed 1 year.

Treatment Protocol for Emicizumab Prophylaxis

All patients received emicizumab as a prophylactic therapy. It was administered subcutaneously in a dose of 3 mg/kg every week for one month (loading dose) followed by 3 mg/kg every two weeks (maintenance dose) for the remaining duration of the study period [10]. Emicizumab was administered in the outpatient hematology clinic under close medical supervision. In this study, emicizumab treatment was covered by health insurance, approved for patients older than 1 year, and provided in the course of regular clinical practice.

All study participants were followed for a period of one year and adverse events were reported in accordance with the standardized Medical Dictionary for Regulatory Activities by System Organ Class, while the toxicity grading scale of the World Health Organization was applied to determine toxicity grades [11].

Classification of Hemophilia Severity

The severity of HA was classified according to plasma levels of FVIII activity [12]. Plasma levels of FVIII activity of <1% indicated severe HA, levels of 1% to <5% indicated moderate HA, and levels of 5% to <40% indicated mild HA.

Definitions

Target joints were defined as single joints in which three or more spontaneous bleeds occurred within a consecutive 6-month period [12].

Muscle bleeds were defined as episodes of bleeding into a muscle, identified clinically and/or by imaging studies and generally associated with pain and/or swelling and limitation of movement [12].

Ethical Approval

This study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki, as revised in 2000. The study was approved by the Research Ethics Committee of the Faculty of Medicine of Zagazig University (protocol number: 8063, date: 01.12.2020). Written informed consent and/or assent was granted by any of the children's parents or guardians.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics 26 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as absolute frequencies. The Shapiro-Wilk test was used to verify assumptions for parametric tests. Quantitative variables were presented as medians and interquartile ranges. To compare the same variables between two points of time within the same group, the paired-samples t-test (for normally distributed data) or the Wilcoxon signed-rank test (for non-normally distributed data) was used. Statistical significance was accepted at $p<0.05$.

Results

In this prospective study, 88 children diagnosed with HA were analyzed. Their ages ranged from 2 to 15 years with a median age of 6 years. At diagnosis the median age was 3 months. Regarding initial clinical presentations, skin and subcutaneous bleeding was present in all patients. Joint bleeding was detected in 94% of patients, mucosal bleeding in 54.8% of patients, and muscle hematoma in 11.4% of patients. Furthermore, 92.2% of the patients had severe HA and 17% of the patients had positive FVIII inhibitors (Table 1).

Among the 94% of hemophilic patients with joint bleeds, 58% had one target joint, 36.4% had more than one target joint, and 5.6% had no target joint. The knee joint, elbow joint, and ankle joint were the most commonly affected joints (68%, 26%, and 25%, respectively) (Table 2).

The median ABR was 48 before treatment with emicizumab versus 0 after the use of emicizumab ($p<0.001$). The percentage reduction in ABR ranged from 95.8% to 100% with a median value of 100% (Figure 1). The median annualized joint bleeding rate was 36 before treatment with emicizumab versus 0 after the use of emicizumab ($p<0.001$), again with a median percentage reduction of 100%.

Only 8 patients suffered mild breakthrough bleeding episodes, including 5 patients with hemarthrosis, 2 patients with head hematoma, and 1 patient with epistaxis. All breakthrough bleeding episodes occurred after trauma. These cases were mild and improved with the infusion of a single dose of FVIII (Table 3). The head hematomas were external and not associated with any intracranial or subdural bleeding. Both head hematomas occurred in young children (ages of these patients: 3 and 4 years). All breakthrough bleeding episodes occurred in the maintenance phase of emicizumab at 1 to 3 days before the scheduled dose.

Table 1. Demographic, clinical, and laboratory characteristics of the analyzed patients.

Variable	Median (interquartile range)	Range
Age, years	6 (4-10)	2-15
Age at diagnosis, months	3 (1-6)	1-24
Initial clinical presentation	**No. of patients (n=88)**	**%**
Cutaneous hemorrhage	88	100
Joint hemorrhage	83	94.3
Mucosal hemorrhage	57	54.8
Muscle hemorrhage	10	11.4
Internal hemorrhage	0	0
Type of hemophilia A		
Moderate hemophilia	6	6.8
Severe hemophilia	82	93.2
Inhibitor status		
Negative	73	83
Positive	15	17

Table 2. Frequency of affected joints among hemophilia A patients.

Affected joints	Patients with hemophilia	
	n=88	%
Knee		
Unilateral	53	60.2
Bilateral	7	9.8
Elbow		
Unilateral	22	25
Bilateral	1	1.1
Ankle		
Unilateral	21	23.9
Bilateral	1	1.1
Wrist		
Unilateral	2	2.27
Bilateral	0	0
Hip		
Unilateral	5	5.6
Bilateral	0	0
Target joints		
One target joint	51	58
More than one target joint	32	36.4
No target joint	5	5.6

The most common adverse events were local reactions at the injection sites (19 patients, 21.6%), headache (12 patients, 13.6%), arthralgia (11 patients, 12.5%), fever (4 patients, 4.5%), and diarrhea (3 patients, 3.4%). All adverse events were tolerable and needed no treatment (Table 3). No thromboembolic events were observed in our study cohort.

There was no significant relationship between the severity of FVIII deficiency and percentage reduction of ABR or the incidence of breakthrough bleeding after emicizumab prophylaxis (p>0.05). Moreover, no significant relationship was found between FVIII inhibitor status and percentage reduction of ABR or the incidence of breakthrough bleeding after emicizumab prophylaxis (p>0.05).

Discussion

In this study, as initial presenting symptoms of HA, skin and subcutaneous bleeding occurred in all patients. Joint bleeding was observed in 94% of patients, mucosal bleeding in 54.8%, and muscle hematoma in 11.4%. Supporting our findings, Levy et al. [13] found that 163/193 (84%) of patients had bleeding episodes that primarily occurred in joints or muscles. Similarly, Callaghan et al. [14] reported that most bleeding episodes occurred in the joints and 61.0% of their hemophilia patients had target joints. Additionally, McCary et al. [15] found that 47.4% of their patients had mucosal bleeding and 36.8% had soft tissue/muscle bleeding.

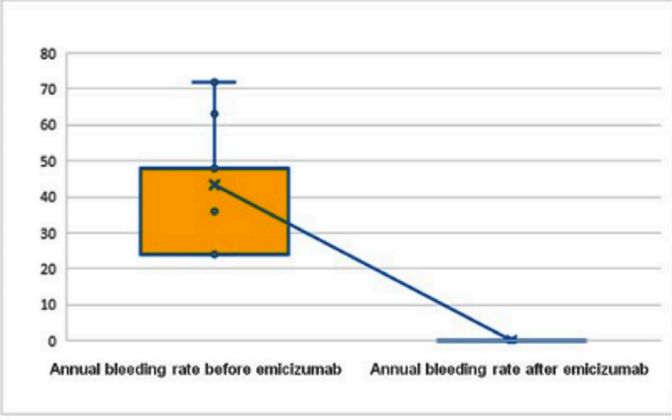

Figure 1. Boxplot showing annualized bleeding rates before and after therapy with emicizumab.

Table 3. Prevalence of breakthrough bleeding episodes and side effects in patients with hemophilia A receiving emicizumab prophylaxis.

Status during emicizumab treatment	n=88	%
No breakthrough bleeding Breakthrough bleeding	80 8	91 9
Sites of breakthrough bleeding	**n=8**	**%**
Hemarthrosis	5	62.5
Head hematoma	2	25
Epistaxis	1	12.5
Reported side effects during treatment with emicizumab		
Injection site reaction	19	21.6
Headache	12	13.6
Arthralgia	11	12.5
Fever	4	4.5
Diarrhea	3	3.4

In our study, 93.2% of the patients had severe HA while 6.8% had moderate HA. Furthermore, 17% of the studied patients tested positive for FVIII inhibitors. The incidence of inhibitors observed in our study can be compared to that in different studies. For example, Shah et al. [16] reported an inhibitor rate of 20.6% in their study cohort (50 out of 243 patients), while Gouw et al. [17] found FVIII inhibitory antibodies in 177 of 574 patients (cumulative incidence: 32.4%). In a large multicenter randomized controlled clinical trial conducted by Peyvandi et al. [18], the cumulative incidence of FVIII inhibitors was 26.8%. A lower incidence of FVIII inhibitors (8.7%) was reported by Kim and You [19].

Approximately 80% of bleeding episodes in patients with hemophilia are intraarticular in nature, two-thirds of which are reported in the knees, elbows, or ankles [20]. In the current study, joint bleeding was observed in 94% of the study population. Among those, 58% had one target joint, 36.4% had more than one target joint, and 5.6% had no target joints. The knee joint, elbow joint, and ankle joint were the most commonly affected joints (68%, 26%, and 25%, respectively). In a large study conducted by Reding et al. [21], a total of 113 target joints were reported among 59 patients. The most common sites were the ankles, elbow and knees (47, 33, and 27 target joints respectively). Moreover, Abdelwahab et al. [22] reported that most of their patients had 3 or 4 target joints.

In Egypt, the health insurance system recently approved emicizumab for young children with HA as primary prophylaxis. It was previously only given to patients with inhibitors. Thus, data about the experience of emicizumab usage in previously untreated Egyptian patients are extremely limited. For this study, the median ABR was 48 before starting emicizumab prophylaxis. The higher ABR in our study compared to previous reports could be attributed to a variety of factors, the most important of which are the limited supply of FVIII concentrates at some points in time, the lack of home therapy, and higher rates of trauma patients presenting to our center.

We observed successful reduction of the ABR for patients receiving emicizumab as the median ABR was 48 before using emicizumab and 0 after the use of emicizumab (p<0.001). The percentage reduction in ABR ranged from 95.8% to 100% with a median value of 100%. Only 8 patients (9%) experienced

mild breakthrough bleeding episodes, including 5 patients with hemarthrosis, 2 with head hematoma, and 1 patient with epistaxis. These cases were mild and the patients improved with a single-dose infusion of FVIII.

In line with our results, Oldenburg et al. [23] evaluated 109 HA patients with inhibitors in the HAVEN 1 study and reported that the ABR was 2.9 events (95% confidence interval [CI]: 1.7-5.0) among patients randomly allocated to receive emicizumab as a prophylaxis therapy (group A, 35 participants) versus 23.3 events (95% CI: 12.3-43.9) among those assigned to receive no emicizumab prophylaxis (group B, 18 participants). This constituted a significant difference of 87% for patients who received emicizumab prophylaxis ($p<0.001$) [23].

Similarly, in a comparative study of adolescents with HA without FVIII inhibitors receiving an emicizumab maintenance dose of 1.5 mg per kilogram of body weight per week (group A), an emicizumab maintenance dose of 3.0 mg per kilogram every 2 weeks (group B), or no prophylaxis (group C), Mahlangu et al. [24] found that the ABR was 1.5 events (95% CI: 0.9-2.5) in group A and 1.3 events (95% CI: 0.8-2.3) in group B compared to 38.2 events (95% CI: 22.9-63.8) in group C. Thus, the rate was 96% lower in group A and 97% lower in group B ($p<0.001$ for both) compared to group C. A total of 56% of patients in group A and 60% in group B had no bleeding events and required no treatment, while all patients in group C developed attacks of bleeding requiring treatment [24].

In a phase 3 open-label, two-stage multicenter study (HAVEN 4) conducted for the evaluation of the efficacy and safety of emicizumab prophylaxis, Pipe et al. [25] found that the ABRs for all treated bleeds, treated spontaneous bleeds, treated joint bleeds, and treated target joint bleeds were all significantly lower for patients receiving emicizumab prophylaxis in comparison to those not receiving prophylaxis.

Shima et al. [26] conducted a multicenter open-label study (HOHOEMI) including young Japanese hemophilia patients aged less than 12 years who had no FVIII inhibitors. They divided the study participants into two cohorts based on the maintenance dose of emicizumab prophylaxis, which was either 3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks for emicizumab prophylaxis. The ABRs for treated bleeding events were 1.3 (95% CI: 0.6-2.9) and 0.7 (95% CI: 0.2-2.6), respectively. They concluded that emicizumab prophylaxis was preferred by all caregivers in comparison to the previous treatment [26].

Callaghan et al. [14], in a study conducted to evaluate the long-term outcomes of emicizumab prophylaxis for patients with HA from the HAVEN 1, 2, 3, and 4 studies with or without FVIII inhibitors, reported that the ABR for treated bleeds was 1.4 (95% CI: 1.1-1.7). ABRs decreased and then stabilized at values of <1 according to an analysis based on 24-week treatment intervals. The mean ABR for treated bleeds was 0.7 (95% CI: 0-5.0). It was further reported that 82.4% of the patients had no treated bleeds, 97.6% had ≤3 treated bleeds, and 94.1% had no treated target joint bleeds. They concluded that target joint bleeding was markedly declined with emicizumab prophylaxis [14].

In line with our results, Abdelwahab et al. [22] found that the initial bleeding rate ranged from 6 to 8 events/year in their prospective cohort study on severe HA patients. The bleeding rate was 0 in 11 (78.6%) patients after 6 months of prophylactic emicizumab treatment. Three patients developed a minimum of one breakthrough bleeding episode but none of it occurred in target joints.

Another single-center retrospective study conducted by Hassan and Motwani [27] on severe HA patients regardless their inhibitor status showed that 56.8% (29/51) of the patients developed no bleeding episodes after receiving emicizumab and 80.3% (41/51) experienced no major treated bleeds during their follow-up period. A total of 29.4% (15/51) developed minor bleeds which recovered spontaneously or with the use of antifibrinolytics. Overall, 19.6% (10/51) of the patients received an additional dose of FVIII to inhibit or stop breakthrough bleeding.

These data are further supported by the study conducted by Young et al. [28], who investigated emicizumab prophylaxis in 85 patients diagnosed with HA with positive FVIII inhibitors in HAVEN 2, a phase 3 trial. The patients were treated with subcutaneous emicizumab at 1.5 mg/kg weekly (group A), 3 mg/kg every 2 weeks (group B), or 6 mg/kg every 4 weeks (group C). The ABRs for treated bleeds were 0.3, 0.2, and 2.2 in group A, group B, and group C, respectively, reflecting a 99% reduction in ABRs. Furthermore, 77% of the patients had no treated bleeding events. The results of different studies on the efficacy of emicizumab are summarized in Table 4.

In the present study, the most common adverse events were local reactions at the injection sites (19 patients, 21.6%), headache (12 patients, 13.6%), arthralgia (11 patients, 12.5%), fever (4 patients, 4.5%), and diarrhea (3 patients, 3.4%). All adverse events were mild and resolved with no treatment. No thromboembolic events were observed in our cohort study and no antidrug antibodies were detected.

Pipe et al. [25] reported that the most commonly observed treatment-related adverse events were injection-site reactions (9 of 41 patients, 22%). Furthermore, no thrombotic events were observed and no patients developed de novo antidrug antibodies with neutralizing potential or FVIII inhibitors [25].

Oldenburg et al. [23] reported 198 treatment-related adverse events in 103 patients on emicizumab prophylaxis, the most frequent of which were injection-site reactions (15% of

Table 4. Results of different studies regarding the efficacy of emicizumab in hemophilia patients.

Authors	Number of patients with on-demand therapy before emicizumab	Number of patients on prophylactic therapy before emicizumab	Number of patients with FVIII inhibitors	Number of patients without FVIII inhibitors	ABR after emicizumab, mean	AJBR after emicizumab, mean	% of patients with no bleeding after emicizumab	% reduction of ABR after emicizumab
Oldenburg et al. [23], 2017	109	0	109	0	2.9	NE	63	79
Mahlangu et al. [24], 2018	152	0	0	152	1.3	NE	60	68
Pipe et al. [25], 2019	41	0	41	0	4.5	1.7	56.1	NE
Shima et al. [26], 2019	0	12*	0	13	14.2	0.9	53.8	NE
Callaghan et al. [14], 2021	353	0	305	48	1.4	NE	82.4	NE
Young et al. [28], 2019	22	66	85	3	0.2	NE	90	99

*One patient (an infant) did not receive any factor VIII. FVIII: Factor VIII; ABR: annualized bleeding rate; AJBR: annualized joint bleeding rate; NE: not estimated.

patients). TMA and thrombosis were reported in 2 patients; those patients had received multiple infusions of aPCC for breakthrough bleeding episodes. No antibodies were detected.

Young et al. [28] found that commonly observed adverse events in their study were injection-site reactions and nasopharyngitis but no thrombotic events were reported. Two of 88 patients developed antidrug antibodies with neutralizing potential associated with decreased emicizumab plasma concentrations. One of those patients experienced loss of efficacy. In the second case, the antidrug antibodies resolved over time with no need for intervention and no breakthrough bleeding occurred [28].

Finally, Callaghan et al. [14] documented in their study that emicizumab had a consistently appropriate long-term safety profile with no unpredicted or new safety issues. No fatalities or TMA events were documented across the HAVEN 1, 2, 3, and 4 studies beyond those described by Oldenburg et al. [23] in the primary analysis conducted for HAVEN 1. Four thromboembolisms were reported, 2 of which (cavernous sinus thrombosis and skin necrosis/superficial thrombophlebitis) were associated with concomitant aPCC use during HAVEN 1. Of the 2 cases not associated with concomitant aPCC, device occlusion was reported in HAVEN 1 in weeks 25-48 for one patient and acute myocardial infraction was reported in HAVEN 3 in weeks 145-168 for one patient. During the HAVEN 1 study, the presence of TMA and thromboembolism was associated with concomitant administration of high doses of aPCC [14].

Study Limitations

One of the main limitations of our study was that it included only pediatric patients with HA. This was because those patients were all covered by health insurance. Another limitation was that our patients received on-demand FVIII replacement therapy before being switched to emicizumab prophylaxis. Larger multicenter studies including patients receiving prophylactic FVIII replacement therapy who will be switched to emicizumab prophylaxis should be conducted.

Conclusion

In the current study, the safety and efficacy of emicizumab were found to be consistent with those reported in previous studies of HA. Emicizumab was effective in terms of reducing the ABR, as the majority of patients developed no bleeding episodes necessitating treatment. Emicizumab also demonstrated a preferable safety profile with no need for discontinuations due to adverse events. Emicizumab prophylaxis seems to be an effective and safe treatment modality for patients with HA.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki, as revised in 2000. The study was approved by the Research Ethics Committee of the Faculty of Medicine of Zagazig University (protocol number: 8063, date: 01.12.2020).

Informed Consent: Written informed consent and/or assent was granted by any of the children's parents or guardians.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: T.H., M.Z., M.F., A.F., E.A., D.G., M.A.H.; Concept: T.H., M.Z., M.F., A.F., E.A., D.G., M.A.H.; Design: T.H., M.Z., M.F., A.F., E.A., D.G., M.A.H.; Data Collection or Processing: T.H., M.Z., M.F., A.F., E.A., D.G., M.A.H.; Analysis or Interpretation: T.H., M.Z., M.F., A.F., E.A., D.G., M.A.H.; Literature Search: T.H., M.Z., M.F., A.F., E.A., D.G., M.A.H.; Writing: T.H., M.Z., M.F., A.F., E.A., D.G., M.A.H.

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