ARTICLE

PREVALENCE OF CUTANEOUS LESION OF CLOPIDOGREL AND MANAGEMENT WITH ANTIHISTAMINE

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ABSTRACT

Background: *Hypersensitivity reactions to clopidogrel are complicated reaction and difficult to management.* ***Objectives:*** *The aim of this study was to describe Prevalence of cutaneous lesion of clopidogrel and manage of it.* ***Methods:*** *Patient's received clopidogrel evaluated for cutaneous manifestation. If diagnose established they received oral antihistamine.* ***Results:*** *Twenty five patients representing 1.4% of the patients receiving clopidogrel developed cutaneous lesion during the study period. The mean age was 57 ± 6 years, 58% of patients were male, and 20% reported prior adverse drug reaction. Cutaneous lesions are manifested as generalized exanthema in 84%, localized skin reaction in 12%, and urticarial in 4% of patients. Complete resolution of cutaneous lesion was observed in 61 patients [96%] with a short course of oral antihistamine.* ***Conclusions:*** *Cutaneous lesion of clopidogrel is manifested commonly as generalized exanthema. This can be managed with oral antihistamine.*

KEY WORDS

Clopidogrel, cutaneous lesion, antihistamine

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INTRODUCTION

Background: Clopidogrel is an oral thienopyridine widely used in the management of patients with cardiovascular disease [1–3]. In addition, long-term administration of clopidogrel with aspirin is recommended after discharge from cardiac care unit due to acute coronary syndrome [4,5]. Development of hypersensitivity reactions after clopidogrel administration is a recognized complication and is difficult to manage. The characteristics and prevalence of clopidogrel hypersensitivity are poorly understood, and treatment options remain limited. In this report, we characterize prevalence and morphological features of clopidogrel hypersensitivity and describe successful resolution with oral antihistamine. The aim of this study is Prevalence of cutaneous lesion of Clopidogrel and Management with Antihistamine

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MATERIALS AND METHODS

Patients

Twenty five patients with suspected clopidogrel hypersensitivity after discharge from cardiac care unit due to acute coronary syndrome at Emam Reza Hospital from March 2016 to March 2017 were included and evaluated. Detailed history and physical examination were performed. All patients diagnosed with clopidogrel hypersensitivity were prescribed a 1-week course of oral antihistamine [cetirizine] with10 mg twice per day. Long-term follow-up was completed in all patients by office visit. Written consent was taken from each subject and the study was approved by the hospital authority.

Hematologic analysis

Complete blood counts with automated differential for leukocyte, lymphocyte, eosinophil, and platelet count were obtained before initiation of clopidogrel therapy and repeated after complete resolution.

Statistical analysis

Continuous data are expressed as mean ± SD, and dichotomous data are expressed as absolute values and percentages. All analyses were performed using SPSS version 17. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 25 patients were referred and evaluated for clopidogrel hypersensitivity during the study period. This represented 1.4% [25 of 3,500] of the patient population undergoing discharge from cardiac care unit due to acute coronary syndrome during the study period. Baseline and procedural characteristics of the patients are shown in [Table 1]. The information for presence of asthma, family history of allergy, and prior drug allergy in individual patients was not systemically collected except for patients presenting with clopidogrel hypersensitivity. There were no significant differences in cardiac risk factors, concurrent medications, and procedural variables between patients with clopidogrel hypersensitivity and the entire patient admitted in cardiac care unit.

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Clinical outcomes

Clinical follow-up was completed in all patients for a median of 100 days. During follow-up, there was 1 target vessel revascularization procedures in patients who underwent percutaneous coronary intervention. No patient died. All patients had completed the minimum recommended duration of clopidogrel therapy.

Table 1: Demographic characteristic

	Patient with cutaneous lesion
Baseline characteristics	
Age, yrs	57 ± 6
Female	11 [44%]
Diabetes	8 [32]
Hypertension	9 [36]
Dyslipidemia	10 [40]
Prior drug allergy	5 [20]

Clinical manifestations of clopidogrel hypersensitivity

Patients with clopidogrel hypersensitivity presented with 3 distinct clinical patterns. Category 1 contained 21 patients [84%] who developed a generalized, pruritic, exanthemata's rash predominantly affecting the trunk with or without involvement of the upper and lower extremities. The rash was limited to the chest, abdomen, and back in 18[86%] and extended to the proximal part of the upper and lower extremities in 4 patients [14%]. Category 2 consisted of 3 patients [12%], in whom the rash was limited to a localized area. These reactions involved the neck, face, back, axilla, palm of the hand, and/or sole of the feet. Category 3 had 1 patients [4%]; with generalized urticarial. The median time to development of clopidogrel hypersensitivity after clopidogrel use was 6 ± 1 days for category 1, 4 ± 3 days for category 2, and 2 ± 1 days for category 3 [p = 0.01].All patients were able to eat antihistamine as prescribed, and all patients report improvement at 5 ± 2 days. The patient with urticarial was prescribed oral steroids. All patients were able to continue clopidogrel for the recommended duration without recurrence of clopidogrel hypersensitivity.

DISCUSSION

The main findings of the present study were that clopidogrel hypersensitivity in most patients was characterized by a generalized exanthemata's rash. Patients with allergic reactions after PCI present difficulty in diagnosis and management. Many patients first have exposure to contrast media and then more recent initiation to standard therapy for coronary artery disease including statins, angiotensin-converting enzyme inhibitors, aspirin, and clopidogrel. No specific assays are available for confirming most drug-induced allergic reactions. In view of these limitations, detailed history of exposure and timing of allergic manifestations is critical for appropriate diagnosis and management.

Clopidogrel is a platelet adenosine diphosphate receptor antagonist that inhibits platelet aggregation by irreversible binding of its active metabolite to the P2Y12 receptor, and it has been shown to reduce adverse cardiac events in patients with both ST and non–ST-segment elevation myocardial infarction [1, 2]. Clopidogrel hypersensitivity is a recognized complication of clopidogrel therapy and presents difficulty in management. The potential ways to manage patients with clopidogrel hypersensitivity include clopidogrel desensitization or treatment with ticlopidine or possibly prasugrel. However, alternative therapy with ticlopidine and prasugrel may not be suitable for all patients because of allergenic cross-reactivity [6, 7] and potential for serious side effects [8–11]. In addition, clopidogrel desensitization as reported previously may not be suitable after PCI because of the need for drug discontinuation and lack of well-defined criteria for selection of patients [8-10].

Adverse drug reactions are classified as type A for predictable reactions related to pharmacological activity of a drug and type B for unpredictable and rare hypersensitivity reactions. Although diverse manifestations for clopidogrel-related type B hypersensitivity, including urticaria [11], angioedema [12], arthritis [13, 14], serum sickness–like reaction [15], and fixed drug reactions [16], have been reported, cutaneous reactions remain the most common presentation.

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Diagnostic confirmation of drug hypersensitivity reactions in clinical practice is difficult because challenge and drug-specific testing are not routinely employed. Drug allergy testing with skin prick and intradermal challenge has been standardized for several drugs responsible for immediate hypersensitivity reactions, but the use of patch testing as a means of controlled challenge in patients with delayed-onset drug hypersensitivity is not widely used. The administration of a single course of oral steroids resulted in complete resolution of clopidogrel hypersensitivity in all but one patient and offers an important treatment option for patients requiring prolonged clopidogrel therapy without drug discontinuation, switching, or desensitization. Furthermore, the steroids were effective in alleviating clopidogrel hypersensitivity in patients presenting with cutaneous manifestations, urticarial, or angioedema. The mechanism of action for successful treatment of clopidogrel hypersensitivity by oral steroids is unclear but is likely related to suppression of the immune response followed by development of immunologic tolerance in sensitive individuals. In our study we treat patients with antihistamines successfully.

CONCLUSIONS

Clopidogrel hypersensitivity was commonly manifested by a generalized exanthemata's eruption. The manifestations of clopidogrel hypersensitivity were successfully treated with an antihistamine.

CONFLICT OF INTEREST

There is no conflict of interest.

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