

Incidence of Major Drugs-Allopurinol, Phenytoin, Carbamazepine-induced SCARs in Korea

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Background/Aims: It is known that allopurinol, phenytoin, carbamazepine are the major drugs causing severe cutaneous adverse drug reaction (SCARs). There have been no studies to date on the incidence of major drugs on severe cutaneous adverse drug reaction in Korea. **Methods:** We used a national medical insurance review system (Health Insurance Review and Assessment) database which contained the claim data of the entire nation from 2010 to 2016. The target population was classified into three categories: allopurinol user (AU), phenytoin user (PU), carbamazepine user (CU). The diagnostic codes of L270 (drug reaction with eosinophilia and systemic symptoms; DRESS), L511 (Stevens-Johnson syndrome, SJS) or L512 (toxic epidermal necrolysis, TEN) from the International Classification of Diseases-10th revision were used to define the case. **Results:** The incidence rates (per 1000 person years) for DRESS and SJS plus TEN in AU were 1.97 and 0.33, respectively. Meanwhile, 6.20 (DRESS) and 0.44 (SJS + TEN) in PU and 2.55 (DRESS) and 0.27 (SJS + TEN) in CU. The hazard ratio (SJS + TEN) was 0.6020 (95% CI, 0.5921 ~ 0.6124) for PU vs AU and 0.6752 (95% CI, 0.6671 ~ 0.6840) for CU vs AU. **Conclusions:** We confirmed that the incidence of major drugs-Allopurinol, Phenytoin, Carbamazepine-induced SCARs ranged 1.97 ~ 6.20 for DRESS and 0.27 ~ 0.44 for SJS + TEN in Korea based on the nationwide population-based database.

Drug	Outcome	Total of person years (PYs)	No. of cases	IR per 1000 PYs (95%CI)	IR difference (vs allopurinol) per 1000 PYs
Allopurinol	ALL SCARs	853434.29	1954	2.3071 (2.3039 ~ 2.3104)	
	SJS/TEN	853434.29	283	0.3311 (0.3299 ~ 0.3324)	
	DIHS/DRESS	853434.29	1671	1.9751 (1.9721 ~ 1.9780)	
Phenytoin	ALL SCARs	24512.09	163	6.6498 (6.6176 ~ 6.6821)	-4.34263
	SJS/TEN	24512.09	11	0.4465 (0.4382 ~ 0.4549)	-0.11534
	DIHS/DRESS	24512.09	152	6.1992 (6.1681 ~ 6.2305)	-4.22417
Carbamazepine	ALL SCARs	750626.92	2108	2.8216 (2.8178 ~ 2.8254)	-0.51449
	SJS/TEN	750626.92	203	0.2699 (0.2688 ~ 0.2711)	0.06121
	DIHS/DRESS	750626.92	1905	2.5507 (2.5471 ~ 2.5543)	-0.57563

IgE Mediated Anaphylaxis to Clavulanate: Case Report

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A 24-years-old woman was referred to the emergency department (ED) after 30 minutes since administration of combination agent of amoxicillin and clavulanate (AMX/ CLV). Her chief complaint was angioedema, urticaria, dyspnea, and abdominal pain. She had no personal or family history of allergic disease. Blood pressure of 104/62mmHg, pulse rate of 170/min, and respiratory rate of 24/min without fever were observed. Congested throat was observed. In the ED, systemic corticosteroids and anti-histamine were administered intravenously along with fluid resuscitation and she was completely recovered. Adverse drug reaction and anaphylaxis to AMX/ CLV were suspected. Specific serum IgE of Amoxicilloyl was not detected. A Skin prick test (SPT) was performed with AMX and CLV separately and SPT was only positive in CLV. CLV allergy was highly suspected. Thus, basophil activation test (BAT) was performed additionally as a safe diagnostic tool in order to find more definite culprit. BAT was performed with AMX and CLV. The result was positive to CLV. Finally an oral drug provocation test (OPT) was performed for confirmative diagnosis. OPT was only positive with CLV. Initially 20mg of CLV was administered. Additional doses of 30mg were administered after 30 minutes interval. 20 minutes after administration of last dose, cumulative dose 50mg, she developed anaphylaxis with numbness of finger tips, angioedema, urticaria and dyspnea with wheezing. As a result, she was diagnosed with CLV allergy with anaphylaxis and received a card reporting the adverse drug reaction and anaphylaxis. Also, she was prescribed an auto-injectable epinephrine for emergencies. Most common form of CLV is combined with AMX. Anaphylaxis due to the administration of AMX is considered relatively common but rare in CLV. In case of drug allergy after taking AMX/ CLV, it needs to consider CLV allergy as well.

Figure 1. Wheal induced by skin prick test (A) and oral provocation test (B)

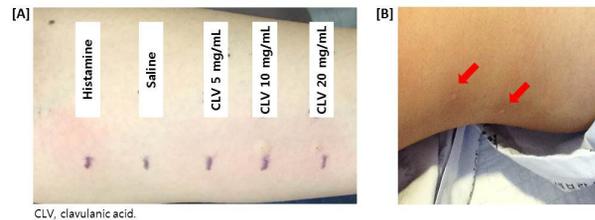


Figure 2. Basophil activation test using clavulanate and amoxicillin

