PP080. Adverse Drug Events in Hospitalized Patients with Acetaminophen Overdose Treated with Intravenous N-Acetylcysteine

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Objectives: Intravenous N-acetylcysteine (IV-NAC) is widely recognized as the antidote of choice for acetaminophen overdose.[1] However, its use is not without adverse drug reactions (ADR) which might affect therapeutic outcome or lead to treatment delay.[2,3] The aims of this study were to investigate the type and incidence of ADR induced by IV-NAC in patients treated for acetaminophen overdose and to assess the causality of individual ADR to IV-NAC using Naranjo's algorithm.[4]

Methods: This is a retrospective study of patients admitted to the hospital for acute acetaminophen overdose over a period of 5 years (January 1, 2004 to December 31, 2008). The primary outcome of interest in this study was the occurrence of ADR during NAC administration. The probability of an ADR was assessed using the Naranjo algorithm, which consists of 10 questions), and has been used to determine the likelihood that an ADR was related to a specific medication. The Naranjo score takes into account other possible influences such as drugs or disease. The association scores were: ≥9 = "definite", 5 to 8 = "probable", 1 to 4 = "possible" and 0 = "doubtful".[4]

Results: During the study period, 305 patients with a diagnosis of overdose of paracetamol-containing compounds were admitted to the hospital for monitoring and treatment. Different types of ADR occurred in 137 patients (137/305; 44.9%). Of those patients who had an ADR, 98 (98/137; 71.5%) had been treated with IV-NAC and 39 (39/137; 28.5%) had not ($p < 0.001$). Comparison of different ADR in all patients showed that the following ADR were significantly associated with IV-NAC administration: nausea ($p = 0.004$), vomiting ($p < 0.001$), flushing ($p < 0.001$), rash ($p < 0.001$), pruritus ($p < 0.001$), chest pain ($p = 0.001$), bronchospasm ($p = 0.015$), coughing ($p = 0.017$), headache ($p < 0.001$), dizziness ($p < 0.001$), convulsion ($p = 0.035$) and hypotension ($p = 0.001$). Based on Naranjo's algorithm, 226 events were judged to be NAC-related – 31.1% probably and 67.9% possibly drug-related. None of the events were definitely drug-related (table I).

Table I. Causality assessment of individual adverse drug reactions to intravenous N-acetylcysteine by Naranjo's algorithm

Clinical features	Number of ADRs				
	Doubtful	Possible	Probable	Definite	Total
Nausea	-	34	-	-	34
Vomiting	-	30	-	-	30
Flushing	-	-	22	-	22
Rash	-	-	17	-	17
Pruritus	-	-	12	-	12
Chest pain	-	3	13	-	16
Bronchospasm	-	3	8	-	11
Coughing	-	9	-	-	9
Headache	-	34	-	-	34
Dizziness	-	27	-	-	27
Convulsion	-	3	-	-	3
Hypotension	-	9	2	-	11
Total (%)	0 (0.0)	152 (67.3)	74 (32.7)	0 (0.0)	226

Conclusions: Adverse drug reactions to IV-NAC were common among patients with acetaminophen overdose but mostly minor, and that all reported adverse reactions were easily managed.

References

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PP081. "Serious" Cutaneous Reactions with Protein Kinase Inhibitors

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Objectives: Results from EMIR study (Effets indésirables Médicamenteux Incidence et Risque), performed in 2007 in France, showed that the incidence of Adverse Drug Reactions (ADRs) who required hospital admission was the highest with vitamin K antagonists and then antineoplastic drugs.[1] Currently, several antineoplastic drugs, orally administered, could be taken at home (ambulatory care). As far as we know, no study described "serious" ADRs with these specific antineoplastic drugs. By using data of spontaneous reporting in France, we aimed to detect, quantify and analyze characteristics of "serious" ADRs related to oral antineoplastic agents use.

Methods: We used the French Pharmacovigilance Database to select "serious" ADR reported from 1st January 2008 to 31st December 2009 with all oral antineoplastic drugs. A "serious" ADR was defined as any untoward medical occurrence that at any dose results in death, requires hospital admission or prolongation of existing hospital stay, results in persistent or significant disability/incapacity or is life threatening.

Results: We found 589 cases of "serious" ADRs with antineoplastic drugs orally administered as "suspect" drugs. Protein kinase inhibitors (PKI) were most frequently involved drugs (271 cases, 46%) with 383 "serious" ADRs reported. "Serious" ADRs with PKI were various but most of them were cutaneous (19%) and particularly skin eruptions (51%, without Stevens-Johnson Syndrome) followed by hand-foot syndrome (18%). Risk to present "serious" cutaneous ADRs was highest in men (62%), in patients 61 years old or exposed to sorafenib (45%). PKI was withdrawn in almost half of patients (43%). Most of patients received a symptomatic treatment (78%). Evolution was favourable in 58% of cases.

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