

Age-specific Contraindication of Therapeutics

Eun Sook Lee

Department of Pharmacy, Seoul National University Bundang Hospital

On the January 16th, 2004, the Korean Ministry of Health and Welfare announced a list of therapeutics that potentially has general and age-specific contraindications. The list consists of 162 combinations of therapeutics that may cause drug interactions leading to an increase in the frequency of adverse drug events or a decrease in therapeutic effectiveness. Previous to the announcement, a guideline for the evaluation committee for drug use was established in an attempt to promote appropriate use of drugs and to discuss such issues as identification of drug interaction based on the drug evaluation report, the determination of proper dosage for specific patient groups (e.g. adult, pediatric and geriatric patients), the duration of therapy, the impact of poly-pharmacy on the therapeutic outcome, the scope of contraindications (e.g., in the presence of the underlying disease or the pregnancy and the dependency of the age of the patient) and the guideline for the allowance in the treatment. Accordingly, the ministry established the "Evaluation Committee for Drug Use" in the Health Insurance Review Agency of Korea to finalize and re-evaluate the scopes. In general, since the incidence of inappropriate prescription is likely to be diminished with a proper evaluation of drug use, which will be leading ultimately to the optimization of pharmacotherapy and promotion of the safety of the patient, computer based monitoring system is apparently required for the effective evaluation of drug use. In the announced list of contraindications, 10 items [diazepam, ketoprofen, lorazepam, sulfamethoxazole/trimethoprim, topiramate, zolpidem, ketorolac, clobetasol (topical formulation), fluticasone (topical formulation)] were specifically included as the contraindication for pediatric patients under 1 year old (Table 1). More recently (March 10, 2005), the ministry added 14 items to the age specific list for contraindications. Particularly, a significant number of items was related to formulations containing benzyl alcohol (i.e., pharmaceutical excipients) or thimerosal (i.e., the preservative). Despite the fact that the ministry is likely to expand the list for contraindications, the recent update in the list apparently suggests the necessity of the detailed categorization of patient groups (e.g., infants, children, young adult) in the evaluation of drug usage. Furthermore, age-specific contraindications in other age groups such as infants and geriatric patients may be studied and identified, considering the fact that these groups may be associated with the alteration in the rate of drug metabolism and, ultimately, potentially increased frequency of adverse effect of drugs.

Considering the fact that the Korean society has an increasing rate of people with advanced age, the identification of age-specific contraindication, especially for geriatric patients, is likely to be socially relevant.

Table 1. Summary of age-specific contraindications announced by the Korean Ministry of Health and Welfare

Item number	Drug	Age	Note
1	benzonatate	Under 7 years old	
2	clobetasol propionate	Topical solution : Under 1 year old	
3	diazepam	Tablet : Under 6 months old Parenteral : Under 4 weeks old	○
4	fluticasone propionate	Cream : Under 2 years old	
5	ketoprofen	Parenteral : Under 4 weeks old	
6	ketorolac tromethamine	Parenteral: Under 2 years old Tablet : Under 17 years	
7	lorazepam	Parenteral : Under 4 weeks old	○
8	sulfamethoxazole, trimethoprim	Under 4 weeks old	○
9	topiramate	Under 2 years old	○
10	zolpidem	Under 16 years old	

Note: '○' mark indicates under review by the Evaluation Committee for Drug Use

Table 2. The recent addition in the list of age-specific contraindication by the Korean Ministry of Health and Welfare

Item number	Drug	Age	Note
11	acetaminophen (for sustained release formulation only)	Under 12 years old	Sustained release tablets for acetaminophen should not be administered for patients less than 12 years old.
12	aloxiporin	Under 15 years old	

13	benorylate	Under 13 years old	
14	butorphanol tartrate	Under 19 years old	Safety of the drug has not been studied for patients less than 18 years old – CCIS
15	diclofenac (sodium or □-dimethyl-aminoethanol salts) (Containing benzyl alcohol in the parenteral formulation)	Under 4 weeks old	Normally, benzyl alcohol is detoxified by the oxidation to benzoic acid. However, the metabolic process is not properly developed in premature infants. Aromatic alcohol typically produces severe neurological effects.
16	hydroxocobalamin (Containing benzyl alcohol in the parenteral formulation)	Under 4 weeks old	See note in item number 15
17	lornoxicam	For parenteral formulation under 19 years old or over 65 years old For tablets, under 19 years	Lornoxicam may not be administered to patients less than 18 years old.
18	meloxicam	Under 19 years old	Meloxicam may not be administered to patients less than 5 years old
19	piroxicam (β-cyclodextrin, potassium salt) (Containing benzyl alcohol in the parenteral formulation)	Under 4 weeks old	Per the manufacturer, dosage recommendations have not been established in children. When the parenteral formulations contain benzyl alcohol, the fact of the age-specific contraindication has to be clearly stated.
20	pyrazinobutazone	Under 15 years old	

21	sodium aurothiomalate (Containing benzyl alcohol in the parenteral formulation)	Under 4 weeks old	When the parenteral formulations contain benzyl alcohol, the fact of the age-specific contraindication has to be clearly stated.
22	sulpyrin	Under 12 years old	
23	talniflumate	Under 13 years old	Talniflumate may not be administered to patients less than 13 years old because the dosage recommendation was not set in the pediatric patients.
24	trometamol tiaprofenate	Under 3 years old	