Drug Safety in Children – Identification of Drugs with High Concern

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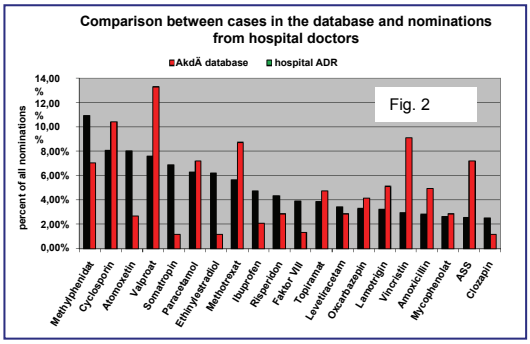
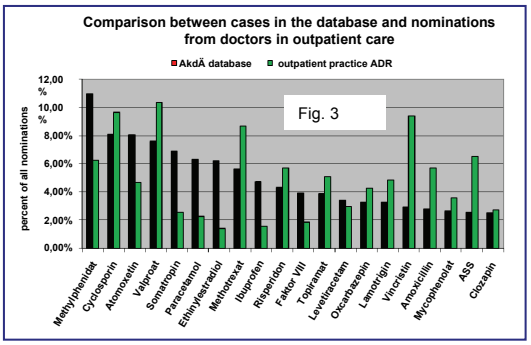
Introduction: Drug treatment in pediatric population is a therapeutic challenge. Children are not simply scaled down adults (see Fig. 1).
Aim of the study presented here was to get more insight into the problems of treating pediatric patients and to identify drugs with a potential for side effects. This study was undertaken within the framework of a project (AMTS) devoted to the safe therapeutic handling of drugs which is initiated by the Ministry of Health and has its secretariat in the Drug Commission of the German Medical Association (AkdÄ) to identify drugs for which more information should be provided how to handle them in order to avoid adverse effects.

Method: We undertook (1) a search in the adverse drug reaction database jointly hold by the Federal Institute for Drugs and Medical Devices und the Drug Commission of the German Medical Association to identify the drugs with side effects in children (the database contains cases from spontaneous reports since 1995) and (2) we did sent out a standardised questionnaire to 10% of all pediatricians in private practice in Germany selected at random (n = 658) as well as all heads of pediatric units in hospitals (n = 343) asking about drugs they experienced problems and side effects in their patients. We used the WHO definition for characterising an adverse reaction: an adverse drug reaction is a response to a drug whic is noxious and unintended and which occurs at doses normally used in man. A serious adverse reaction is any untoward medical occurrence that at any dose results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity or is congenital malformation/birth defect (EMA).





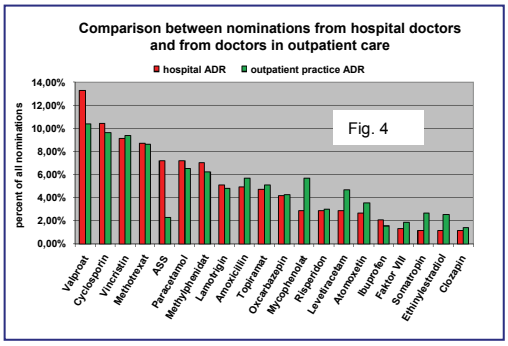
Results The search in the side effect database resulted 177 drugs. The rank order of the drugs with reports in the database is given stratified according to age ranges in table 1. It is different in different age groups and represents the therapeutic use of drugs in the age range, e.g. ethinylestradiol in female adolescents and the special therapeutic situation, e.g. morphine in neonatal intensive care units.
We stratified also according to the severity and sorted out cases with fatal outcome. Table 2 gives the drugs with fatal outcome of the cases reported in the database.
The results from the questionnaire showed some difference as compared to the search in the AkdÄ database. Compared to the rank order in the database the pediatricians working either in hospitals or in private praxis ranked cyclosporin, valproate, methotrexate, vincristine and ASS higher whereas methylphenidate was judged to represent a less serious problem in handling the drug (Fig. 2, Fig. 3 and Fig. 4).

age range	0–28 days	29 days–3 years	3–12 years	12–18 years
rank order				
1	Ibuprofen	Cefuroxim	Methyl-phenidat	Ethinyl-estradiol
2	Zidovudin	Clarithro-mycin	Ato-moxetin	Methyl-phenidat
3	Morphine	Cyclosporin	Soma-tropin	Paracetamol
4	Methylpred-nisolon	Valproat	Valproat	Somatropin
5	Surfactant	Topiramat	Cyclo-sporin	Risperidon

Table 1: Rank order according to the number of reports in the database

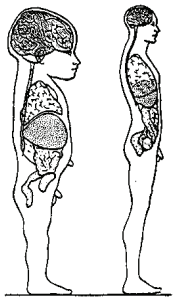
age range	0–28 days	29 days–3 years	3–12 years	12–18 years
rank order				
1	Ibupro-fen	Vincri-stine	Metho-trexat	Metho-trexat
2	Surfac-tant	Clarithro-mycin	Vincri-stine	Vincri-stine
3	No cases	Cyclo-sporin	Cyclo-sporin	Cyclo-phos-phamide

Table 2: Rank order according to the number of reports with fatal outcome in the database



Conclusion: For drugs with an cytostatic (e.g. vincristine, methothrexat, cyclophosphamid) and with immunosuppressiv profile (cyclosporin) measures should be taken to help how to safely handle treatment with them.

Fig. 1



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