Is pediatric drug information the same for all children around the world?

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BACKGROUND

- Several governmental initiatives were implemented around the world in the last decade to increase clinical research and available data for drugs used in pediatrics
- USA enacted the Pediatric Labeling Rule in 1994, followed by other acts requiring more information about pediatrics that should be contained in product monographs
- Europe enacted the EU Paediatric Regulation in 2006
- In Canada, no pediatric regulation was enacted
- However, pediatric initiatives and requirements concerning the information contained in product monographs can differ between countries depending on the legislation where the drug is marketed

DESCRIPTION

We compared product monograph requirements for pediatric information between Canada, USA and Europe

ACTION

- Retrospective descriptive and transversal study
- We retrieved product monographs requirements concerning pediatrics using governmental agencies web portals
- For Canada, Health-Canada web portal was used
- For USA, Food and Drug Administration (FDA) web portal was used
- For Europe, European Medicines Agency (EMA) web portal was used
- Requirements about pediatric information were identified
- Product monograph templates in Canada, USA and Europe were also analyzed
- We reported if each requirement was mandatory in Canada, USA and Europe
- We analyzed consequences of these differences in clinical practice

EVALUATION

- We reported in Table I the list of 15 requirements about pediatric information on drugs that should be contained in the product monograph
- These pediatric requirements are: pediatric section, neonate section, age, pediatric dosing, pharmacology in pediatrics, pharmacokinetics in pediatrics, drug interactions, specific pediatric side effects, particular drug monitoring in pediatrics, pediatric precautions, pediatric warnings, pediatric contraindications, inactive ingredients potentially dangerous for neonates and overdose management in pediatrics
- For Canada, USA and Europe, we reported if these requirements were mandatory or not

Table I. Comparison of Canadian, US and European regulations concerning drug product monographs requirements for pediatrics

Requirements	Canada	USA	Europe
Pediatric section	Yes	Yes	Yes
Neonates section	**No**	Yes	**No**
If no pediatric studies were conducted	Detailed in pediatric section	Detailed in pediatric section	Detailed in pediatric section
Age	Yes	Yes	Yes
Pediatric dosing	Yes	Yes	Yes
Pharmacology in pediatrics	Yes	Yes	Yes
Pharmacokinetics in pediatrics	Yes	Yes	**No**
Drug interactions	**No**	**No**	Yes
Pediatric side effects	**No**	Yes	Yes
Particular drug monitoring in pediatrics	Yes	Yes	**No**
Pediatric precautions	**No**	Yes	Yes
Pediatric warnings	**No**	Yes	Yes
Pediatric contraindications	**No**	Yes	**No**
Inactive ingredients potentially dangerous for neonates	**No**	Yes	**No**
Overdose management	**No**	**No**	Yes
	7/15 in Canada	**13/15 in USA**	**10/15 in Europe**

Consequences of these regulation differences in clinical practice

Why such differences between countries?

- Different pediatric regulations have been enacted in USA and Europe
- In USA, there were the Pediatric Rule in 1994, the FDA Modernization Act (FDAMA) in 1997, the Best Pharmaceuticals for Children Act in 2002, the Pediatric Research Equity Act in 2003 and the FDA Safety and Innovation Act in 2013
- In Europe, there were the EU Paediatric Regulation in 2006
- All of these acts reinforced the requirements for adequate paediatric information contained in drug monographs
- No pediatric regulation has been enacted in in Canada

What should we expect?

- Better Canadian monographs for neonates and children

What can Canadian clinicians do in the meantime?

- Consult Canadian monographs first but do always consider other drug monographs and relevant information
- Whenever available, use USA and European drug monographs (e.g. systematically if importation of drug through the Special Access Program of Health Canada or any unanswered questions from Canadian drug monographs)
- Whenever a patient need a drug with poor scientific evidence available (e.g. emerging drug), consider Canadian, American and EMA drug monographs as well as drug evaluations from relevant governmental institutes (e.g. FDA in USA, Center for Drug Evaluation and Research in USA, EMA in Europe, Haute Autorité de Santé, Agence nationale de sécurité du médicament in France, National Institute for Health and Care Excellence in United Kingdom and Life Saving Drugs Program in Australia), pediatric information databases (e.g. Micromedex® or Lexicomp's Uptodate®) and scientific literature

CONCLUSION

- Canadian drug monographs require less information than US and European regulations/guidelines
- Clinicians should consider not only Canadian drug monographs when they prescribe drug for neonates and children
- In hospital practice, pharmacy should make available the best sources of information to allow optimal drug prescribing and use by all clinicians

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