

Therapeutic efficacy & safety of ACE inhibitors in the hypertensive paediatric population: a review

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Background & purpose

Since 1997, strong incentives have been introduced worldwide to improve access to safe and effective medicines addressing the therapeutic needs of children.

Angiotensin-1 converting enzyme (ACE) inhibitors = Most prescribed antihypertensive drugs in the paediatric population
= Prototype drugs targeted by the legislation initiatives



Evaluate and describe the current evidence of the efficacy and safety profile of ACE inhibitors in the paediatric population

Methods

A literature search was performed in PubMed, including abstracts from 1980 to April 2015.

Search terms hypertension, child, paediatric, ACE (inhibitors), RAAS and kallikrein-kinin system, and following drugs: captopril, lisinopril, enalapril, ramipril and fosinopril. + “snowball method”

Inclusion intervention studies, observational studies and reviews of ACE inhibitors in hypertensive children (0-18 years)

Exclusion not published in English, editorial pieces and opinions were excluded.

Information Design, number of patients, age, ACE inhibitor, dose, formulation, primary end-points and adverse events.

Results & Discussion

Incentives = increase in trials evaluating efficacy & safety of ACE inhibitors + 3/5 paediatric labelling by the FDA Reports

ACE inhibitors = potency to **decrease the systolic and/or diastolic blood pressure**
= an overall **favourable safety profile in a short-term period**

**≠ THE TRUE CLINICAL
RELEVANCE!!**

However ... Efficacy based on **surrogate outcome** (blood pressure)

Safety only on **short term**, without information of ACE inhibitors on growth, pubertal development & maturation

Incomplete inclusion of paediatric population: only mild disease, without comorbidities & low risk adverse events

Younger children (<6 years): poor availability of labelled ACE inhibitors, no RCT, only observational data

Absence of **age-appropriate formulations**

⇒ The promising legislative initiatives and the improved paediatric labelling, have hardly narrowed the gap between the availability of ACE inhibitors labelled and indicated for paediatric use and the actual drug usage in children

⇒ 25,5 to 33,1% of the children are receiving **unlabelled or not indicated** antihypertensive medications

⇒ 7% of all the prescribed antihypertensive drugs were **prescribed “off-label”**

Conclusions

The recent legislative initiatives increased the availability of paediatric labelling of ACE inhibitors. Nevertheless, many drugs used by hypertensive children have an insufficiently mapped out efficacy and safety profile and lack paediatric labelling. Moreover, many clinical questions remain and consequently complicate the selection of the most appropriate and effective ACE inhibitor in hypertensive children. The legislative initiatives also failed to fulfil several of paediatric needs: absence of long-term safety data on growth and maturation, absence of commercially available child-friendly formulations and incomplete evaluation of the entire paediatric hypertension population. Additional efforts are needed to close the gap between the availability of drugs that are labelled and indicated for paediatric use and the actual drug usage in children, especially in young children, neonates and children with severe hypertension, renal transplantation or severe renal impairment.