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A Review On: "Anti-Hypertensive Drugs In Children and Adolescents''

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ABSTRACT: -
Worldwide the prevalence of essential hypertension in children and adults continues to increases. They used "of label" drugs to treat Hypertension.That means these drugs are not preformed in patient populations. The providers have extrapolated dosing safety and efficacy from trials in adults. This practice is sub-optimal as children demonstrate unique differences in drug metabolism and drug response. Use of unstudied drugs has more risk. These agencies have created financial incentives for industry to conduct clinical trials. They have spurred over 30 clinical trials of anti-hypertension drugs over the last 15 years and have result found 10 new drugs by U.S. drug administration for the treatment of hypertension in children and adults but the financial incentive focus on new drugs and drug classes this all-reviewsanti-hypertensive drugs trials with focus on safety, drug dosing, efficiency and end point. I also review the available data for some of the more commonly prescribed, but less studied antihypertensive drugs.
Key words: Hypertension, children, safety, Clinical Trials, Dosing,

I. INTRODUCTION: -

All nations are developed world are facing epidermic of pediatric hypertension that are continuously increases prevalence of childhood obesity. The recent studies are greater than one out of that seven united states children and adults

Prehypertension with over 3% meeting diagnostic criteria for hypertension.Prevalence trends are similar on the based-on population assessments in numerous other nations. High blood pressure during child age and adult age is connected with end organ damage. Most similarly left ventricular hypertrophy and is chances of hypertension in adult's age. With the increasing of hypertension there is a need of all data support and efficacy of antihypertensive drugs. Whenever the more variety of antihypertensive drugs are studied in clinical trials in adults there has been a possibility of evidence to support safety and efficiency of drugs. This practice is sub-optional as in children and adults and off label drugs added more risks in the disease treatment and safety. Most drugs are created for used in adults do not have pediatric specific tablets or formulation. This initiative has very successful and over the preceding 15 years more than 20 clinical trials of antihypertensive agents and completed in child more than 10 drugs approval by US food and drug administration for treatment of hypertension in child and adolescents.

In this review I collect the available data and experience supporting to used of antihypertensive drugs in child and adolescents.

Identification of clinical trials: -

To identify anti-hypertensive drug trials in children and adolescents, that can used four principal sources: the United States FDA website (http://www.accessdata.fda.gov/),the FDA approved drug label, the European Medicines Agency (EMA) website (http://www.ema.europa.eu/) and PubMed. The FDA website and drug label include detailed information summarizing clinical trials completed in response to an FDA issued written request includes trials design, drugs dosing, and safety data. And the EMA published the all results of reviews conducted for EMA drug approval. I also viewed publications on PubMed for relevant clinical trials. Publications were identified following a PubMed search restricted to children and adolescents.

Angiotensin converting enzyme inhibitors: -

ACE inhibitors target to the renin angiotensin aldosterone system. ACE converts angiotensin 1 to the angiotensin 2, the peptide that causes vasoconstriction and increases aldosterone production. ACE inhibitors lower blood pressure by down the ang2 and observed its effects in adults. ACE inhibitors are the most commonly used antihypertensive drugs and the one more benefit of

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reducing cardiovascular and renal events in pediatric populations, ACE inhibitors is mostly prescribed antihypertensive for both primary and secondary hypertensions. ACE inhibitors have anti proteinuria effects. ACE inhibitors approved for treatment of pediatric hypertension by the FDA in clued enalapril, eosinophil,benazepril and lisinopril.

Enalapril: -

Enalapril is the first ACE inhibitor approved by the US FDA for pediatric hypertension following completion of the various clinical trials in 2002. Compared to placebo children treated with high dosage (2.5 or 20 mg for children < 50kg and 5mg or 40mg for children >50kg) for the significantlylowered blood pressure DBP and systolic blood pressure (SBP). The low dose groups did not demonstrate lowering of DBP or SBP, there is no difference in anti-hypertensive effects depends on the age, sex or Tanner Stage.

Fosinopril: -

Fosinopril was approved for treatment of pediatric hypertension by the US FDA after the trials were completed in 2003 in the clinical trials, all three dose levels (0.1,0.3 and 0.6 mg/kg) of fosinopril were equally effective at reducing SBP and DBP with no dose response in the overall cohort. It remains unclear whether the lack of dose response was attributable to the dose levels goes to high, and overly narrow dose range and right absence of a dose response. Further analysis showed that fosinopril was effective at reducing SBP in a dose responsive manner in black children.

Lisinopril: -

Lisinopril was approved for pediatric hypertension by the US FDA in 2003 in the pivotal Trial Lisinopril demonstrated a dose response reduction in SBP and DBP that was consistent across the age, groups, tanner, stages, and ethnicity. lisinopril was safe and well tolerated in the 4-week trials with serious adverse events. The most common adverse events were little bit pain in the head and abdominal pain.

Benazepril: -

Pediatric trials for benazepril have not been published in the literature, but the US FDA approved it for pediatric hypertension in 2004 and the trials are summarized on the FDA label. Benazepril significantly lowered SBP but did not exhibit a dose not report if any patients discontinued the trials due to drug related adverse events.

Captopril: -

Captopril is not approved for treatment of in children it is an off-patent agent with no financial incentive for industry to sponsor clinical trials. Because captopril was one of the earliest ACE inhibitors approved for use in adults, there is a substantial body of clinical experience in children and adolescents and several trials have demonstrated clinical efficacy. However, a major disadvantage of captopril is the need for frequent dosing.

Angiotensin receptor blockers: -

Angiotensin receptor blockers target the Angiotensin 2 type 1 receptors located on the heart, kidney, blood vessels, and adrenal glands. By blocking the final step of the RAAS, ARBs inhibit vasoconstriction and lower blood pressure Similar to ACE inhibitors, ARBs are particularly beneficial in reducing left ventricular hypertrophy in adults with heart failure. In adults and children, ARBs are effective at reducing proteinuria secondary to diabetes and may be particularly useful in patients with chronic kidney disease. Adults who experience cough and can of the study, there were no serious adverse events and few subjects discontinued therapy due to adverse events. Headache and dizziness were the most commonly reported adverse events in the dose response phase.

Candesartan: -

Candesartan was approved for pediatric use by the US FDA in 2009. Pediatric clinical trials are summarized in Figure 1. In the dose ranging study, Candesartan demonstrated a significant decrease in SBP and DBP compared to placebo at all dose levels but not a dose response. The lack of dose response was attributed to a narrow dose range. In the extension study, the 1-year response rate was 52%. Black children had a lesser reduction in SBP and DBP and a lower response rate compared to white children (response rate in black vs white 43 vs 61%

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African Americans [26,39-42]. Adults who experience cough and cannot be tolerate ACE inhibitors often take ARBs as an alternative. ARBs approved for the treatment of pediatric hypertension include losartan, valsartan, candesartan, and Olmesartan.

Losartan: -

Losartan was the first ARB approved for pediatric hypertension by the United States FDA in 2004 following completion of the required clinical trials. Losartan demonstrated a dose response reduction in SBP and DBP with efficacy demonstrated for the moderate and high dose groups (2.5 or 25 mg for children < 50 kg and 5.0 or 50 mg for children ≥ 50 kg) but no significant difference in BP between the low dose Losartan or placebo groups. There were too few non-white patients to evaluate race related differences in dose repose. Losartan was well tolerated with few discontinuations due to adverse events.

Valsartan: -

Valsartan was approved for pediatric use by the US FDA in 2007. The Valsartan pediatric clinical trials are summarized in. Valsartan demonstrated a dose response reduction in SBP and DBP but no statistically significant difference in blood pressure between the low or medium-dose groups (10, 20 mg for children < 35 kg and 20, 40 mg for children ≥ 35 kg). Valsartan's antihypertensive effects were observed across all subgroups including sex, age, tanner stage and race of the study, there were no serious adverse events and few subjects (1.6%) discontinued therapy due to adverse events. Headache (11.6%) and dizziness (2.7%) were the most commonly reported adverse events in the dose response phase.

Candesartan: -

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Calcium Channel Blockers: -

Calcium channel blockers encompass a diverse group of agents with different targets and functions. Second and third generation dihydropyridine CCBs, such as felodipine and amlodipine, are highly selective for vascular smooth muscle and are commonly prescribed for pediatric hypertension. They target L type long-acting voltage sensitive calcium channels and inhibit further influx of calcium into already depolarized smooth muscle cells, ACE inhibitors and ARBs, dihydropyridine CCBs do not demonstrate any anti-proteinuria effects in adults. and other studies have shown Reno protective effects in renal transplant patients.

Amlodipine: -

Amlodipine was approved for pediatric hypertension by the United States FDA in 2004. It is the most commonly prescribed CCB for pediatric hypertension. In pediatric trials, amlodipine demonstrated a dose response reduction in SBP and DBP. SBP reduction was slightly greater in females compared to males.and SBP reduction across race, age, and etiology of HTN did not any differenceconstantly. Amlodipine was generally well tolerated with few discontinuations due to adverse events.And the adverse event commonly seen in adults, was reported in 3.8% of children in dose ranging phase and 2.3% of children in placebo withdrawal phase.

Nifedipine: -

Nifedipine is a calcium channel blocking agent that was previously frequently prescribed to children and adolescents but was off patent and did not qualify for financial incentives and therefore has not been specifically studied for FDA labeling. Data are lacking on efficacy of short acting nifedipine and concerns have been raised about the dosing formulations which can lead to significant blood pressure fluctuations. Sustained release nifedipine perhaps has more utility but also has not been formally studied in children and adolescents.

II. CONCLUSION:

Regulatory initiatives in the US and Europe over the last one and half decades have multiple clinical trials of antihypertensive agents in children. That result is the increases the maximum num of US FDA gives permissions to the treatment of hypertension in children. this is very nice with the only caveat that most of the medications was

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studied in trials and also not belongs to any classes of drugs. and also, in us is approved more than 11 drugs since 2000 this is also a very good thing. And remains a clinical trial data of safety and efficiency of mostly used antihypertensive drugs. and they also provide clinical trial data for others gets some more knowledge, information and some guidance for many treatmentsof hypertension in children and adolescents. And FDA also labeled that antihypertensive drug has all safe.

And there is no any type of deaths happened during the clinical trials and only rarely some serious happened and that's all reported in clinical trials.

These clinical trials have highlighted the differences between drug safety and efficiency in children .as the prevalence of under age kids has a risk of hypertension the clinical trials data of clinical trials of antihypertensive drugs in children, proved that they are familiar with children. These clinical data guide to treatment

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