The incidence of headache in hypertensive patient on losartan therapy

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ABSTRACT

Background :- Losartan is the first of a new class of antihypertensives, is an angiotensin II receptor (type AT 1) antagonist. Losartan also provides a reduction in the combined risk of cardiovascular death, stroke and myocardial infarction in hypertensive patients with left ventricular hypertrophy and renal protection for type II diabetic patients with proteinuria. Side effects: Losartan has been found to be generally well tolerated in controlled clinical trials for hypertension, side effects have usually been mild and tranisient in nature and have not required discontinuation of therapy. the overall incidence of side effects reported with Losartan was comparable to placebo. in controlled clinical trials for essential hypertension, dizziness was the only side effect reported as drug related that occurred with an incidence greater than placebo in one percent or more of patients treated with Losartan. in addition, dose related orthostatic effects were seen in less than one percent of patients. rarely, rash was reported, although the incidence in controlled clinical trials was less than placebo. in these double-blind controlled clinical trials for essential hypertension, the following adverse experiences reported with Losartan occurred in ≥1 percent of patients, regardless of drug relationship: Body as a whole: abdominal pain , asthenia/ fatigue ,chest pain , edema/ swelling, Cardiovascular : palpitation, tachycardia /Digestive :diarrhea ,dyspepsia, nausea /Musculoskeletal: back pain, muscle cramps /Nervous / psychiatric: dizziness, headache, insomnia/ Respiratory: cough, nasal congestion, pharyngitis, sinus disorder Patients & methods:- An eighty-five hypertensive patients on losartan therapy were included by this study . All patients either newly diagnosed , or added losartan to their therapy or newly change their therapy to losartan .Any patient complaining of headache was excluded .Follow up the patients if they developed headache . Results :- patients age range (41-78 years old) average age(58.3)years old. Only three (3.5%) patients developed headache as side effects. The three patients age above 63 years old & they either change their therapy or losartan added to their therapy .average period of occurrence of headache within the first three days. One patient(1/3) need to stop therapy due to complaining of sever headache(early morning headache) that disappear on therapy discontinue .No relation between headache & the starting or initial therapy dose & blood pressure. Conclusion :- if the hypertensive patient presented complaining of headache better to not start therapy with losartan, if should a diuretics to be start to lower blood pressure then we add losartan , the patient should be a ware that he may develop headache & this is due to therapy & may disappear within few days .

Key words: hypertension , Losartan . headache

Introduction

Losartan is the first of class of anti-hypertensives, is an angiotensin II receptor (type AT 1) antagonist. Losartan also provides a reduction in the combined risk of cardiovascular death, stroke and myocardial infarction in hypertensive patients with left ventricular hypertrophy and renal protection for type II diabetic patients with proteinuria(1-5). Losartan is recommended as first-line treatment in patients under the age of 55 who cannot tolerate an ACE inhibitor.(6-8). The maximal effects on blood pressure usually occur within 3-6 weeks upon starting losartan(9).

Mechanism of action and pharmacological actions:-Losartan is a selective, competitive angiotensin II receptor type 1 (AT1) receptor antagonist, reducing the end organ responses to angiotensin II. Losartan administration results in a decrease in total peripheral resistance (afterload) and cardiac venous return (preload) All of the physiological effects of angiotensin II, including stimulation of release of aldosterone, are antagonized in the presence of losartan. Reduction in blood pressure occurs independently of the status of the renin-angiotensin system. As a result of losartan dosing, plasma renin activity increases due to removal of the angiotensin II feedback.(1,2)

Pharmacokinetics:

Following oral administration, losartan is well absorbed and undergoes significant first-pass metabolism to produce 5-carboxylic acid metabolite, designated as EXP3174. This metabolite is a long-acting (6 to 8 hr), noncompetitive antagonist at the AT1 receptor, and contributes to the pharmacological effects of losartan. EXP3174 is 10-40 times more potent in blocking AT1 receptors than losartan.. Biliary excretion contributes to the elimination of losartan and its metabolites.its bioavailability about 32%. .Peak plama concentration & its metabolite occur about 1&4 respectively orally .its 98% bound to plasma proteins. Only 4% excrete unchanged in urine .

Indications:

1-Hypertension 2-Heart failure 3-Reduction in the risk of cardiovascular morbidity and mortality in hypertensive patients with left ventricular hypertrophy. 4-Renal protection in type 2 diabetic patients with proteinuria(2,10)

Dosage and adminstration :Losartan may be administered with other antihypertensive agents, and with or without food.

Adult Hypertensive Patients

-Losartan may be administered with other antihypertensive agents, and with or without food.Dosing must be individualized. The usual starting dose is 50 mg once daily, with 25 mg , It can be administered once or twice daily with total daily doses ranging from 25 mg to 100 mg. -The maximal effect occurred in 3-6 weeks .

-If blood pressure is not controlled by losartan alone, a low dose of a diuretic may be added.

-Hydrochlorothiazide has been shown to have an additive effect

-No initial dosage adjustment is necessary for elderly patients or for patients with renal impairment, including patients on dialysis.

Pediatric Hypertensive Patients 6 years of age

The usual recommended starting dose is 0.7 mg/kg once daily (up to 50 mg total) administered as a tablet or a suspension . It is not recommended in pediatric patients <6 years of age or in pediatric patients with glomerular filtration rate <30 mL/min/1.73 m.

Hypertensive Patients with Left Ventricular Hypertrophy

-The usual starting dose is 50 mg of losatan once daily. Hydrochlorothiazide 12.5 mg daily should be added and/or the dose of losartan should be increased to 100 mg once daily followed by an increase in hydrochlorothiazide to 25 mg once daily based on blood pressure response

Nephropathy in Type 2 Diabetic Patients

-The usual starting dose is 50 mg once daily. The dose should be increased to 100 mg once daily based on blood pressure response .losartan may be administered with insulin and other commonly used hypoglycemic agents (e.g., sulfonylureas, glitazones and glucosidase inhibitors)(1,2,11).

Contraindications:

Hypersensitivity to any component of this medication, Breast feeding,Pregnancy. Pregnancy Categories C (first trimester) and D (second and third trimesters) ,Anuria ,Hypotension (3,4,5,13).

Side effects: dizziness was the only side effect reported as drug related that occurred with an incidence greater than placebo, dose related orthostatic effects were seen in less than one percent of patients. rarely, rash was reported. in these double-blind controlled clinical trials for essential hypertension, the following adverse experiences reported with Losartan occurred in ≥1 percent of patients, regardless of drug relationship: Body as a whole: abdominal pain , asthenia/ fatigue ,chest pain , edema/ swelling, Cardiovascular : palpitation, tachycardia /Digestive :diarrhea ,dyspepsia, nausea /Musculoskeletal: back pain, muscle cramps /Nervous / psychiatric: dizziness, headache, insomnia/ Respiratory: cough, nasal congestion, pharyngitis, sinus disorder (1-5). Losartan is a uricosuric. Because losartan can cause hyperkalemia, potassium supplements or salt substitutes containing potassium should not be used without appropriate monitoring by a physician(5).

Aim of study

to estimate incidence of headache among hypertensive patients receiving losartan therapy .

Patients & methods

An eighty-five hypertensive patients on losartan therapy were included by this study . All patients either newly diagnosed , or added losartan to their therapy or newly change their therapy to losartan .Any patient complaining of headache was excluded .Follow up the patients if they developed headache . Questioner including age , sex, duration of therapy , smoking, pulse rate , blood pressures

Statistical analysis done by using chi square.

Results

patients age range (41-78 years old) average age(58.3)years old. A 38 were female &47 were male. Only three (3.5%) patients developed headache as side effects. The three patients age above 63 years old & they either change their therapy or losartan added to their therapy .average period of occurrence of headache within the first three days. One patient(1/3) need to stop therapy due to complaining of sever headache(early morning headache) that disappear on therapy discontinue .No relation between headache & the starting or initial therapy dose & the measured blood pressure. All the three patients were male , two of them were smoker .Two of them their blood pressure were elevated

Discussion

Headache, which is often one of the most common adverse events in this study involving hypertensive patients,headache is important since some of hypertensive patients their presentation with headache. Headache frequently has a higher incidence in old patients treated with ARBs .our study estimate that 3.5% of the patients developed headache this in agreement with other study that estimate incidence of headache over 2% up to 8% (14-15-16-) .The blood pressure in those losartan added to their therapy was within normal vales but this was inagreement with other study that indicate high blood pressure & relate it to the headache Wiklund et al (17)showed that the incidence of headache (4%)was reduced after 6 months of antihypertensive treatment in all three target groups in the HOT trial, a finding that supports the conclusion that lowering elevated blood pressure reduces the incidence of headache in hypertensive patients.

No significant difference statistically were found regarding sex , smoking & starting or adding dose of losartan therapy in spite of that all patient above 63 years old & they were male . (2/3) smoker & of normal blood pressure at time of presentation .Non of them previously receive the drug or ACE inhibitors .

The patient discontinue therapy complaining of sever headache early morning headache but agonize type .The blood pressure was normally since losartan was added to their therapy nifedipine (10 mg twice daily)in spite of fact that no drug interaction between both drug .

Conclusion

if the hypertensive patient presented complaining of headache better to not start therapy with losartan, if should a diuretics to be start to lower blood pressure then we add losartan , the patient should be a ware that he may develop headache & this is due to therapy & may disappear within few days .

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