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E: ISSN NO.: 2349-980X **Shrinkhla Ek Shodhparak Vaicharik Patrika**

Effects of Propranolol and Hydrochlorothiazide Combined Therapy on Body Weight, Kidney Weight and Biochemical Parameters in the Kidney of *Rattus norvegicus*

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Abstract

Author studied the effects of propranolol and hydrochlorothiazide combined drug therapy on the body weight, kidney weight, and their ration with other biochemical parameters in the kidney of Rattus norvegicus (Albino rat). The drug combination were given orally at a dose of propranolol 40mg/kg and hydrochlorothiazide 25mg/kg body weight daily for 10, 20. 30 and 40 days, through feeding tube. Body weight recorded at start and after treatment days, while organ weight observed after decapitation of each rats. Total protein, cholesterol were increased significantly. In conclusion these result consistence with primary action of propranolol and hydrochlorothiazide combined drug therapy on kidney to promote the cholesterol and protein due to the side effects and ions distribution in proximal tubules in the kidney. Therefore the morphological parameters i.e. body weight, kidney weight and kidney weight/ body weight ratio and biochemical parameters, such as protein, cholesterol ALP the kidney after propranolol and hydrochlorothizde combined treatment would determine the significance and relationship to drug and clinical evidences of their metabolic side effects.

Keywords: Propranolol, Hydrochlorothiazide, kidney, PRO, CHO, GLY, TOTAL LIPIDS

Introduction

Propranolol and hydrochlorothiazide both *are antihypertensive drugs agents.*Antihypertensives are a class of drugs that are used to treat hypertension (high blood pressure). Beta blockers cause retention of sodium and water. Diuretics can cause mild volume reduction that leads to an increase in renin secretion by the kidney. The rationale for combining beta blockers with diuretics is twofold: beta blockers blunt the increase in the plasma renin level that is induced by diuretics, and diuretics decrease the sodium and water retention that is caused by beta blockers.

Review of Literature

Furaman (1970) noted the diuretic induced hyporglycemia in mice while renal lesion studied hypercholesterolemia in normal and subdiabetic rabbits after long term diuretic uses (Wellmann and Volk, 1971) Bucher et al (1990) noted the carcinogenic and toxicity of diuretic drugs in mice and rats. Arthur (2000) studied diuretics complications in rats and others mammals. Maheshwari (2002), Singh and Maheshwari (2004) reported the effects of carbonic anhydrase inhibitor, acetazolamide on kidney and blood biochemical parameters in rat, while Maheshwari (2004) noted combined effects of propranolol and hydrochlorothiazide in renal histo-Architecture and biochemical alterations in the kidney , liver and adrenal glands of rats. while Zal F (2014) shows combined effect of furasemide and propranolol on GSH homeostasis on ACHN kidneyl cell and Prieto I et al (2016) angiotensinase effect on blood pressure, heart and kidney Frindt G**,** (2017) Responses of distal nephron Na+ transporters to acute volume depletion and hyperkalemia in man. De Almeida (2018) diuretic and saluretic effect of nothofagin in hypertensive rat kidney, while Maheshwari (2018) reported that an increase protein and cholesterol level due to the combined effects of PROP and HCTZ in albino rats.\\

Aim of the Study

The purpose of present study is to see the combined effect of propranolol and hydrochlorothia zide drug therapy on the kidney biochemistry and morphological alterations in rats.

Tools

Present study has been made on acclimatized specimens of albino rat *Rattus norvegicus.* Animals were breeded in the laboratory with GLP. Animals were housed in controlled temperature, humidity and light cycle. They fed standered goldmohar brand feed and water ad libitum. For Present study propranolol (trade name –ciplar40) with hydrochlorothiazide (trade name- aquazide25) were selected. We use Lowery et al (1951) methods for tissue protein and Zlatkis et al (1953) for cholesterol. Rex Montgommery (1957) methods for glycogen and Total lipids by Folch et. al. (1957) methods.The results were subjected to statistical analysis (Fisher and Yates, 1963).

Experimental Protocol

Each dose propranolol 40 mg\kg and hydrochlorothia zide 25mg\kg body weight daily for 10, 20, 30 and 40 days. Drugs were dissolve in N-saline water and given to rats orally through cathedral tube. The selected rats of both sexes were divided in to eight groups of 10 in each. The groups of A,C, E and G treated As control groups and given to equal volume of N- saline water while groups B,D.F and His treated as experimental groups and given propranolol and hydrochlorothiazide drugs daily for 10, 20, 30 and 40 days respectively.

Collection of Kidney

After sacrificing the rats and dissected, the kidney detached out from their body was very carefully.

Results and Findings

In present study the combined drug propranolol and hydrochlorothiazide therapy for 10, 20, 30, and 40 days carefully studies on kidney morphological and kidney biochemical parameters in rat. An increase in body weight, kidney weight and their ratio with kidney total protein, total lipids and cholesterol with increase in time period of combined drug therapy is very highly significant ($p<0.001$) (Table 1,2,3,4,and 5) due to adverse effect of propranolol and hydrochlorothiazide combined drug treatment for 10, 20, 30 and 40 days combination also increase lipid contents, glucose level in the body, which also correlated with infilammation and lesions in kidney of rats (Maheshwari, 2004). Arther (2002) and Gluck (1978) reported that have been reported cholesterol and protein increase after treatment of antihypertensive drug on plasma potassium and catchacholamine levels in blood and also significant changes in the glucose tolerance and acetyle Co-A in liver, which is might results from increase the synthesis of lipids and disturb the catabolism by the activation of lipolysis .

Discussion and Suggestion

Diuretics in our therapeutic armament arum have predictable effects which is based on their nepharon sites of action and may exert their by interfering with cell metabolism (Breater, 2000). In the present study, therefore, an attempts been made to study in detailed the of such combination due to the biotransformation of these drugs compound in the liver and metabolic activites of lipids , glycogen and proteins in various tissues. An effect of diuretic drugs depends upon the bioavailability, distribution and extent of elimination and responsiveness of drug. In antihypertensive drug therapy are reliable of impacts of such drugs on the blood pressure due to effects on heart. The side effects are excreted to be more using combined therapy as potentially serious hypercalemia, glomerular sclerosis, various llesion in the kidney and other organs (Pereire et. al, 2002). The use of certain ditretic,β- blockers constimations at least at short term or long term produced some alterations in metabolism with these therapy and obtain additive synergetic effects in human and animals and a possible influence or can concommittent administration (Arther, 2000). An increase in body wt., kidney wt. and their ratio have been reported Katsumata et al (1990) and Sakemi and Baba (1993) in rats due to the side effects of antihypertensive drugs and proteinuria while Middeke et al.(1997) in humans due to side effects of combination of hydrochlorothiazide and captoprile drug treatments, and to metabolic side effects of diuretic drugs (Unlucerci et al, 2001). An additional studies have also demonstrated that a potent affects for hyperlipidemia and hypercholesterolemia in accelerating the developments of glomerulosclerosis the chronic renal disease by promoting macrophage infiltration or by the activation of messengial cells prosclerotic and fibronectin growth factors (Pawluezy k et al,2000). Total protein, cholesterol, total lipids and glycogen increase due to the effects of propranolol and hydrochlorothiazide combined drug treatment and can correlated to increase body wt. and kidney wt. with their ratio.

Conclusion

The result of present study is indicating that combined drug therapy of propranolol and hydrochlorothiazide not better for renal failure patients and obesity persons.

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Table - 01

Combined Effects of *Propranolol and hydrochlorothiazide* therapy on Morphological Parameters of *Rattus norvegicus*

S.No.	Drug Administration Time (in days)	No.of Rats	Bodyweight (in gm)				Kidney wt. (in gm.)				Kidney wt./ Body wt, Ratio			
			Control Groups		Treated Groups		Control Groups		Treated Groups		Control Groups		Treated Groups	
			MEAN	SEM +_	MEAN	SEM +_	MEAN	SEM +_	MEAN	SEM +_	MEAN	SEM +_	MEAN	SEM +-
1	10	10	147.3	3.43	181.6	2.08	2.471	0.024	2.680	0.022***	0.014	0.002	0.015	0.0003***
2	20	10	152.6	2.58	203.3	3.02	2.581	0.014	2.809	0.016***	0.013	0.002	0.016	0.0003***
3	30	10	163.2	3.14	213.3	2.50	2.462	0.019	2.884	0.020***	0.012	0.002	0.014	0.0003***
4	40	10	168.6	3.6	222.6	2.43	2.522	0.024	3.055	0.045***	0.013	0.002	0.014	0.0003***

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Table - 02

Combined Effects of *Propranolol and hydrochlorothiazide* therapy on total protein (Kidney) of *Rattus norvegicus*

S.No	Drug Administration Time(in days)	No. of Rats	Total Protein Kidney (in µg/dl)					
			Control Group			Treated Group		
			Range	Mean	+_S.Em	Range	Mean	+_S.Em
1	10	10	111.11-155.55	136.66	5.5	355.55-444.44	395.55	5.5***
2	20	10	111.11-166.66	145.55	6.2	422.22-522.22	465.55	5.5***
3	30	10	144.44-200.00	176.66	5.6	477.77-522.22	499.99	5.5***
4	40	10	155.55-211.11	187.21	6.6	505.55-577.77	531.1.	5.5***

Table - 03

Combined Effects of *Propranolol and hydrochlorothiazide* therapy on total lipids (Kidney) of *Rattus norvegicus*

S.No	Drug administration Time(in days)	No. of rats	total lipids IN Kidney (in mg/gm. Tissue weight)					
			Control group			Treated group		
			Range	Mean	+_S.Em	Range	Mean	+_S.Em
1	10	10	40-56	48.2	1.68	60-72	66	1.14***
2	20	10	42-55	49.3	1.35	68-82	74.4	1.49***
3	30	10	42-58	50.6	1.58	74-90	82.5	1.78***
4	40	10	42-56	49.4	1.38	78-96	86.8.	1.98***

Table - 04

Combined Effects of *Propranolol and hydrochlorothiazide* therapy on total cholesterol (Kidney) of *Rattus norvegicus*

S.No	Drug administration Time(in days)	No. of rats	total cholesterol Kidney (in mg/gm. Tissue weight)					
			Control group			Treated group		
			Range	Mean	+_S.Em	Range	Mean	+_S.Em
1	10	10	0.096-0.116	0.105	5.5	0.136-0.172	0.156	5.5***
2	20	10	0.096-0.119	0.107	5.5	0.160-0.224	0.194	5.5***
3	30	10	0.104-0.124	0.118	5.5	0.180-0.240	0.204	5.5***
4	40	10	0.112-0.134	0.126	5.5	0.240-0.304	0.264	5.5***

Table - 05

Combined Effects of *Propranolol and hydrochlorothiazide* therapy on Glycogen (Kidney) of *Rattus norvegicus*

S.No	Drug Administration Time(in days)	No. of Rats	Glycogen in Kidney (In mg/gm bogy weight)					
			Control Group			Treated Group		
			Range	Mean	+_S.Em	Range	Mean	+_S.Em
1	10	10	0.031-0.039	0.034	0.0009	0.024-0.028	0.026	\0.0004***
2	20	10	0.029-0.038	0.032	0.0009	0.019-0.023	0.021	0.0004***
3	30	10	0.028-0.035	0.031	0.0006	0.014-0.020	0.017	0.0006***
4	40	10	0.027-0.034	0.029	0.0007	0.014-0.017	0.015	0.0003***

*** very highly significant SEM - standard error of mean