ORIGINAL ARTICLE

HYDRALAZINE? ESSENTIAL OR HAS A POTENTIAL FOR COMPLICATIONS IN DERMATOLOGY

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ABSTRACT: BACKGROUND: Hydralazine is a drug which is vasodilator, it lowers blood pressure and allows blood to flow more easily in veins and arteries. Hydralazine is used to treat hypertension. **OBJECTIVES**: The purpose of this prospective study is to determine role of – Hydralazine in dermatological complications. **METHODS:** In this descriptive, prospective, observational, cross sectional study, all patients who presented to the department of dermatology during this study period of 12 months from January 2010-December 2010 in. were included. **RESULTS:** Total number of males in the present study was 19(74%), females in the study was 6(26%). Mean age was 55.28±15.74 (SD) years, number of patients in the age group 31-40 years was 3(12%), 41-50 years was 5(20%), 51-60 years was 7(28%), number of patients in 61-70 years was 4(16%), number of patients in the age group 71-80 years was 4(16%), number of patients in the age group 71-80 years was 2(8%). Maximum number of patients was in their middle age between 41-60 years. Flushing was seen in 8(32%) patients, Urticarial rashes were seen in 10(40%) patients, Lupus-like syndrome was seen in 5(20%) patients, Hypersensitivity reactions was seen in 5(20%) patients, ANA-positivity was seen in 5(20%) patients, out of all the dermatological manifestations Urticarial rashes were seen in maximum number of patients i.e., in 10(40%) patients. Lupus-like syndrome was seen in 5(20%) patients all of whom belonged to the age group 31-60 years. Flushing was seen in 6 (31.57%) patients in males, Urticarial rashes were seen in 8(42.10%) male, lupus like syndrome was seen in 5(26.31%) males, hypersensitivity was seen in 4(21.05%) males and ANA positivity was seen in 5(26.31%) males. Flushing was seen in 2(33.33%) patients in females, Urticarial rashes were seen in 2(33.33%) females, hypersensitivity was seen in 1(16.66%) females and ANA positivity & lupus like syndrome was not seen in females. P value of all symptoms being insignificant. **CONCLUSION:** There is significant percentage of patients who report with dermatological manifestations with hydralazine in first 6months after initiation as an add on drug.

KEYWORDS: Hydralazine, Lupus-like syndrome, Flushing, Hypersensitivity reactions.

INTRODUCTION: The peripheral vasodilator hydralazine is commonly added to antihypertensive treatment when a combination of a 3 blocker and a thiazide diuretic has failed to control the blood pressure. Used in this way it proved to be superior to labetalol, minoxidil, methyldopa, and prazosin over a six month period. With more prolonged treatment hydralazine, particularly at high dosage, may cause a syndrome resembling systemic lupus erythematosus.[1]

In recent years the maximum daily dose of hydralazine has usually been limited to 200 mg to avoid the lupus syndrome, which has generally been believed to be rare with these lower

doses.[3] These findings confirm many well known facts about hydralazine induced lupus. The syndrome is dose related.[2]

These findings confirm many well known facts about hydralazine induced lupus. The syndrome is dose related, is commoner in women than men, and tends to develop after at least three months of treatment.[3]

The dose should be limited to 100 mg daily, and patients should be followed up closely and advised to report persistent ill health, joint pains, weight loss, rash, chest pain, or any other unexplained symptom.

Lupus like syndrome was first described in 1953, and 6 well-recognized risk factors have been identified: (1) cumulative dose (150 vs 76 g), (2) female sex, (3) white race, (4) slow acetylation, (5) human leukocyte antigen (HLA) DR4, and (6) C4 null.[4]

MATERIALS & METHODS:

STUDY DESIGN: Prospective, observational, cross sectional study.

SAMPLE SIZE: 25 cases over a span of 12 months from January 2010-December 2010 were included.

Method of Collection of Data: The data for the purpose of the study was collected in a predesigned and pretested proforma which include various socioeconomic parameters like age, sex, occupation, religion, etc. About 25 cases were selected on the basis of the simple random sampling method. Patients who were started on hydralazine in the last 6 months. Patients who presented with dermatological manifestations during the period of treatment with hydralazine.

The statistically data was analyzed with the help of software SPSS.16.0, Chi-square test was done. Questionnaires, physical, radiographic examination was done in all patients

INCLUSION CRITERIA: Patients with dermatological manifestations, and who were initiated with hydralazine as an add on therapy 25mg PO BD to TDS dose for better control of hypertension in the last 6 months.

EXCLUSION CRITERIA:

- Patients who were on long term hydralazine >6 months.
- Patients with overt allergy to hydralazine or known allergy to other known drugs.

RESULTS: Table 1 Shows total number of males in the present study was 19 (74%), females in the study was 6(26%). Mean age of the patients was 55.28±15.74 (SD) years, maximum age being 89 years and minimum age being 34 years.

Table 2 Shows age distribution according to groups in present study, number of patients in the age group 31-40 years was 3(12%), 41-50 years was 5(20%), 51-60 years was 7(28%), number of patients in 61-70 years was 4(16%), number of patients in the age group 71-80 years was 4(16%), number of patients in the age group 71-80 years was 2(8%). Maximum number of patients was in their middle age between 41-60 years.

Table 3 showing distribution of symptoms in present study, flushing was seen in 8(32%) patients, Urticarial rashes were seen in 10(40%) patients, Lupus-like syndrome was seen in 5(20%) patients, Hypersensitivity reactions was seen in 5(20%) patients, ANA-positive was seen in 5(20%) patients, Urticarial rashes were seen in maximum number of patients i.e. in 10(40%) patients.

Table 4 shows that Lupus-like syndrome was seen in 5(20%) patients who were in between 31-60 years.

Table 5 shows symptoms in different sex distribution. Flushing was seen in 6(31.57%) patients in males, Urticarial rashes were seen in 8(42.10%) male, lupus like syndrome was seen in 5(26.31%) males, hypersensitivity was seen in 4(21.05%) males and ANA positivity was seen in 5(26.31%) males.

Flushing was seen in 2(33.33%) patients in females, Urticarial rashes were seen in 2(33.33%) females, hypersensitivity was seen in 1(16.66%) females and ANA positivity & lupus like syndrome was not seen in females. P value of all symptoms being insignificant.

DISCUSSION: This prospective, observational study titled "Hydralazine? Essential or has a potential for Complications in dermatology"

Hydralazine is one of the commonest add-on therapies used while treating resistant hypertension, usually in chronic kidney disease (CKD) patients. One of the most limiting factor in using hydralazine is its dosage, there is enough proof to limit the dose to 200mg. Hydralazine above 200 mg / d are not recommended for the treatment of hypertension because of the risk of drug-induced lupus[6]

Arthropathy was the presenting complaint in 80% of patients, mostly affecting the small joints of the hands, followed by the wrists and then the elbows, ankles, knees, and toes.[7]

Where as in our study dermatological manifestations are more common, none of our patients has any manifestations of joint involvement.

Dermatitis is a less common manifestation of drug induced lupus, variously reported in 10% to 34%,[4] 33%,[6] and 11%[5] of patients with hydralazine-induced lupus.[8] An important differentiating characteristic of drug-induced lupus is occasional generalized distribution with involvement of the lower extremities, which is lacking in idiopathic lupus.[9]

subacute cutaneous lupus with generalized annular papulosquamous lesions is a different disease than drug-induced systemic lupus and is predominantly associated with other antihypertensive agents: calcium channel blockers, angiotensin-converting enzyme inhibitors, and thiazide diuretics.[3,4,10]

Positive antinuclear antigen (ANA) staining occurs in a diffuse homogenous pattern, in association with positive anti-single stranded DNA antibody and antihistone antibody, but, compared with idiopathic lupus, antibody response to native double-stranded DNA (anti-ds DNA ab), extractable nuclear antigen, and cardiolipid is usually absent in drug-induced lupus.[1–3, 9] Another distinction from idiopathic lupus is that serum complement levels are normal in drug-induced disease.[1,4,9]

Our study shows there is predominance of dermatological symptoms among the male subjects and the female being affected in lesser proportion, even though major symptom profile

studied here is very limited and purely concentrated on the dermatological manifestation. The number of patients included in our study is limited, but still this study shows a new symptom profile. Since the manifestations seen may be a secondary manifestation to CKD because most of the patients in our study were CKD patients who needed better control of their blood pressure and were on add-on therapy of hydralazine and the consumed was also less. Further, randomised control studies will help in this regard to understand the drug complication profile in all the individuals.

REFERENCES:

1. Finks SW, Finks AL, Self TH. Hydralazine-induced lupus: maintaining vigilance with increased use in patients with heart failure. South Med J. 2006; 99: 18–22.
2. Hydralazine-induced lupus syndrome (HILS) was first reported in 1953.[1] Aylward PE, Tonkin AM, Bune A. Cardiac tamponade in hydralazine-induced systemic lupus erythematosus. Aust N Z J Med 1982; 12: 546-12.
3. Katz U, Zandman-Goddard G. Drug-induced lupus: an update. Autoimmun Rev. 2010; 10: 46–50.
4. Bernstein RM. Rheumatic complications of drugs and toxins. In: Maddison PJ, Isenberg DA, Woo P, Glass DN, eds. Oxford Textbook of Rheumatology, 2nd edn. New York, NY: Oxford University Press; 1998: 1689–1700.
5. Official Journal of the American Society of Hypertension, Inc. The Journal of Clinical Hypertension Vol 14; No 2; February 2012; 132-136.
6. Cameron HA, Ramsay LE. The lupus syndrome induced by hydralazine: a common complication of low dose treatment. BMJ. 1984; 289: 410–412.
7. Perry HM. Late toxicity to hydralazine resembling systemic lupus erythematosis or rheumatoid arthritis. Am J Med. 1973; 54: 58–72.
8. Bernstein RM. Rheumatic complications of drugs and toxins. In: Maddison PJ, Isenberg DA, Woo P, Glass DN, eds. Oxford Textbook of Rheumatology, 2nd edn. New York, NY: Oxford University Press; 1998:1689–1700.
9. Marzano AV, Vezzoli P, Crosti C. Drug-induced lupus: an update on its dermatologic aspects. Lupus. 2009; 18: 935–940.
10. Hobbs RN, Clayton AL, Bernstein RM. Antibodies to the five histones and poly (adenosine diphosphate-ribose) in drug-induced lupus: implications in pathogenesis. Ann Rheum Dis. 1987; 46: 408–416.

Group	Number of patients	Percentage (%)
Females	19	76
Fefemales	6	24
Total	25	100

Table 1: Showing prevalence of present study

Age	Frequency	Percentage (%)
31-40	3	12
41-50	5	20
51-60	7	28
61-70	4	16
71-80	4	16
81-90	2	8
Total	**25**	**100**

Table 2: Table showing age distribution according to groups in present study

Symptoms	Present	(%)
Flushing	8	32
Urticarial rash	10	40
Lupus-like syndrome	5	20
Hypersensitivity reactions	5	20
ANA-positive	5	20

Table 3: Table showing symptoms according to groups in present study

Age	Frequency
	Present
31-40	3
41-50	0
51-60	2
61-70	0
71-80	0
81-90	0
Total	**5**

Table 4: Showing distribution of Lupus-like syndrome in different age groups

Symptoms	Females (n=19)	(%)	Females (n=6)	(%)	P value
Flushing	6	31.57	2	33.33	0.65
Urticarial rash	8	42.10	2	33.33	0.54
Lupus-like syndrome	5	26.31	0	0	0.29
Hypersensitivity reactions	4	21.05	1	16.66	0.65
ANA-positive	5	26.31	0	0	0.21

Table 5: Showing distribution of symptoms in different age groups

LIST OF ABBREVIATIONS

SD-standard deviation
WHO-World Health Organization
i.e.-that is

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