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Adverse drug reaction following mass drug administration during the program to eliminate lymphatic filariasis in banke district, Nepal

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ABSTRACT

This study aimed to find out types of adverse drug reaction following mass drug administration during the program to eliminate lymphatic filariasis in Banke distict of Nepal.The retrospective study of the prescription of the patient with the history of adverse drug reaction was done .The totals of 602 patient were reported to have adverse drug reactions after intake of medication against filariasis under mass drug administration program. Nausea, Vomiting, Abdominal pain, Fever, Diarrhoea, Malaise, Asthenia ,Angioedema , Dermatitis, Hydrocoel , Itching, Dyspnoea , Syncope, Convulsion, Anxiety were different types of adverse drug reactions reported during my study. Ethnic variation in adverse drug reactions was also studied which shows disadvantage non dalit terai caste group had highest reported cases of adverse drug reactions followed by religious minorities.

Keywords: Filariasis, Diethylcarbamazi, Mass Drug Administration, Adverse drug reactions.

INTRODUCTION

The government of Nepal has been launching a national campaign against filariasis since 2002 under WHO [1].As a part of the campaign against filariasis the government of Nepal had launched mass drug administration Programme to Eliminate Lymphatic Filariasis in 36 district in the year 2011 where two drugs named Diethylcarbamazine and albendazole were administered to 14.5 million people aged above two years. But when there is a drug the possibility of its adverse reaction cannot be overlooked. Adverse drug reaction as per WHO is "any noxious, unintended and undesired effect of a drug which occur at doses used in human for prophylaxis, diagnosis or therapy"[2] In one of the study carried out by *Babu BV.et.al* in Orissa State, India it was found that the frequency and severity of adverse reactions are the main reasons for low compliance of mass drug administration (MDA) [13] It also reports of all the adverse reactions, systemic adverse reactions typically associated with microfilarial death were more frequent and the frequency of adverse reactions was higher in microfilaraemics compared with amicrofilaraemic controls[3]. In the study carried out by *Jeevan B Sherchand.et.al* it was found the overall prevalence of lymphatic filariasis from a 4,488-sample population studied from 37 districts was 582 (13%). The ICT Filariasis (immunochromatographic test – used to screen for circulating filarial antigen) positive percentage for Banke was 20.8% and for Bardiya it was found to be 41% which shows high prevalence of micro filaria in these region[4]. Banke and Bardiya lies in Bheri zone in the Mid-Western Region of Nepal.Hence ,the present study was carried out with the objective to study the frequency and types of adverse reactions during mass drug administration in the year March 2011 in the Banke District,Nepal.

MATERIALS AND METHODS

The retrospective study of the prescription of the patient with the history of adverse drug reaction after intake of the medication named Diethylcarbamazine and albendazole during Mass Drug Administration

program to eliminate filiariasis was done at Bheri zonal hospital, Nepalgunj Medical college hospitals and Nepalgunj district public health office.

Bheri Zonal Hospital located in Nepalgunj, Banke district, is the largest referral government hospital in the mid western region providing services to more than 100,000 people of the mid and far western region of Nepal per year.Nepalgunj Medical college Hospital is the 220 bedded private super specialty hospital located at Nepalgunj. Beside these the case report of Adverse drug reaction during MDA program were reported from other hospitals and Health post at Nepalgunj district public health office from where patient reports were collected. The observational and linguistic biases in the assignment of terms of adverse drug reaction was verified as per the criteria of council of international organization of medical science which has been defined in their publication entitled Reporting Adverse Drug Reactions [5] and terms were assigned as per the criteria as far as possible.

Ethical Consideration: The research proposal was ethically approved by IRB of Maharajgunj Medical Campus and to carry out research work the permission was granted by Ministry of Health and Population,Nepal.

Data PROCESSING, ANALYSIS and reporting: The data were coded and processed using Statistical Package for Social Sciences (SPPS) software (version 17).

RESULTS AND DISCUSSION

The total no of 602 patients (305 Female (50.7%) and 297 Male(49.3%)) were reported to have ADRS after intake of medicine against fialriasis under Mass Drug Administration program in Banke District. In a study done in Orissa State, India it shows similar results with female (20.5%) and Male (12.7%) according to household coverage survey done in year 2004.[13] Also various studies in large population sample have shown female to be more prone towards adverse drug reactions.[6, 7] The ADRS were found to be more prevalent in the age group 20 to 30 years (21.6%) followed by age group 10 to 20 years (20.9%).(Table I) In a similar study done in Orissa State, India the majority of patients experiencing ADR after intake of medication against filariasis were in the age group 31-45 years in the year 2002 and it was reported more in age >45 years in the year 2004 [3].It also says the frequency of adverse reactions increased with age[3]. Also various surveys conducted in other endemic areas have shown an increased frequency of ADRs with age.[8, 9.] But my study results slightly deviates from the above finding and it might be due to the fact the the hospital allocated by government for treatment of ADRs was quite far from the village areas and was not easy accessible to all. The Ethnic group wise distribution of ADRs reveals that People from disadvantage non dalit terai caste group had highest reported cases of ADRs (232 cases i.e. 38.5%) followed by religious minorities(196 cases i.e 32.6%)(Table I).The maximum number of case of ADRs was reported from Nepalgunj city (173 cases i.e 28.7%) followed by Belbhar (48 cases i.e 8.0 %).From Radhapur, Narainapur, kalaphanta, Mahadevpuri, Bhawaniapur, Salyan, Holia, Banke, Bardiya, Bethani a single case of ADRs was reported(Table II). It might be due to the fact that the two hospitals allocated by government for treatment of ADRs is located at Nepalgunj city area and it's quite far from other remote village areas around Nepalgunj.

Malaise was found to be predominant ADRs followed by acute abdominal pain(Table III). In a study done in Orissa State, it state of the total adverse reactions, dizziness was predominant, followed by headache, nausea, fatigue, fever, myalgia, abdominal pain, diarrhoea, etc[13]. But in the study done in Indonesia fever was found to be most reported ADRs followed by myalgia, adenolymphangitis, itching and Headache[10]. In the study done in Australia in dogs the clinical signs associated with reactions to diethylcarbamazine therapy in dogs infected with Dirofilaria immitis include depression, vomiting and diarrhoea followed by bradycardia , softened heart sounds, weakened apex beat, low amplitude arterial pulse, pale mucosa, poor mucosal capillary refill and polypnoea [11]. Subsequently the dogs become laterally recumbent and exhibit tachycardia and dyspnoea, with associated hepatomegaly and abdominal wall contractures[11.]

Nausea, vomiting, abdominal symptoms pains were found to be reported more in the age group 20-30 years.Fever and diarrhea was more predominant in age group 0-10 years. Asthenia was more in age group 20-30 years(50 cases) followed by 30-40 years(49 cases) and then in 10 -20 years (47 cases).Malaise was predominant in age group 20-30 years and 30-40 years with 10 cases respectively. 5 cases of angioedema was reported among which 2 cases were from age group 10-20 years and 1 cases each from age group 0-10 years, 30-40 years and 50-60 years. Dermatitis was found more prominent in age group 30-40 years.Hydrocoel was reported more in age group of 20-30 years and 30 -40 years with 9

cases in each.One case each of itching and dyspnoea was reported in age group 10-20 years and 30-40 years respectively. The two cases of syncope was reported in age group 10-20 years.Total of 8 cases of convulsion were reported among which 6 cases was from age group 0-10 years and 2 were from age group 10-20 years. Similarly two cases of anxiety were also reported. (Table IV).Similarly 2 cases were reported as others among which one was diagnosed as HCR which was not defined and the in next case chief complaints were missing. Asthenia was found to be predominant ADR in all ethnic group except in relatively advantage janajatis where predominant ADRs was acute abdominal pain (Table V). In the study carried out by Cartel JL.et.al on A single diethylcarbamazine dose for treatment of Wuchereria bancrofti carriers in French Polynesia: efficacy and side effects it was found the percentage decrease in microfilaria density reached 95% by day 180 and Side effects were observed in 10 patients (71%) of whom 3 only were unable to perform usual activities for less than 24 hours [12]. In the study carried out by M. Haarbrink.et.al. on Strong Association of Interleukin-6 and Lipopolysaccharide-Binding Protein with Severity of Adverse Reactions after Diethylcarbamazine Treatment of Microfilaremic Patients it was found that patients experienced no or mild, moderate, or severe adverse reactions. It also shows that increasing pretreatment microfilarial counts were associated with escalating severity of adverse reactions. Plasma concentrations of DEC were not different among patients suffering from varying degrees of illness. Interleukin (IL)–6, IL-10, lipopolysaccharide-binding protein (LBP), and soluble tumor necrosis factor receptors (sTNF-Rs) increased after treatment. IL-6 and LBP, however has showed the strongest association with adverse reactions [13].The finding of this the study is supported by my study as the microfiarial load for Banke was 20.8%[4] and therefore the adverse drug reactions was quite prone after intake of medictation against filariasis in the Banke district. Similarly in the study carried out by Bockarie MJ.et.al on Efficacy of single dose diethylcarbamazine compared with diethylcarbamazine combined with albendazole against Wucheria Brancrofti infection in Paupa New Guinea the results suggest use of diethylcarbamazine combined with albendazole in mass treatment programs on the basis of greater activity against adult worms [14].

Regarding the prevalence of ADRs the study carried out by Shrestha R. et. al. in five major hospital from different parts of Nepal,the prevalence of drug related complication was found to be 0.4% [15].Similarly in a study carried out by Jha N.et.al.in five major hospitals of Kathmandu the prevalence of ADR was found to be 0.8%.[16] This study however could calculate the prevalence of ADRS after intake of medication against filariasis under mass drug administration because the exact data regarding compliance were lacking. Also various studies have shown the fear of adverse reactions as a cause for noncompliance in mass drug administration Program to eliminate lymphatic filariasis [17,18].

CONCLUSION

This study depicts the occurrence of adverse reactions following mass drug administration Program to eliminate lymphatic filariasis in Banke District,Nepal which reflects the strong and urgent need to strengthen medicine safety systems. Improving quality of care to patients by providing ADR screening is an approach for early identification and subsequently treatment of adverse drug reactions. Also a more field based study regarding impact of adverse drug reactions, factors affecting compliance to MDA program has to be conducted which is a key to the success of mass drug administration Program to Eliminate Lymphatic Filariasis.

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Table I: Basic characteristic of patients (n=602)(Mean age in years: 30.66)

Variables	Frequency	Percentage
Age in years		
0-10	84	14.0
10-20	126	20.9
20-30	130	21.6
30-40	106	17.6
40-50	77	12.8
50-60	41	6.8
60-70	35	5.8
70-80	2	.3
80-90	1	.2
Gender of patients		
Male	297	49.3
Female	305	50.7
Ethnicity		
Dalit	37	6.1
Disadvantaged janajatis	79	13.1
Disadvantaged non-dalit Terai caste	232	38.5
Religious minorities	196	32.6
Relatively advantaged janajatis	13	2.2
Upper caste groups	45	7.5

Table II: Place wise distribution of Patients

Place	Frequency	Percentage	Place	Frequency	Percentage
Saigun	8	1.3	Bankatti	10	1.7
Udayapur	37	6.1	Jaispur	3	.5
Nepalgunj	173	28.7	Bhawaniapur	1	.2
Baijapur	4	.7	Phattepur	5	.8
Manikapur	8	1.3	Kohalpur	7	1.2
Ganapur	12	2.0	Raniyapur	6	1.0
Indrapur	44	7.3	Salyan	1	.2
Paraspur	39	6.5	Udharapur	25	4.2
Sitapur	9	1.5	Belhar	7	1.2
Radhapur	1	.2	Bankatawa	5	.8
Belbhar	48	8.0	Holia	1	.2
Gangapur	2	.3	Samsergunj	8	1.3
Narainapur	1	.2	Khurda	6	1.0
Kalaphanta	1	.2	Rajena	2	.3
Katukuta	19	3.2	Khajura	2	.3
Kachanpur	4	.7	Bageshwori	4	.7
Kamdi	36	6.0	Sonpur	3	.5
Khaskusma	2	.3	Banke	1	.2
Mahadevpuri	1	.2	Bardiya	1	.2
Puraini	25	4.2	Betahani	1	.2
Hirminiya	14	2.3	Basudevpur	6	1.0
Puraina	9	1.5			

Table III: Gender wise distribution of ADRs

Category	Male	Female	Total
Nausea,Vomiting	7	8	15
Abdominal pain	57	77	134
Fever	11	18	29
Diarrhoea	43	29	72
Malaise	119	129	248
Asthenia	14	19	33
Angioedema	0	5	5
Dermatitis	9	10	19
Hydrocoel	30	0	30
Itching	0	1	1
Dyspnoea	0	1	1
Syncope	1	1	2
Convulsion	5	3	8
Anxiety	0	2	2
Others	1	2	3
Total	297	305	602

Table IV: Age-wise distribution of ADRS

Category	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90
Nausea,Vomiting	1	5	6	0	1	1	1	0	0
Abdominal pain	14	31	34	19	19	9	8	0	0
Fever	12	6	2	1	1	2	4	1	0
Diarrhoea	18	17	14	9	5	5	4	0	0
Malaise	28	47	50	49	36	20	16	1	1
Asthenia	1	5	10	10	6	0	1	0	0
Angioedema	1	2	0	1	0	1	0	0	0
Dermatitis	3	4	3	6	1	1	1	0	0
Hydrocoel	0	4	9	9	6	2	0	0	0
Itching	0	1	0	0	0	0	0	0	0
Dyspnoea	0	0	0	1	0	0	0	0	0
Syncope	0	2	0	0	0	0	0	0	0
Convulsion	6	2	0	0	0	0	0	0	0
Anxiety	0	0	1	1	0	0	0	0	0
Others	0	0	1	0	2	0	0	0	0
Total	84	126	130	106	77	41	35	2	1

Table v: Ethnic group wise distribution of ADRs

Category	Dalit	Disadvantaged janajatis	Disadvantaged non-dalit Terai caste	Religious minorities	Relatively advantaged janajatis	Upper caste
Nausea,Vomiting	2	4	3	3	2	1
Abdominal pain	6	20	60	32	4	12
Fever	0	2	12	11	1	3
Diarrhoea	7	2	33	21	2	7
Malaise	14	36	89	92	3	14
Asthenia	4	5	11	10	1	2
Angioedema	0	2	1	1	0	1
Dermatitis	3	1	6	7	0	2
Hydrocoel	1	5	11	13	0	0
Itching	0	0	0	1	0	0
Dyspnoea	0	0	1	0	0	0

Syncope	0	0	1	1	0	0
Convulsion	0	2	2	2	0	2
Anxiety	0	0	1	1	0	0
Others	0	0	1	1	0	1
Total	37	79	232	196	13	45

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