ORIGINAL ARTICLE

Prevalence of Thiamine Deficiency at a Drug Rehabilitation Centre in Malaysia

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Summary

A possible outbreak of beriberi occurred at a drug detention and rehabilitation centre, Pusat Serenti Bukit Cabang, Perlis, Malaysia in February 2004. This outbreak was identified following the presentation of a large number of inmates at a health centre with signs and symptoms of ankle oedema and shortness of breath. Further investigations revealed the death of three inmates at the General Hospital with similar clinical presentations during the period from October 2003 till February 2004. A cross sectional comparative study was carried out at the rehabilitation centre to find out the prevalence of thiamine deficiency among the inmates both symptomatic and asymptomatic. A total of 154 inmates were examined (57 symptomatic and 97 asymptomatic cases). It was found that 74% from the sample study (114 cases) had thiamine deficiency (44 symptomatic and 70 asymptomatic). Further statistical analysis showed that ankle oedema is consistent with the diagnosis of thiamine deficiency but lack sensitivity ($p<0.05$, sensitivity 24.6%, specificity 95%). This outbreak could have been triggered by poor diet intake of thiamine by the inmates coupled with possible intake of certain thiamine antagonists in their diet.

Key Words: Prevalence, Thiamine deficiency, Beriberi, Malaysia

Introduction

Pusat Serenti Bukit Cabang is a detention and rehabilitation centre for convicted drug addicts. It is situated in Padang Besar about 25km from the town of Kangar and 10km from the Malaysia-Thailand border. It is the requirement of the law that drug addicts must undergo compulsory rehabilitation for two years.

A possible outbreak of beriberi was identified in February 2004 when a group of 35 inmates presented with the clinical signs and symptoms of ankle oedema, shortness of breath, weakness and numbness of the lower limbs at a nearby health centre. The health personnel alerted the Health Department and a committee was set up to investigate the outbreak.

It was found that since late 2003, a number of cases with similar presentations were either treated at the in-house clinic or the nearby health centre. Many of them were referred to the General Hospital and some were admitted into the wards. They were treated symptomatically with oral frusemide and potassium supplement. Their symptoms resolved with the above treatment but tend to recur.

It was later revealed that three inmates had died and they presented with similar signs and symptoms at the General Hospital between the months of November 2003 and February 2004. The first case had symptoms of ankle oedema for two months with a brief history of shortness of breath and was treated as heart failure. However, his cardiac status deteriorated rapidly resulting in death the following day of hospitalisation. The second and third cases had similar symptoms of ankle oedema for a few weeks with sudden onset of cardiac decompensation and died within a few hours

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upon admission at the hospital. None of the deceased had echocardiography done to establish the specific cause of heart failure symptoms.

During the initial investigations of the outbreak, a few differential diagnoses were considered, e.g. infections, exposure to toxins and thiamine deficiency. Immediate control measures were carried out based on the differential diagnosis as cleaning and disinfection especially the 'detoxification area' of the camp. The 'detoxification area' is a section in the camp where the inmates are placed for a period of two weeks to one month to undergo the drug 'detoxification' process and are not allowed to mingle with other inmates.

Bearing in mind that thiamine deficiency was one of the differential diagnosis, all the inmates were treated with 100 mg of thiamine as intramuscular vitamin B complex for symptomatic and oral thiamine for asymptomatic inmates during the course of the investigation after blood samples for thiamine were taken. The majority of the inmates showed marked improvement of signs and symptoms within a few days and this narrowed down the diagnosis to thiamine deficiency. At the same time a study was conducted to determine the prevalence of thiamine deficiency as well as possible risk factors that precipitated the outbreak.

Materials and Methods

The study design is a cross-sectional comparative study between symptomatic and asymptomatic cases. The study sample consisted of symptomatic cases defined as inmates presenting with at least one of the following symptoms; ankle or leg swelling, dyspnoea, leg numbness or leg weakness between October 2003 and February 2004 and asymptomatic cases defined as inmates not presenting with any of the symptoms stated. The asymptomatic cases were chosen through a systematic random sampling.

All the study subjects were interviewed by trained paramedics and their symptoms and physical signs were determined by a doctor. Blood samples were taken for full blood count, liver and renal functions and thiamine levels. Thiamine level measurements were carried out by the Institute of Medical Research in Kuala Lumpur. The laboratory used the thiamine pyrophosphate effect (TPPE) to confirm the diagnosis of thiamine deficiency (TPPE $\geq$ 25% as thiamine deficient; 0-24% as marginally adequate/ acceptable).

Other information such as length of stay and HIV status were obtained from the records of the inmates. Diet recall was done on 10 inmates (5 symptomatic and 5 asymptomatic) by a nutritionist through a convenience sampling. The results of the study were subjected to chi-square test or Fisher's exact test for categorical variables and t-test for continuous variables. Statistical significance was set with a p value of less then 0.05.

Results

There were 416 inmates during study period and all were males and Malays. The total inmates in the study group were 154; 57 symptomatic and 97 asymptomatic. Other socio-demographic profiles of the study group are shown in Table I. It was found that only the number of admissions to the centre had a significant association to develop thiamine deficiency ($p<0.05$) whereas other factors were not.

Blood investigations of these inmates found that 114 of them had thiamine deficiency. The prevalence of thiamine deficiency was 74%, almost equal in both symptomatic (77.2%) and asymptomatic inmates (72.2%). There was no difference between symptomatic or asymptomatic subjects to be thiamine deficient ($p>0.05$) (Table II). Out of 57 symptomatic inmates, 44 had thiamine deficiency while 13 had adequate thiamine levels.

Among the symptomatic inmates, numbness was the commonest complaint followed by ankle oedema, weakness and dyspnoea as shown in Figure 1. Majority of them had more than one symptom, 24 had all the four symptoms, 17 had 3 symptoms, 13 had 2 symptoms and only three a single symptom.

As shown in Table III, the sensitivities of history and physical findings were low, although the specificities were higher for some items. Only leg oedema occurred more commonly in thiamine deficient inmates than thiamine non-deficient inmates ($p<0.05$). None of the blood tests done to evaluate the nutritional status and presence of liver or renal dysfunction was significant between thiamine deficient and non-thiamine deficient subjects (Table IV).

To determine the status of thiamine intake through their diet, ten inmates were randomly selected (five who were thiamine deficient and five who had thiamine acceptable levels). Through a 24 hours diet recall

questionnaire, the results showed that the mean thiamine intake was 0.47 mg/day with a median of 0.45 mg/day. Only one subject had adequate thiamine intake of 1.2 mg/day. The mean calorie intake was 1900 kcal/day. However, the 24 hours diet recall as shown in Table V did not statistically determine the thiamine status; deficient or acceptable ($p>0.05$).

Table I: Socio-demographic profile of the study group

		Thiamine Deficient n=114 (%)	Thiamine Adequate n=40 (%)	Significant test
Age (years)	<30	52 (45.6)	22 (55.0)	$\chi^2 = 1.95$
	30-39	39 (34.2)	12 (30.0)	$p = 0.58$
	40-49	19 (16.7)	5 (12.5)	
	≥50	4 (3.5)	1 (2.5)	
No of	1	60 (52.6)	19 (47.5)	$\chi^2 = 7.51$
Admission	2	36 (31.6)	7 (17.5)	$p = 0.02$
	≥3	18 (15.8)	14 (35)	
Duration of	< 3 months	39 (34.2)	13 (32.5)	$\chi^2 = 1.12$
Admission	3-6 months	25 (21.9)	12 (30.0)	$p = 0.57$
	> 6 months	50 (43.9)	15 (37.5)	
Duration of	≤ 2 weeks	41 (36.0)	16 (40.0)	
detoxification	> 2 - 4 weeks	49 (43.0)	15 (37.5)	$\chi^2 = 1.77$
	> 4 - 6 weeks	16 (14.0)	4 (10.0)	$p = 0.62$
	> 6 weeks	8 (7.0)	5 (12.5)	
History of	Yes	59 (51.8)	21 (52.5)	$\chi^2 = 0.07$
injecting drug use	No	55 (48.2)	19 (47.5)	$p = 0.94$
Body mass index (BMI)	< 23	80 (70.1)	22 (55.0)	$\chi^2 = 3.05$
	≥ 23	34 (29.9)	18 (45.0)	$p = 0.08$
HIV Status	Positive	3 (2.6)	2 (5.0)	$p = 0.39$
	Negative	111(97.4)	38 (95)	(Fisher's exact test)

Table II: Thiamine levels among the study inmates

Category of inmates	Adequate level of thiamine (%)	Thiamine deficient (%)	Total (%)
Asymptomatic	27 (27.8)	70 (72.2)	97 (100)
Symptomatic	13 (22.8)	44 (77.2)	57 (100)
Total	40 (26.0)	114 (74.0)	154 (100)

Table III: Sensitivities and specificities in the detection of thiamine status according to signs and symptoms

Factors	Thiamine deficient (n=114)	Not thiamine deficient (n=40)	Sensitivity	Specificity
Symptoms				
Any symptoms	38.6%	32.5%	38.6%	67.5%
Leg swelling	35.1%	27.5%	35.1%	72.5%
Dyspnoea	20.2%	20.0%	20.2%	80.0%
Numbness of leg	37.7%	32.5%	37.7%	67.5%
Leg weakness	23.7%	30.0%	23.7%	70.0%
Signs				
Leg oedema	24.6%	5.0%	24.6%	95.0%
Muscle weakness	9.6%	12.5%	9.6%	87.5%
Sensory loss	10.5%	10.0%	10.5%	90.0%

Table IV: Nutritional status, liver function and renal function of sample subjects

Factors	Thiamine deficient, mean (SD)	Not thiamine deficient, mean (SD)	t-test, p value
Hb (gm%)	13.97 (1.34)	14.20 (1.59)	0.666
PCV (%)	89.40 (5.46)	88.80 (7.10)	0.783
Creatinine (umol/l)	83.70 (11.78)	79.84 (9.15)	0.199
Total protein (g/l)	81.12 (5.40)	82.51 (5.02)	0.172
Albumin (g/l)	42.42 (3.27)	43.51 (3.51)	0.086
Alkaline phosphatase (U/L)	88.67 (36.36)	80.22 (17.59)	0.177
SGPT (U/L)	70.16 (150.28)	54.89 (56.74)	0.548
SGOT (U/L)	70.16 (150.28)	36.19 (17.57)	0.309
Gamma GT (U/L)	24.66 (29.73)	25.30 (20.52)	0.954

Table V: Thiamine intake and Thiamine Status

Thiamine status	Thiamine intake		Total
	Normal	Low	
Deficient	1	4	5
Acceptable	0	5	5
Total	1	9	10

(p=0.5, Fisher's exact test)

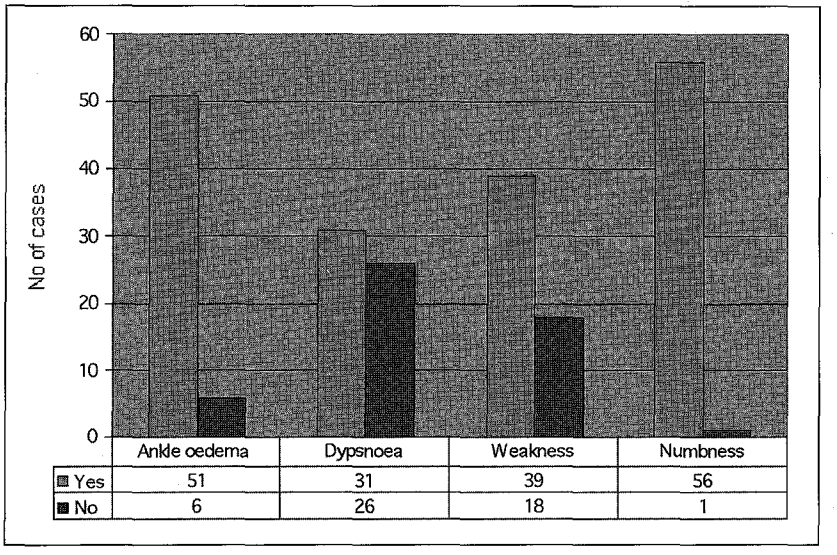

Fig 1: Category of Symptoms

Discussion

In the past, outbreaks of beriberi have occurred in many parts of the world especially among refugees and displaced population e.g. in Thailand (1980's) and Nepal (1993-95)[1]. In late 1992 and early 1993 there was an outbreak of B vitamin deficiency in Cuba related to polyneuropathy affecting 50,000 people. It was reported to be the combination of a nutritional problem associated with a possible toxic substance[2]. Such outbreaks have also occurred in a well nourished Amazonian population whereby the actual trigger cause was not known[3].

Recently, twenty-seven inmates from a drug addict detention centre in Perak were reported to have presented with ankle oedema and prompt clinical response to thiamine replacement therapy was noted in most of them on follow up[4]. There was also an unpublished report of a possible beriberi outbreak in a drug rehabilitation centre in Pusat Serenti Sungai Ruan, Pahang which caused six deaths.

The clinical presentations of ankle oedema, dyspnoea, weakness and numbness of limbs in this disease outbreak were consistent with thiamine deficiency as most cases presented with features of wet beriberi had responded dramatically with thiamine replacement. Usually the response to treatment in wet beriberi occurs within hours although improvement is often slow for those with peripheral neuropathy symptoms[5]. All symptomatic cases received thiamine 100mg as a stat dose followed by 10mg daily for three months. A prophylactic dose of 1mg daily is then given to them and all other inmates. Following this intervention, no new cases were reported.

The prevalence of thiamine deficiency in this camp was remarkably high at 74% and this is possibly true in the overall drug addict population in Malaysia. It is known that in countries where polished rice is the main dietary constituent, biochemical thiamine deficiency is prevalent among the population even if frank clinical thiamine deficiency has become rare. People exposed to subclinical thiamine deficiency are predisposed to the manifestation of frank beriberi under appropriate circumstances, occasionally in epidemic proportions. The incidence may be augmented by anti-thiamine factors in the diet that are present in e.g. tea leaves, shell fish, and fermented fish and betel nuts[6].

The cause of thiamine deficiency in this study was undetermined but a few conditions could have precipitated the outbreak. Frequent and extreme washing of rice grains before cooking is known to actually wash away whatever little thiamine that is present in the rice. This is especially so in highly

milled white rice whereby only 0.08 mg/100g of thiamine is present compared to 0.33 mg/100 g in brown rice[1]. In this drug rehabilitation centre a special pot is used for steaming the rice. Water used for washing the rice grains is drained before the rice is steamed. Together with a diet that is lacking in other sources of thiamine such as green vegetables and legumes, the lack of thiamine in the diet could have contributed to the outbreak.

From the diet recall that was conducted albeit a small sample, it was found that the mean dietary intake of thiamine was 0.47mg/day. The recommended intake by WHO is 0.4 mg/1000 kcal[1]. The mean calorie intake was 1900 kcal which required 0.76mg of thiamine/day. Therefore, there was a gross inadequate of thiamine intake.

At the same time, there are some foods that have an antagonistic effect on thiamine. These are foods that contain thiminase, among them coffee, tea, betel nut, alcohol and certain bacteria found in food such as *Bacillus thiamineolyticus*[6]. It was noted that tea was the drink that was being served at all meal times in this centre. It had also been postulated that alcohol which the inmates may have obtained from illegal self-made alcohol could be a contributing factor. The inmates that had presented with bilateral ankle oedema and were treated with frusemide, their conditions further aggravated as a result of increase loss of thiamine through diuresis[7].

From the socio-demographic data, only inmates admitted to rehabilitation centre for the first time were associated with thiamine deficiency whereas age, duration of admission, duration of detoxification, HIV status and history of injecting drug use were not. Body Mass Index (BMI) was also not a risk factor in our study as compared to the outbreak of beriberi among Chinese immigrants in Taiwan where BMI was negatively associated with the illness[8]. The nutritional status from the laboratory investigations of haemoglobin, serum protein and albumin levels were found to be similar among thiamine deficient and acceptable groups. This is probably because in this population, they had adequate intake of calorie but lack micronutrients such as vitamins. Liver enzymes were also not significantly different in both groups.

Many clinical categories had been recommended at the field to determine cases of thiamine deficiency but none really showed significant correlation between signs and symptoms. Symptoms or clinical case category are not suitable to classify patients who are thiamine deficient as the disease involves many bodily functions which manifest themselves in various ways[1]. Even combination of many symptoms to increase the possibility of diagnosis did not have significant correlations.

The clinical presentation of ankle oedema assessed by doctors was the only significant clinical finding of thiamine deficiency in this study as it was a very objective form of evaluation. Assessment of neurological status through muscle power, reflexes and sensation are too subjective especially so in drug addict populations who tend to be manipulative. However, due to the lack of sensitivity to detect cases and many subjects were subclinical, it was recommended that the whole affected population should also receive prophylactic treatment.

There were many limitations during the course of the study. Many inmates were uncooperative especially in revealing their illegal activities, such as alcohol intake and current drug use at the centre which could be associated with the occurrence of the outbreak. In addition, only a few of the inmates could be roped in for the diet recall interview.

Conclusion

The prevalence of thiamine deficiency in this drug rehabilitation centre is high at 74%, almost equal in both symptomatic (77.2%) and asymptomatic inmates (72.2%). A possible solution to overcome the problem of thiamine deficiency in this centre is to propose a menu adequate in thiamine. The proposed new menu would include more legumes such as corn and green beans in their daily diet. Other nutritious drinks are recommended as an alternative to tea, as tea is a thiamine antagonist. Methods of cooking especially rice also need to be changed in order to avoid unnecessary removal of vitamins.

Another easier alternative would be to provide supplement of thiamine and other vitamins to the inmates. Daily supplement of vitamin B complex is suitable as it is cheap and contains enough thiamine for a daily intake. However as in any other medications the compliance for long-term use might be a problem and this would require commitment from the camp authorities.

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