The effect of pyridoxine supplementation on quality of life of patients with chronic lymphocytic leukaemia

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Abstract

Objective: Pyridoxine, is essential in the metabolism of many classes of food, we aimed at determining the effect of its supplementation on the quality of life (QoL) of patients with chronic lymphocytic leukaemia (CLL).

Methods: This study compared the (QoL) and haematological parameters of CLL patients before and after the administration of pyridoxine. Data obtained were analyzed using SPSS version 19.

Results: There was improvement in the QoL of the patients after pyridoxine supplementation; Majority of the parameters that make up the physical functional scales was significantly higher after pyridoxine supplementation. There were also significant improvements in insomnia, appetite loss and constipation after pyridoxine supplementation.

Conclusion: Pyridoxine supplementation in patients with CLL marginally improved quality of life.

Keywords: Pyridoxine, Supplementation, Quality of life, Leukaemia, CLL

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Effet de la supplémentation en pyridoxine sur la qualité de vie des patients atteints de leucémie lymphoïde chronique

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Abstrait

Objectif: La pyridoxine, essentielle au métabolisme de nombreuses classes d'aliments, nous avons cherché à déterminer l'effet de sa supplémentation sur la qualité de vie des patients atteints de leucémie lymphoïde chronique (LLC).

Méthodes: Cette étude a comparé les paramètres (qualité de vie) et hématologiques des patients atteints de LLC avant et après l'administration de pyridoxine. Les données obtenues ont été analysées avec SPSS version 19.

Résultats: La qualité de vie des patients s'est améliorée après la supplémentation en pyridoxine; La majorité des paramètres constituant les échelles physiques et fonctionnelles était significativement plus élevée après la supplémentation en pyridoxine. Il y avait aussi des améliorations significatives dans l'insomnie, la perte d'appétit et la constipation après une supplémentation en pyridoxine.

Conclusion: La supplémentation en pyridoxine chez les patients atteints de LLC a légèrement amélioré la qualité de vie.

Mots-clés: pyridoxine, supplémentation, qualité de vie, leucémie, LLC

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INTRODUCTION

Pyridoxine is a vitamin that is essential in the metabolism of protein, carbohydrates, fatty acids, and several other substances, including brain amines (1), where as chronic lymphocytic leukaemia (CLL) is a blood cancer that affects mainly the elderly. Pyridoxine's benefit in patients with tuberculosis has been established as it is known to prevent the development of peripheral neuropathy during isoniazid therapy. Chronic lymphocytic leukaemia is the commonest form of leukaemia in adults in Nigeria (2). Low emotional wellbeing score for CLL patients has been reported compared to the general population and with patients with other forms of cancers (3). The use of chemotherapy alone in the treatment of CLL has not improved on these parameters significantly (4), therefore there is the need to search for agents that could improve the QoL of this group of patients.

Pyridoxine is a compound that has vitamin B6 activities. Large proportions of the naturally occurring pyridoxine are not bioavailable as they occur in glycosylated poorly absorbable form. It performs a wide range of activities especially as a co-enzyme assisting in many metabolic activities amongst which are metabolism of carbohydrate and lipid. Pyridoxine acts by converting tryptophan to niacin or serotonin, breaking down of glycogen to glucose-1-phosphate, conversion of oxalate to glycine, synthesis of gamma aminobutyric acid (GABA) within the CNS, and synthesis of heme necessary for the production of red blood cells.

As stated earlier, pyridoxine has been found to be very useful in preventing polyneuropathy in tuberculosis patients that are on isoniazid (1). It is also useful in reducing pains and may therefore be useful in improving the QoL of patients with CLL in whom pain is one of the major contributors to poor quality of life (5). It has been revealed that there is a 60% increase in daily requirement of pyridoxine in physiologic states with increased metabolic activities like pregnancy, lactation and exercise (6). Since one of the cardinal features of CLL is increased metabolism (hypermetabolic state), pyridoxine may be of great value in this condition. Investigations of the benefit of vitamins in various medical conditions have been going on. An example was a study in children with malaria which showed improved haematological indices on those that had vitamin A supplementation during treatment (7). Rich sources of pyridoxine include beef liver, fish, and starchy vegetable, and because of prevalent poor economy, most of the patients may not be able to afford these food items and may therefore be deficient of this vital vitamin.

We therefore aim to determine the beneficial effect or otherwise of pyridoxine supplementation (an important coenzyme) in CLL patients, an agent which is of immense benefit to patients with tuberculosis.

MATERIALS AND METHODS

This was a longitudinal study that sought to determine the impact of pyridoxine supplementation on the quality of life and on the haematological parameters of CLL patients in Makurdi north-central, Nigeria. Ethical clearance for this study referenced BSUTH/MKD/HREC/2013B/2018/0019 (Appendix A) was obtained from the Health Research and Ethics Committee of the Benue State University Teaching Hospital, Makurdi. The study population comprised chronic lymphocytic leukaemia patients that attended the outpatient clinic of the Benue State University Teaching Hospital, (BSUTH) Makurdi and the Federal Medical Centre, (FMC) Makurdi within the period of the study (January-August 2018).

The sample size was calculated using the formula developed by Xavier *et al* (8) for longitudinal studies. The calculated minimum sample size was 50. An additional 50 patients were recruited to make up for those that would be lost to follow up. Participants were recruited from the Haematology out-patient clinic of the BSUTH, Makurdi and FMC, Makurdi. They were recruited consecutively as they presented for routine consultations, until a total of 100 participants was reached.

Exclusion criteria included: Objection to participate in the study, patients less than 18 years of age and patients with diagnosis other than CLL. Immediately after the details of the study were explained to the participants and their consent obtained, the EORTC (version 3) quality of life questionnaires (QLQ-C30) were issued to them, and baseline samples for complete blood count were collected. The questionnaires were administered by the research assistant, who also guided the participants in filling them.

The EORTC (version 3) Quality of life questionnaire (QLQ-C30) is a 30-item Likert-type validated questionnaire, which has the advantage of self-administration to respondents. This questionnaire was field-tested in a cross-cultural sample of cancer patients in 13 countries to confirm the hypothesized scale structure, to establish reliability and to evaluate validity (8). It

demonstrated internal consistency for the group under study with a calculated Cronbach alpha of 0.73 in a pilot study. A high score for a functional scale represents a high / healthy level of functioning, a high score for the global health status / QoL represents a high QoL, but a high score for a symptom scale / item represents a high level of symptomatology / problems.

On completion of the questionnaire, 2ml of venous blood was withdrawn from the cubital vein using a 5ml syringe and observing aseptic procedures. The blood was dispensed into an EDTA bottle for analysis of haematological parameters. These parameters included red blood cell count, haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), white blood cell count, differential leukocyte count, and platelet count using the Sysmex haematology auto-analyzer (Sysmex Corporation of America) at the Haematology laboratory of BSUTH, Makurdi. These tests were done within 24 hours after collection. The performance of the auto-analyzer was validated using quality control samples which were run with each batch of the sample specimen and by manual counts. Participants were there after given supplemental tablets of pyridoxine at a dose of 25mg daily to be taken in addition to their chemotherapy for a period of four months. The participants were mainly on a combination of chlorambucil and prednisolone for varying number of cycles depending on their responses. The pyridoxine was sourced from pharmaceutical outlets where the researchers had no conflict of interests. At the end of this period, the questionnaires were re-administered and their full blood count taken again for comparison.

Data obtained from these analyses were analyzed by the statistical package for social sciences version 19. The differences in quality of life and haematological indices were tested for significance using the student t-test.

RESULTS

A total of 100 (one hundred) chronic lymphocytic leukaemia patients were recruited, but 74 (seventy-four) completed the study. Fifty-one were males while 23 were females, translating to a male to female ratio of 2.2: 1. The mean age of the participants was 62 ± 8.5 years. Majority (66.2%) of the participants had late stages (stages III and IV) of the disease. Table 1

The quality of life (QoL) of the participants prior to pyridoxine administration was significantly lower than the published data in the EORTIC QLQ-C30 reference value manual (10). All the parameters in the functional scale were significantly lower in our study compared to the reference values. In the symptom scales, our participants were worse off with fatigue, pain and financial difficulty but fared better with nausea, vomiting, dyspnoea, insomnia appetite loss, constipation and diarrhea. Table 2.

There was improvement in the global health status of the patients after pyridoxine supplementation; however, this was not statistically significant, but majority of the parameters that make up the physical functional scales (Physical functioning, role functioning, emotional functioning and cognitive functioning) was significantly higher after pyridoxine supplementation. Result also showed statistically significant improvements in symptoms after pyridoxine supplementation except for fatigue, Nausea, vomiting and financial difficulties. Table 3. The total white cell count, lymphocyte count and granulocyte count were significantly lower after pyridoxine supplementation and chemotherapy while the haemoglobin concentration and the platelet count were significantly higher after supplementation. Table 4.

DISCUSSION

The quality of life (QoL) of the participants in our study prior to pyridoxine administration was significantly lower than published data in the EORTIC QLQ-C30 reference value manual (10). The low QoL in our participants may be related to late presentation of our patients which is demonstrated by the high number (66.2%) that had the late stages (Ria III and IV) of the disease compared to those used for calculating the reference values mainly stages I and II. It may also be as a result of fewer numbers of participants in our study (74) as compared to 23,555 used for the calculating the reference range or it could be the effect of geographical and racial influences on the quality of life of this category of patients. The above adduced concerns will require further studies. The low QoL from our study was however in keeping with the report of other studies (4,10,11,12,13) around the globe which demonstrated that the different dimensions of QoL were deteriorated by haematological malignancies and, probably, by the side effects of their treatments. Our result revealed that all the parameters in the functional scales of the QoL questionnaire were significantly lower compared to the reference values. This implied that the functional aspect of quality of life of our patients was worse affected

than the symptom aspect. In the symptom scales, our participants had higher scores for fatigue, pain, and financial difficulties but there were not statistically significant. This implied that our participants had worse symptoms (fatigue, pain and financial difficulties) compared to the reference range and this is in keeping with the fact that our participants presented with the late stages of the disease. We however recorded significantly milder symptoms in the rest of the parameters (dyspnoea, insomnia, appetite loss, constipation, and diarrhoea).

There was marginal improvement in the global health status of our patients after pyridoxine supplementation; but this was not statistically significant. However, parameters in the functional scales revealed that physical functioning, role functioning, emotional functioning and cognitive functioning were significantly higher after pyridoxine supplementation. Researchers had earlier reported a decline in QoL especially when patients were undergoing chemotherapy (14,15). The improved QoL of our patients after pyridoxine supplementation may be an indication that pyridoxine is beneficial in this group of patients. This finding is however contrary to what Jannique *et al* (16) discovered while working on the effect of vitamin B supplementation on quality of life in community-dwelling adults with mild cognitive impairment. Although pyridoxine deficiency has been noted to lead to increased circulating homocysteine, which is a risk factor for neuropsychiatric disorders including seizures, migraine, chronic pain and depression, Malouf *et al* (17) in a systematic review revealed no evidence for short-term benefit from pyridoxine in improving mood (depression, fatigue and tension symptoms) or cognitive functions.

Our result also showed statistically significant improvements in insomnia and appetite loss after pyridoxine supplementation. Although vitamins have not been reported to have soporific effects, B vitamins have been advanced as preventive for insomnia based on research that suggests deficiencies in vitamin B6 promote psychological distress and ensuing sleep disturbance (18) and report by Morin *et al* (19) earlier indicated that vitamin intakes improve sleep. Another study has identified vitamin B complex as a helpful treatment of nocturnal leg cramps (20) and this may improve the sleep quality of the individual. The precise mechanism for this observation was not however clear. The significant improvement in appetite following pyridoxine supplementation in our study is in keeping with what researchers demonstrated in Rex Rabbit where it was discovered that pyridoxine increased food intake significantly and in a dose-dependent manner (21).

Other symptoms (fatigue, nausea and vomiting, and pain) also improved but not significantly after pyridoxine supplementation. Report of mood changes resulting from pyridoxine deficiency and leading to depression, anxiety, irritability and pain is well documented (22-24). These effects were attributed to the fact that pyridoxine is involved in the production of several neurotransmitters especially gama-aminobutyric acid (GABA) and serotonin which help control anxiety, depression and pains. Improvement in fatigue post pyridoxine may be linked to the fact that pyridoxine plays a vital role in haemoglobin-the protein that carries oxygen round the body-synthesis. Besides feeling tired from anemia, pyridoxine deficiency could also potentially contribute to tiredness due to its role in making the sleep-promoting hormone melatonin (25-26).

The total white cell count, lymphocyte count and granulocyte count were significantly lower after pyridoxine supplementation while the haemoglobin concentration and the platelet count were significantly higher after supplementation. The haematological changes cannot be immediately differentiated from the actions of chemotherapeutic agents. A study involving those patients that are off chemotherapy will help in differentiating the two. But the improvements in haemoglobin concentration and platelet count may be attributed to the pyridoxine since it has been established as a necessary factor in the synthesis of heme.

CONCLUSION

Pyridoxine supplementation in patients with CLL improved the physical functioning, some symptoms, haemoglobin concentration, platelet count and overall quality of life.

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Table 1: Socio-demographic characteristics of the participants

Socio-demographic variables	n (%)
Age (years)	
50-59	35 (47.3)
60-69	24 (32.4)
70-79	15 (20.3)
Mean ± SD	62 ± 8.5
Sex	
Male	51 (68.9)
Female	23 (31.1)
Educational level	
None	8 (10.8)
Primary	11 (14.9)
Secondary	0 (0.0)
Tertiary	55 (74.3)
Occupation	
Unemployed	41 (55.4)
Civil/Public servant	14 (18.9)
Self-employed	19 (25.7)
Ria stage	
I and II	25 (33.8)
III and IV	49 (66.2)

Table 2: Comparing quality of life of the participants prior to pyridoxine administration with the EORTIC QLQ-C30 reference values

Parameters	Reference values n(SD) n=23,553	Scores before pyridoxine supplementation n(SD) n=74	p-value
Global health status/QoL	61.3 ± 24.2	50.2 ± 20.3	0.0001
Functional scales			
Physical functioning	76.7 ± 23.2	65.3 ± 15.4	0.0001
Role functioning	70.5 ± 32.8	59.0 ± 10.2	0.0001
Emotional functioning	71.4 ± 24.2	60.1 ± 12.1	0.0001
Cognitive functioning	82.6 ± 21.9	56.5 ± 12.6	0.0001
Social functioning	75.0 ± 29.1	53.3 ± 11.4	0.0001
Symptom scales			
Fatigue	34.6 ±27.8	39.0 ± 16.8	0.1736
Nausea and vomiting	9.1 ± 19.0	8.2 ± 14.4	0.6839
Pain	27.0 ± 29.9	34 ± 17.5	0.0541
Dyspnoea	21.0 ± 28.4	4.6 ± 10.5	0.0001
Insonmia	28.9 ± 31.9	10.4 ± 5.7	0.0001
Appetite loss	21.1 ± 31.3	9.3 ± 6.9	0.0013
Constipation	17.5 ± 28.4	9.5 ± 4.3	0.0154
Diarrhoea	9.0 ± 20.3	1.1 ± 0.7	0.0008
Financial difficulties	16.3 ± 28.1	21.9 ± 14.3	0.0866

QoL= quality of life

Table 3: Quality of life of the participants before and after pyridoxine supplementation

Parameters	Scores before pyridoxine supplementation n(SD) n=74	Scores after pyridoxine supplementation n(SD) n=74	p-value
Global health status/QoL	50.2 ± 20.3	52.1 ± 19.3	0.5604
Functional scales			
Physical functioning	65.3 ± 15.4	75.0 ± 21.2	0.0018
Role functioning	59.0 ± 10.2	66.7 ± 12.6	0.0001
Emotional functioning	60.1 ± 12.1	68.0 ± 14.2	0.0004
Cognitive functioning	56.5 ± 12.6	66.7 ± 13.4	0.0001
Social functioning	53.3 ± 11.4	52.1 ± 18.2	0.6315
Symptom scales			
Fatigue	39 ± 16.8	36 ± 15.7	0.2636
Nausea and vomiting	8.2 ± 14.4	6.3 ± 12.4	0.3911
Pain	34 ± 17.5	31 ± 20.3	0.3372
Dyspnoea	4.6 ± 10.5	4.7 ± 12.0	0.9570
Insonmia	10.4 ± 5.7	7.3 ± 4.1	0.0002
Appetite loss	9.3 ± 6.9	6.2 ± 2.4	0.0004
Constipation	9.5 ± 4.3	7.3 ± 6.5	0.0164
Diarrhoea	1.1 ± 0.7	1.2 ± 0.4	0.2877
Financial difficulties	21.9 ± 14.3	23 ± 12.2	0.6154

Table 4: Haematological parameters of participants before and after pyridoxine supplementation and chemotherapy

Parameter	Before pyridoxine supplementation (mean ± SD)	After pyridoxine supplementation (mean ± SD)	p-value
TWBC ($x10^9$/L)	46.0 ± 43.6	23.5 ± 15.6	0.0001
Lym ($x10^9$/L)	33.0 ± 37.3	18.2 ± 9.4	0.0013
Gr ($x10^9$/L)	6.9 ± 4.7	5.4 ± 2.1	0.0139
Hb (g/dL)	9.0 ± 1.8	10.1 ± 0.9	0.0001
MCV (fL)	95.0 ± 12.7	96.0 ± 13.4	0.6442
MCH (pg)	28.5 ± 1.9	28.7 ± 1.2	0.4480
MCHC (g/dL)	30.1 ± 2.4	29.4 ± 1.7	0.0330
Platelet ($x10^9$/L)	143.4 ± 63.8	172.1 ± 54.5	0.0040
PDW (fL)	9.0 ± 2.3	8.7 ± 1.9	0.3917
MPV (fL)	9.9 ± 1.2	8.7 ± 0.8	0.0001

Key: TWBC-Total white blood cell count, Lym- lymphocyte count, Gr- Granulocyte count, Hb-Haemoglobin concentration, MCV-Mean cell volume, MCH-Mean cell volume, MCHC-Mean corpuscular haemoglobin concentration, PDW-Platelet distribution width, MPV-Mean platelet volume,