Original Article

The Effect of Dhamma Practice on Depression Outcomes in Hemodialysis Patients

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Background: Depression impairs the quality of life (QOL), increases risk of hospitalization and death in hemodialysis patients. Antidepressant medications can lead to more severe side effects. Dhamma practice by Chanting and Anapanasati meditation may relieve depressive symptoms in hemodialysis patients.

Objective: To evaluate the effect of Dhamma practice on depression outcome and QOL in hemodialysis patients.

Materials and Methods: The authors conducted a quasi-experimental research, a time series design. Patients who were hemodialyzed three times a week at Bhumirajanagarindra Kidney Institute Hospital were enrolled. Participants were trained to practice the Chanting with Anapanasati meditation for 35 minutes every hemodialysis session for six months. Comparison of depression scores, severity of depression, QOL, vital signs, laboratory data, and biomarkers (F2-isoprostanes) was made between the beginning and the end of the study.

Results: Forty patients were eligible for participation in the present study. The average age was 63.7±13.1 years. Median dialysis vintage was 29.5 months. After Dhamma practice for six months, diastolic blood pressure was decreased significantly (p=0.015). Median depression score decreased from 9.5 to 4 (p<0.001). The proportion of depressive patients were decreased from 17.5% to 2.5%. The severity of depression trended to decrease, but without statistical significance. F2-isoprostanes was decreased significantly (p<0.001). Both physical aspects (role physical, bodily pain, and physical component scale) and mental aspects (vitality, role emotional, mental health, and mental component scale) of QOL were significantly improved.

Conclusion: Dhamma practice by Chanting and Anapanassati meditation significantly decreased blood pressure, and depression, and improved QOL both physically and mentally, in hemodialysis patients.

Keywords: Depression, Quality of life, Hemodialysis, Meditation, Buddhist chanting, Dhamma.

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End stage renal disease (ESRD) is an important non-communicable disease (NCD). In Thailand, the number of ESRD patients increases every year[1]. While hemodialysis can extend ESRD patients' life expectancy, their mortality rate is still high, attributable to both physical and psychological disorders[2]. Depression is a common psychological disorder in chronic kidney disease (CKD) patients. The prevalence of depression in CKD patients is around 25%[3,4] and higher in CKD patients with rapid progression and high risk of dialysis initiation[5] or hemodialysis patients[6].

From a previous study in Thailand, depression prevalence of hemodialysis patients was 25%, which included 15% mild depression, 5% moderate depression, and 5% severe depression[7]. Risk factors of depression in hemodialysis patients are old age, unmarried status, number and severity of associated diseases, decreased ability to do daily activities or work, financial problem, lack of family and social support, lack of interaction with surrounding people, diet and fluid restriction, and sexual dysfunction[8,9].

Depression impairs the mental aspect of the quality of life (QOL)[10]. Depression is associated with increased risks of hospitalization and mortality in hemodialysis patients[10]. Worsening of depression

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was also associated with higher mortality in these patients[10].

An imbalance in serotonin levels may influence mood in a way that leads to depression. Depressed patients have lower serotonin level than normal population[11]. In the electroencephalogram (EEG), the alpha waves in depression groups were found to be lower compared to non-depressed groups[12,13]. Depression is associated with an increased in serum epinephrine and serum norepinephrine level[14]. There is evidence suggesting that oxidative stress may be increased in depression. Depression is associated with a decreased of antioxidants[15,16], therefore, an increase of oxidative damage[17] to lipids, proteins, DNA [reflected by high 8-hydroxydeoxyguanosine (8-OHdG), and F2-isoprostanes level][18].

The treatment of depression improves the QOL and survival in hemodialysis patients[19]. However, antidepressant medications can cause a wide range of unpleasant side effects such as dry mouth, blurred vision, constipation, dizziness, syncope, headache, agitation, insomnia, drowsiness, seizure, indigestion, nausea, and diarrhea[20]. Previous studies found that Dharma practice by Chanting and Anapanassati meditation decreased anxiety and depressive symptoms in patients with chronic diseases[21,22]. Other studies in hemodialysis patients also found that Dharma practice by Chanting and Anapanassati meditation decreased depression[7,23] and improved the physical aspects of the QOL in these patients[7]. After improving depression, C-reactive protein (CRP) level, which is a representative as biomarker of inflammation, and F2-isoprostane level, which is a representative as oxidative stress biomarker, was decreased in both plasma and urine samples[18,24-26].

The authors conducted the present study to evaluate the effect of Dhamma practice on depression outcome, QOL, and biomarkers associated with depression in hemodialysis patients.

Materials and Methods

The author conducted the quasi-experimental research, a time series design at Bhumirajanagarindra Kidney Institute Hospital between February and July 2016. The present study was approved by the Ethical Review Committee for Research in Human Subjects Bhumirajanagarindra Kidney Institute Hospital, Thailand (Ref. no. 3/2016). Written informed consents were obtained from all the enrolled patients. Inclusion criteria were hemodialysis patients who regularly received hemodialysis session three times/week for at least two months, all genders, age more than 18 years, and Buddhist. Exclusion criteria were patients who had acute complications such as sepsis or congestive heart failure, during the study, had irregular hemodialysis schedule, missed more than two hemodialysis sessions/month, had sense disabilities such as mental retardation, deafness, blindness, or illegibility, had mental disorders, or had associated disease with predicting prognosis of less than six months such as advanced cancer. At the beginning of the study, all patients filled out the questionnaire about baseline characteristics that included gender, age, status, occupation, medical reimbursement, family history, cause of ESRD, dialysis vintage, associated diseases, antidepressant medication, height, weight, body mass index, personal history such as smoking, alcohol drinking, exercise, diet, and sleep behavior, social history, and Buddhist activities.

Participants were trained to practice Dharma for 35 minutes every hemodialysis session for six months. During the hemodialysis session, the patients received wireless headphones to listen the Buddhism chanting for 15 minutes, the Anapanasati meditation's instruction for five minutes, and practiced Anapanasati meditation for 15 minutes. The co-author (Vareesangthip J) preached to patients for 15 minutes before Dharma practice once a month. The authors recorded blood pressure, heart rate, and respiratory rate before and after Dharma practice.

At the beginning, at the third month, and at the sixth month of the study, patients were encouraged to answer the questionnaire to evaluate depression and QOL. Depression score was assessed by using The Thai Depression Inventory (TDI)[27]. QOL was evaluated by using the SF-36 Questionnaire for Hemodialysis Patients (IN THAI)[28].

Laboratory data and biomarkers

At the beginning and the end of the present study, blood sample was collected for complete blood count, blood urea nitrogen (BUN), serum creatinine, serum electrolyte, serum calcium, serum albumin, serum phosphate, CRP. Meanwhile dialysis adequacy was determined using the single pool formula Kt/V (spKt/Vurea)[29] and normalized protein nitrogen appearance (nPNA) using the two-BUN formula, single-pool, and variable-volume model[29].

Serum F2-isoprostanes (8-iso-PGF2α) was measured at the beginning and the end of the study. The method of determine the serum F2-isoprostanes level was enzyme-linked immunosorbent assay

(ELISA) by using 8-iso-PGF2α-HRP conjugate enzyme[30].

Statistical analysis

Variables were expressed as mean ± standard deviation (SD), median and quartile in quantitative data or percentage, and frequency in categorical data.

Primary outcomes were depression score, SF-36 score, plasma level of F2-isoprostanes (8-iso-PGF2α), and CRP. Secondary outcomes were vital signs, laboratory data, and dialysis adequacy.

All statistical analyses were performed using the IBM SPSS Statistics software, version 24.0 (IBM Corp., Armonk, NY, USA). To compare the same parameter between beginning and the end of the study, paired t-test was used for normally distributed data and related-samples Wilcoxon signed rank test for non-normally distributed data. The criteria for significance was a p-value of less than 0.05.

Results

Fifty-six hemodialysis patients were assessed for eligibility. Two patients were excluded due to hearing loss, one patient because of sepsis, and one patient because of pain during hemodialysis. Ten patients withdrew from the study due to unwillingness to keep up with Dharma practice, one patient because of kidney transplantation, and one patient died . At the end of the present study, 40 patients completed the Dharma practice program, and blood sample were collected from 38 patients for biomarker.

Most patients in the present study were male (n=22, 58%) (Table 1). The average age was 63.7±13.1 years. Causes of ESRD were hypertension (47.5%), and diabetes (40%). Median dialysis vintage was 29.5 months before enrollment. Most of the patients were married (70%) and had children (85%). About 40% of the patients were not working. One-third of the patients had secondary education and one-third of the patients had a bachelor's degree. Almost all the patients had Government or State Enterprise insurance for medical reimbursement. A small number of patients smoked (5%) and drank alcohol (7.5%). Most patients could eat (90%) and sleep (75%) normally. Only 45% of the patients had normal exercise. The average height was 1.6±0.1 meters and average weight was 60.1±12.7 kilograms. Mean body mass index (BMI) was 23.4±4.9. Only one patient (2.5%) was taking antidepressant drugs. About Buddhist activities, all patients made merit. Most patients went to the temple (87.5%), prayed (77.5%), and observed the Five Precepts (72.5%).

Table 1. Baseline characteristics

Parameters	n=40; n (%)
Sex: male	22 (55.0)
Age (year); mean±SD	63.7±13.1
Cause of ESRD	
Hypertension	19 (47.5)
DM	16 (40.0)
Other	5 (12.5)
Dialysis vintage (month); median (Q1, Q3)	29.5 (16, 43.5)
Married status	29 (72.5)
Have child/children	34 (85.0)
Occupation	
None	17 (42.5)
Government officer	9 (22.5)
Educational background	
Under associate degree	15 (37.5)
Bachelor degree	13 (32.5)
Medical reimbursement	
Government or State Enterprise	37 (92.5)
Smoking	2 (5.0)
Alcohol drinking	3 (7.5)
Eating normally	36 (90.0)
Normal sleep	30 (75.0)
Normal exercise	18 (45.0)
Height (m); mean±SD	1.6±0.1
Weight (kg); mean±SD	60.1±12.7
BMI (kg/m^2); mean±SD	23.4±4.9
Antidepressant medications	1 (2.5)
Buddhist activities	
Making merit	40 (100)
Going to the temple	35 (87.5)
Praying	31 (77.5)
Observing the five precepts	29 (72.5)
Vipassana meditation	20 (50.0)

BMI=body mass index; SD=standard deviation

Fifty percent of the patients did Vipassana meditation.

There was no significant difference in heart rate, respiratory rate, and systolic blood pressure between before and after Dharma practice. Diastolic blood pressure was decreased statistically significant from 72.1±16.5 to 67.1±14.1 mmHg ($p<0.02$) without dosage adjustment of current antihypertensive medications.

The average hemoglobin, hematocrit, BUN, serum albumin, serum potassium, serum bicarbonate, serum phosphate, Kt/V, and nPNA were not significantly different when compared between before

Table 2. Laboratoty data and dialysis adequacy compared between before and after Dharma practice for 6 months

Laboratory data	n=40; mean±SD		p-value
	Before	After	
Hemoglobin (g/dL)	10.7±1.5	10.7±1.1	0.968
Hematocrit (%)	33.2±4.3	32.8±3.0	0.728
BUN (mg/dL)	60.5±18.5	58.1±21.4	0.379
Creatinine (mg/dL)	9.0±2.9	9.5±3.2	0.012
Albumin (g/dL)	3.7±0.3	3.7±0.3	0.195
Sodium (mEq/L)	135.5±3.7	136.7±2.9	0.012
Potassium (mEq/L)	4.6±0.8	4.5±0.7	0.231
Bicarbonate (mEq/L)	22.3±1.7	23.1±2.3	0.081
Calcium (mg/dL)	9.0±0.6	8.7±0.7	0.007
Phosphorius (mg/dL)	4.5±1.3	4.6±1.6	0.944
Dialysis adequacy			
Kt/V	2.1±0.5	2.2±0.5	0.264
nPNA	1.1±0.4	1.1±0.4	0.612

BUN=blood urea nitrogen; nPNA=normalized protein nitrogen appearance; SD=standard deviation

and after Dharma practice (Table 2). After Dharma practice, serum creatinine was increased from 9.0±2.9 to 9.5±3.2 mg/dL, and serum sodium was increased from 135.5±3.7 to 136.7±2.9 mEq/L (p=0.012), while serum calcium was decreased from 9.0±0.6 to 8.7±0.7 mg/dL (p=0.007).

Depression and quality of life

After Dhamma practice for six months, median depression score was decreased significantly from 9.5 to 4.0 (p<0.001). The proportion of non-depressed patients by patient-administered questionnaire

Table 3. Depression score compared between the beginning and the end of the study

Depression	n=40		p-value
	Before	After	
Depression score; median (Q1, Q3)	9.5 (6, 17)	4 (2, 9)	<0.001
Range	1 to 39	0 to 26	
Severity of depression; n (%)			0.057
None	33 (82.5)	39 (97.5)	
Mild	3 (7.5)	-	
Moderate	2 (5)	1 (2.5)	
Severe	2 (5)	-	
Very severe	-	-	

increased from 33 patients (82.5%) to 39 patients (97.5%), but without statistical significance (Table 3).

At the end of the present study, QOL was improved significantly (Table 4) in the aspect of role-physical (p=0.002), bodily pain (p=0.035), vitality (p=0.007), role-emotional (p=0.007), and mental health (p=0.001). After Dharma practice, hemodialysis patients improved QOL in both physical and mental aspects. Physical component scale increased significantly from 61.4±22.4 to 69.5±19.4 (p=0.01). Mental component scale also increased significantly from 67.0±22.9 to 77.5±14.2 (p<0.004).

Serum CRP level and serum F2-isoprostanes (8-iso-PGF2α) level

Serum CRP was not significantly different when compared before and after Dharma practice (Table 5), but median serum F2-isoprostanes (8-iso-PGF2α) level decreased by more than a half from 31,536.54

Table 4. Quality of life score (SF-36) compared between the beginning and the end of the study

SF-36	n=40; mean±SD		p-value
	Before	After	
Physical functioning; median (Q1, Q3)	65 (40, 85)	60 (30, 83.75)	0.182
Role-physical (physical role-limitation); median (Q1, Q3)	87.5 (0, 100)	100 (100, 100)	0.002
Bodily pain; median (Q1, Q3)	73 (41, 100)	100 (62, 100)	0.035
General health	50.3±25.5	55.6±23.3	0.219
Vitality	62.0±20.8	70.8±18.9	0.007
Social functioning; median (Q1, Q3)	75 (50, 100)	87.5 (50, 100)	0.131
Role-emotional (emotional role-limitation)	81.7±38.5	100±0	0.007
Mental health	75.1±24.1	87.0±13.6	0.001
Physical component scale	61.4±22.4	69.5±19.4	0.01
Mental component scale	67.0±22.9	77.5±14.2	0.004

SF-36=36-Item Short Form Survey; SD=standard deviation

Table 5. Serum C-reactive protein (CRP) and serum F2-isoprostanes (8-iso-PGF2α) level compared between before and after Dharma practice for 6 months

Biomarkers	n=38; median (Q1, Q3)		p-value
	Before	After	
CRP (mg/dL)	0.21 (0.14, 0.66)	0.18 (0.09, 0.40)	0.396
F2-isoprostanes (8-iso-PGF2α) (pg/mL)	31,536.54 (13,438.73, 52,761.47)	10,411.04 (7,726.18, 13,307.66)	<0.001

CRP=C-reactive protein

to 10,411.04 pg/mL (p<0.001), which was statistically significant, after Dharma practice.

Discussion

Meditation is widely used as alternative therapy for the treatment of depression in patients with chronic diseases and CKD patients. In Western countries, they mostly used meditation techniques, which were not associated with religious belief, such as yoga, mindfulness meditation, Transcendental Meditation[31-33]. Most of the Thai people are Buddhist, so the present investigators used Dharma practice by Chanting and Anapanassati meditation, which is associated with Buddhism, to treat depression in hemodialysis patients.

The results of the present study demonstrated that after Dhamma practice by Chanting and Anapanassati meditation, hemodialysis patients had lower Diastolic Blood Pressure, lower depression score, better QOL in many aspects, and the proportion of depressed patients trended to decrease. In agreement with the previous studies, Dhamma practice by Chanting and Anapanassati meditation decreased depression and improved the QOL both physically and mentally in hemodialysis patients[7,23].

During meditation, EEG studies have reported a significant increase in alpha waves[12,13]. Metabolic pathway changes from glucose metabolism to fatty acid metabolism[34,35] and serum lactate also decreases during meditation[36]. Meditators have a hypometabolic state. Meditation reduces activity in the nervous system. The parasympathetic activity predominates while the sympathetic activity is decreased, so serum epinephrine and serum norepinephrine level decreases 30% to 40%[14]. The present study confirmed the previous report that meditation lowers heart rate, systolic blood pressure, and diastolic blood pressure[37].

Meditation increases in gamma-aminobutyric acid (GABA) production by enhancing hypothalamic GABAergic tone to promote anxiolytic effect[34,35]. Meditators also exhibit a higher serotonin level after meditation[38]. These are the reasons why meditation helps to decrease anxiety levels and decrease depression. It mimics the effect of antidepressant drugs such as serotonin reuptake inhibitor (SSRI)[11,39].

From the present study, the authors found that meditation improved the QOL in the aspect of bodily pain. In meditation, calmness stimulates to release β-endorphin, which relieves pain by inhibiting the firing of peripheral somatosensory fibers[40]. Meditation also improved mental aspects of the QOL. These results were consistent with previous studies that meditation improved the QOL in patients with ESRD[21,31] and other diseases such as cancer[22].

Plasma F2-isoprostanes (8-iso-PGF2α) decreased significantly after Dharma practice. This result indicated that oxidative stress was decreased after Dharma practice. Although many factors such as uremia[41], congestive heart failure[42], blood-membrane incompatibility reaction[43], and intravenous iron infusion[44] are associated with increased oxidative stress in hemodialysis patients, these factors cannot explain the change of oxidative biomarker after Dharma practice because all these factors are not present or constant in the present study. It may be that Dharma practice decreased depression and decreased oxidative stress that lower F2-isoprostanes level as shown in a previous study[18].

There are some differences between the present study and the previous study[7]. The previous study compared different mental practice intervention groups and found that depression was decreased only in the meditation group. The present study was a pre-post comparison study and found that Chanting and Anapanassati meditation decreased depression and improved the QOL both physically and mentally.

There are several limitations in the present study. The study was only a single center study. The study was not a randomized controlled trial (RCT) trial and did not have a control group to compare. Around 25% of the enrolled hemodialysis patients withdrew from the study, which may lead to decrease reliability of the study. The present study used

Chanting and Anapanassati meditation, which is a Buddhism activity in Thailand, to treat depression. So, this method cannot apply to patients with other religious belief.

The present investigators have suggested that further research should be conducted in the form of RCT to compare depression, QOL, and biomarkers between a Dharma practice group and a control group. In cases of applying to other religious patients, the authors suggested to adjust the method to that religion, perhaps using the prayers of each religion or meditation techniques that were not associated with religious belief to help patients understand meditation well.

Conclusion

Dhamma practice by Chanting and Anapanassati meditation significantly decreased blood pressure and depression, and improved the QOL both physically and mentally, in hemodialysis patients. However, further RCT is needed to confirm the effect of Dharma practice on depression outcome.

What is already known on this topic?

Depression impairs the QOL, and increases risk of hospitalization and death in hemodialysis patients. The treatment of depression improves the QOL and survival, but antidepressant medications can cause a wide range of unpleasant side effects in hemodialysis patients. An alternative treatment of depression may be the Dharma practice. Some studies evaluated the effect of Dharma practice by Chanting and Anapanassati meditation on depression outcome in hemodialysis patients. However, none of these studies evaluated the biomarkers associated with depression.

What this study adds?

The author conducted the present study to evaluate the effect of Dhamma practice on depression outcome, the QOL, and the biomarkers associated with depression in hemodialysis patients.

The present study found that Dhamma practice by Chanting and Anapanassati meditation significantly decreased depression, confirmed by lowering depression score and biomarkers associated with depression, in hemodialysis patients. Dhamma practice by Chanting and Anapanassati meditation also improved the QOL both physically and mentally in hemodialysis patients. The present study added that Dhamma practice by Chanting and Anapanassati meditation can be an alternative treatment in the treatment of depression in hemodialysis patients.

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Conflicts of interest

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. There are no conflicts of interest.

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