Role of Meditation in Reducing Sympathetic Hyperactivity and Improving Quality of Life in Lupus Nephritis Patients with Chronic Kidney Disease

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Background: *Lupus nephritis is an important leading cause of chronic kidney disease (CKD) among the young population in Thailand. Systemic lupus erythematosus (SLE) is often characterized by the presence of sympathetic hyperactivity, which results in a perishing outcome. Some physiological studies reveal that meditation may reduce this autonomic dysfunction. The authors hypothesized that meditation could be beneficial in alleviating the sympathetic hyperactivity and improving quality of life in lupus nephritis patients with CKD.*

Material and Method: *The authors performed a prospective pilot study, which enrolled lupus nephritis patients and categorized enrollees into meditation group and control group. Method of meditation was instructed by an expert in Buddhist studies for a duration of 60 minutes every month. Participants in the intervention group were advised to meditate every day for 24 weeks. To evaluate change in sympathetic activity, normetanephrine level was measured at beginning and the end of study and compared between both groups. Quality of life was determined by SF-36. Heart rate variability was also assessed in meditation group.*

Results: *Thirty eligible patients were recruited into the study. Fifteen patients were stratified in the meditation group and 15 patients in the control group. After meditation for 6 months, serum normetanephrine level decreased, but without statistical significance (0.105 vs. 0.059, p = 0.28). The reduction in normetanephrine level was also observed in the control group (p = 0.11). In the aspect of quality of life, scores of physical and mental components improved significantly. In meditation group, physical component score increased from 21.4 (5.0-50.2) to 62.2 (51.8-88.4) points (p<0.01) and mental score increased from 16.9 (4.4-46.0) to 72.4 (45.1-81.6) points (p<0.01). Quality of life score in the meditation group significantly increased more than in control group (p<0.01). The parameter of heart rate variability in time and frequency domain also improved in the meditation group.*

Conclusion: *In lupus nephritis patients with CKD, meditation shows a trend of benefits in reducing sympathetic overactivity and improving quality of life. Our results support the important role of meditation as a valuable adjunctive treatment of lupus nephritis with CKD.*

Keywords: *Meditation, Sympathetic hyperactivity, Quality of life, Chronic kidney disease, Normetanephrine, Heart rate variability*

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Lupus nephritis (LN) is an important cause of chronic kidney disease (CKD) among the young population in Thailand. Systemic lupus erythematosus (SLE) is often characterized by the presence of sympathetic hyperactivity resulting in a poor outcome[1]. There is clinical evidence revealed that SLE accompanied autonomic dysfunction[2], diminished cardiovascular autonomic nervous system response, decreased heart rate variability and increased sympathetic outflow[3].

Sympathetic outflow directly affects multiple

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organs such as the heart and the vascular structure. Chronically elevated sympathetic outflow not only contributes to high BP but also has adverse effects on these organs, particularly the heart, where sympathetic activation has been demonstrated to induce left ventricular hypertrophy and arrhythmias. Stimulation of the renin-angiotensin-aldosterone system, alteration in the L-arginine/NO pathway and aggravation of hypertension are common sequelae of sympathetic hyperactivity. A large number of additional factors may further aggravate both the increase in BP and target organ damage, thereby contributing to cardiovascular morbidity and mortality in lupus nephritis patients[4].

Some physiological studies showed that meditation could reduce respiratory rate, serum cortisol and norepinephrine levels and also decrease sympathetic nerve activity in healthy participants[5-7]. Another clinical study also revealed that meditation could reduce sympathetic activity and improve quality of life in congestive heart failure patients[8]. Nowadays, there has not been any study about role of meditation in management of CKD. The authors hypothesized that meditation could be beneficial in alleviating the sympathetic hyperactivity and improving the quality of life in LN patients with CKD.

Material and Method

The authors conducted a prospective study for a 6 months period. The present study population was comprised of 30 adult patients, age between 20-70 years old, from Siriraj Nephrology clinic, who were diagnosed as SLE with CKD stage 1-5. Patients who were receiving beta-adrenergic antagonists, or having severe concomittent disease or life-threatening conditions were excluded. Enrolled patients were allocated into two groups, the meditation and control groups. All subjects in both groups were receiving regular medication such as anti-hypertensive and immunosuppressive agents.

The interventional group was given a meditation program, which was instructed by an expert in Buddhist studies for a duration of 60 minutes every month for 3 months. The meditation practice consisted of two parts, Buddhism chanting for 25 minutes and a meditation part for 15 minutes. Process of meditation was controlled breathing, with deep and slow breaths that were also known among practitioners of yoga as "Anapanasati". The aims of this technique were to reduce breathing rate and to learn how to mobilize in sequence-that is, within the same breath-the diaphragm, the lower chest, and then the upper chest during inhalation, and the reversed sequence during exhalation. The participants in the meditation group were advised to practice at home every day.

To assess sympathetic activity, serum normetanephrine level, which is metabolite of norepinephrine, was measured in all patients at beginning of study, 3 months after study and end of study. Blood was collected in sitting position in the morning. Method of determine normetanephrine level was liquid chromatography-mass spectrometry (LC-MS) assay. Heart rate variability (HRV), a non-invasive measure of autonomic dysfunction was also performed at beginning and the end of study. HRV was done by recording EKG for 30 minutes, which was used to detect beat-to-beat variability reported as time domain and frequency domain. Time domain assessed variability in RR interval whereas frequency domain evaluated cyclical changes in heart rate by fast Fourier transformation into spectral representation[9].

Quality of life (QOL) was evaluated using The Short Form (36) Health Survey (SF-36, Thai version) at beginning and the end of study[10]. All patients were encouraged to answer this form themselves without any assistance or pressure. We also determined blood pressure, heart rate, urine protein/creatinine ratio, blood urea nitrogen, serum creatinine every month.

Statistical analysis

Variables were expressed as mean $\pm$ SD or median with range depend on types of data. Categorical variables were compared using Chi-squared test. Continuous variables were compared using Independent Student's t-test or Mann-Whitney U-test according to distribution of data. To compare the same parameter between beginning and the end of treatment, paired t-test was used for normally distributed data and Wilcoxon test for non-normally distributed data. Analysis of co-variance was used to compare change in quality of life score between both groups. The criteria for significance was $p \leq 0.05$. All statistical analyses were performed using the SPSS version 17.0 software.

Results

Baseline patient characteristics

Thirty patients were allocated equally into two groups. Baseline patient characteristics are displayed in Table 1. The average age was 35.8 ± 10.4 years and 34.3 ± 12.6 years in meditation and control group, respectively. The majority of patients were female (n = 28, 93.3%). Nine patients (60%) in meditation group and seven patients (46.7%) in control group had active

Table 1. Baseline characteristics compared between meditation and control group

Parameters	Meditation (n = 15)	Control (n = 15)	p-value
Age (year)	35.8±10.4	34.3±12.6	0.73
Female gender (n)	13 (86.7%)	15 (100%)	0.48
Body mass index (kg/m^2)	22.5±4.7	22.5±4.3	0.98
Heart rate (bpm)	86.7±3.8	86.9±5.3	0.94
Mean arterial pressure (mmHg)	97.2±10.8	95.8±12.3	0.74
Active lupus nephritis (n)	9 (60%)	7 (46.7%)	0.46
Immunosuppressive agents (n)			
Cyclophosphamide	7 (46.7%)	1 (6.7%)	0.04
Azathioprine/MMF	8 (53.4%)	9 (60%)	0.74
Prednisolone	13 (86.7%)	14 (93.3%)	1.00
ACEI	10 (66.7%)	10 (66.7%)	1.00
ARB	2 (13.3%)	4 (26.7%)	0.65
Hemoglobin (g/dl)	11.2±2.7	11.6±1.7	0.57
Leukocytes (/mm^3)	6,730 (2,200-12,520)	6,010 (3,560-15,580)	0.84
Platelet (/mm^3)	222,200±40,281	272,200±88,308	0.06
BUN (mg/dl)	13.3 (4.9-40.1)	17.5 (7.5-71.6)	0.30
Creatinine (mg/dl)	0.8 (0.6-3.1)	0.9 (0.5-2.3)	0.75
FBS (mg/dl)	101.6±24.1	102.5±21.9	0.93
LDL (mg/dl)	135.8±59.4	149.5±57.4	0.66
Albumin (g/dl)	3.6±0.8	3.7±0.8	0.57
UPCR (g/gCr)	1.7 (0-6.8)	1.4 (0.2-10.1)	0.63

MMF = mycophenolate mofetil; ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BUN = blood urea nitrogen; FBS = fasting blood sugar; LDL = low density lipoprotein; UPCR = urine protein creatinine ratio

LN at enrollment. The average hemoglobin, serum creatinine, albumin and urine protein creatinine ratio were 11.2±2.7 g/dl, 0.8 (0.6-3.1) mg/dl, 3.6±0.8 g/dl and 1.7 (0-6.8) g/gCr in meditation group, consecutively, which was not significantly different when compared with the control group. However, patients in meditation group tended to receive cyclophosphamide at recruitment more than control group (46.7% vs. 6.7%, p = 0.04).

Serum normetanephrine level

Serum normetanephrine level tended to decrease over time during the study period in both groups, but without any statistical significance (Fig. 1). The median of serum normetanephrine level at baseline, 3rd month and 6th month were 0.105 (0.004-0.585) ng/ml, 0.078 (0.003-0.256) ng/ml and 0.059 (0.001-0.253) ng/ml, respectively, in meditation group versus 0.126 (0.011-0.363) ng/ml, 0.066 (0.004-0.539) ng/ml and 0.054 (0.009-0.235) ng/ml, consecutively, in control group. The authors also compared change in normetanephrine level during the study in both groups and this revealed no significant difference (p>0.05, Wilcoxon test).

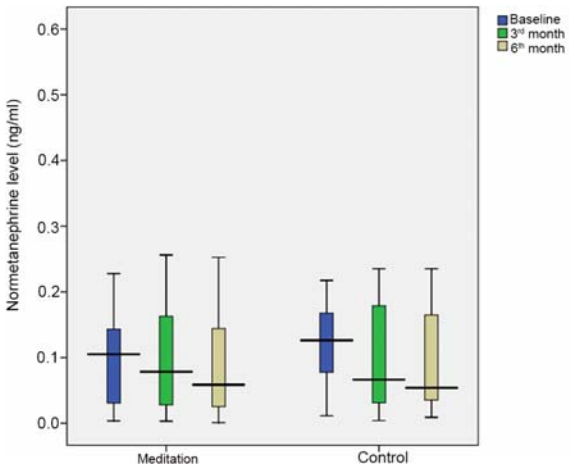

Fig. 1 Serum normetanephrine level were given as box plots compared between meditation and control group at baseline, 3rd month and 6th month.

Heart rate variability

Heart rate variability was measured only in the meditation group due to time constraint. The authors found significant improvement of parameter of both time domains; SDNN, SDSD, RMSSD and frequency

Table 2. Heart rate variability in meditation group

Parameters	Before (n = 15)	After (n = 15)	p-value
Time domain			
SDNN (ms)	23.38 (13.08-36.32)	34.50 (22.33-60.41)	<0.01
SDSD (ms)	15.30 (7.55-23.68)	26.72 (13.66-54.41)	0.03
RMSSD (ms)	15.28 (7.54-23.64)	26.68 (13.65-54.34)	0.03
Frequency domain			
Total power (ms^2)	570.04 (155.50-1,242.71)	1,330.04 (532.79-3,234.22)	0.01
VLF (ms^2)	254.21 (51.12-735.64)	608.41 (155.55-2078.84)	0.03
LF (ms^2)	151.02 (22.34-443.09)	282.49 (74.24-772.50)	0.07
HF (ms^2)	144.87 (22.32-343.69)	348.57 (62.88-1,248.44)	0.09
LF/HF	1.21 (0.17-2.36)	1.24 (0.10-2.81)	0.92

SDNN = standard deviation of all NN intervals; SDSD = standard deviation of differences between adjacent NN intervals; RMSSD = the square root of the mean of the square of successive NN intervals; VLF = power in very low frequency range; LF = power in low frequency range; HF = power in high frequency range; LF/HF = ratio of low to high frequency power

Table 3. Change of physical and mental component score in meditation and control groups

Quality of life score	Meditation (n = 15)	Control (n = 15)	p-value
Change of physical component	46.6±12.9	34.9±8.7	0.02
Change of mental component	48.7±14.2	32.4±9.2	<0.01

domains; total power, VLF (Table 2).

Quality of life

Quality of life scores, by SF-36, were summarized in Fig. 2. The median of physical and mental component score at baseline were 21.4 (5-50.2) and 16.9 (4.4-46) in meditation group while 19.4 (10.4-49.2) and 13.9 (7.7-44.2) in control group, respectively. The median of physical and mental component score at the end of study were 62.2 (51.8-88.4), 72.4 (45.1-81.6) in meditation group and 55.4 (36.4-83.4), 45 (29.8-77.6) in control group, consecutively. The significant improvement in the quality of life scores of both groups were observed.

Change of quality of life score during study compared between both groups was determined by analysis of co-variance (ANCOVA) and found statistically, significantly higher for both physical and mental component scores in the meditation group (Table 3).

The significantly greater improvement in important modality of SF-36 consisted of general health, vitality, social function and mental health, which were also demonstrated in patients who performed meditation (p<0.01) (Fig. 3).

For clinical parameters at the end of study, 6 months period, heart rate was meaningfully lower in meditation group (78.5±4.7 vs. 82.2±4.2 , p = 0.03) while no differences were found in other markers (Table 4).

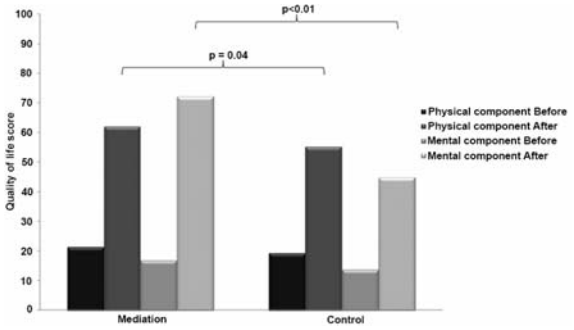

Fig. 2 Quality of life (QOL) score in both groups; physical and mental components at baseline and end of study.

Discussion

To the best of our knowledge, the present study represents the first analysis of meditation in a prospective manner in non-dialysis CKD (stages 1-4) patients. The authors have investigated the effect of meditation, which is simple, feasible, and easily performed in outpatient population on autonomic function in patients with SLE. Two different assessment methods were applied for this purpose, including the

measurement of autonomic parameters by serum normetanephrine level and heart rate variability.

Normetanephrine is a main metabolite of norepinephrine created by action of Catechol-O-methyltransferase on norepinephrine. It is a marker for catecholamine secretion, which is implying sympathetic hyperactivity. From the present study, serum normetanephrine level tended to decrease during follow-up period, but without statistical significance, in both meditation and control groups. Explanation of this finding could be for three reasons: amelioration of activity of lupus nephritis, which is evidenced in both groups may lower normetanephrine levels itself and obscure the effect of meditation, relatively small sample size and short period of practice.

Heart rate variability is a method to evaluate cardiac autonomic function response. Chandra et al[9] studied 305 subjects with CKD and found that lower HRV was significantly associated with higher risk of poor cardiovascular and renal outcomes. The present study showed significant increased HRV after meditation for 24 weeks. Whether meditation results in better HRV outcomes and improves cardiovascular and renal outcomes in this high-risk population, it deserves further study.

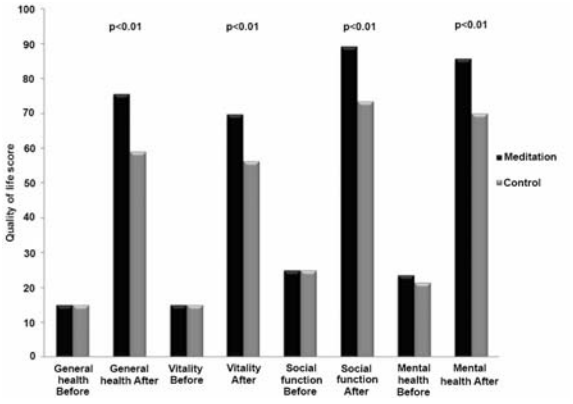

Fig. 3 Quality of life (QOL) score in important modalities between two groups at baseline and end of study.

The crucial finding of the present study is that quality of life is improving in lupus nephritis patients. The authors also demonstrate that quality of life scores at the end of study are significantly superior in meditation group. Vareesangthip J[11] studied of role of meditation in 80 hemodialysis patients and showed that Dhamma practice by the method of doing the "Anapanasati" meditation significantly decreased the depression and improved the physical aspect of the quality of life. Moreover, the heart rate and respiratory rate in the chanting group were significantly decreased.

The present study emphasized that the benefits in the quality of life as an effect of meditation in lupus nephritis patients corresponded with previous studies. The main reason for better quality of life scores after 24 weeks of follow-up period in both groups may be the effect from remission of active disease by medication. However, the change in quality of life scores is significantly higher in meditation group, although with comparable baseline score. The authors did not reveal significant change in clinical parameters at the end of study; that may be from the relatively short duration of follow-up.

There are some limitations in the study such as no randomization of allocation, lack of heart rate

Table 4. Clinical and laboratory data at the end of study compared between the 2 groups

Parameters	Meditation (n = 15)	Control (n = 15)	p-value
Body mass index (kg/m^2)	22.4±4.8	22.4±3.9	0.97
Heart rate (bpm)	78.5±4.7	82.2±4.2	0.03
Mean arterial pressure (mmHg)	93.4±11.2	96.7±14.3	0.50
Hemoglobin (g/dl)	11.7±2.0	11.7±1.2	0.93
Leukocytes (/mm^3)	6,110±3,033	6,540±4,157	0.22
Platelet(/mm^3)	258,730±52,066	266,200±93,613	0.79
FBS (mg/dl)	102.2±21.5	100.7±21.4	0.91
LDL (mg/dl)	148.8±20.9	132.5±50.3	0.68
Albumin (g/dl)	3.7±0.5	3.6±0.6	0.98
BUN (mg/dl)	13.5 (6.7-47.5)	15.9 (3.0-47.2)	0.68
Creatinine (mg/dl)	0.8 (0.6-4.6)	0.8 (0.5-2.4)	0.82
UPCR (g/gCr)	1.1 (0-7.5)	0.5 (0.1-4.1)	0.97

FBS = fasting blood sugar; LDL = low density lipoprotein; BUN = blood urea nitrogen; UPCR = urine protein creatinine ratio

variability data in control group, half of the patients in study had active lupus nephritis, no observation of meditation practice at home and a relatively short period of intervention.

However, our findings support the benefit of practice the "Dhamma" which is one of pivotal importance in Thai culture in making life more desirable. Further study on the role of meditation in slowing progression of chronic kidney disease might be worth conducting, focusing on this objective evidence.

Conclusion

In lupus nephritis patients with CKD, meditation shows a trend of benefits in reducing sympathetic overactivity and improving quality of life. Our results support the important role of meditation as a valuable adjunctive treatment of CKD from lupus nephritis.

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Potential conflicts of interest

None.

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บทบาทของธรรมปฏิบัติต่อการทำงานของระบบประสาทซิมพาเทติกและคุณภาพชีวิตในผู้ป่วยโรคไตอักเสบลูปัส

ศิรวิทย์ บัณฑรวรรณ, วัฒนา วัฒนาภา, พวงเพชร หัสรินทร์, สมฤดี ฉัตรสิริเจริญกุล, นัฐสิทธิ์ ลาภปริสุทธิ, ธัญญารัตน์ ธีรพรเลิศรัฐ, จุฑามาศ วารีแสงทิพย์, เกรียงศักดิ์ วารีแสงทิพย์

ภูมิหลัง: โรคไตอักเสบลูปัส (Lupus nephritis) เป็นสาเหตุที่สำคัญของภาวะไตวายเรื้อรังซึ่งพบได้บ่อยในประชากรไทย โดยเฉพาะช่วงวัยรุ่นและวัยผู้ใหญ่ ภาวะระบบประสาทซิมพาเทติกทำงานมากเกินไป (Sympathetic hyperactivity) พบได้บ่อยในผู้ป่วยโรคเอสแอลอี ซึ่งทำให้ผลการรักษาไม่ดีเท่าที่ควร การศึกษาทางสรีรวิทยาจำนวนหนึ่งพบว่าการปฏิบัติสมาธิอาจช่วยลดความผิดปกติของระบบประสาทอัตโนมัติได้ การศึกษานี้จัดทำขึ้นโดยสมมติฐานว่าธรรมปฏิบัติอาจได้ประโยชน์ในการลดการทำงานของระบบประสาทซิมพาเทติกและช่วยเพิ่มคุณภาพชีวิตในผู้ป่วยโรคไตอักเสบลูปัสที่มีภาวะไตวายเรื้อรัง

วัสดุและวิธีการ: การศึกษาจัดทำในแบบเก็บข้อมูลติดตาม (Prospective study) ผู้ป่วยโรคไตอักเสบลูปัสจำนวนทั้งสิ้น 30 ราย เป็นเวลา 6 เดือน โดยแบ่งผู้เข้าร่วมการศึกษาออกเป็น 2 กลุ่ม คือ กลุ่มธรรมปฏิบัติและกลุ่มควบคุม ซึ่งกลุ่มธรรมปฏิบัติจะได้รับการสอนวิธีการและรายละเอียดในการปฏิบัติธรรมโดยผู้เชี่ยวชาญทางด้านพระพุทธศาสนาครั้งละ 60 นาที เป็นประจำทุกเดือนและแนะนำให้ไปปฏิบัติต่อเองที่บ้านทุกวันต่อเนื่องเป็นระยะเวลา 24 สัปดาห์ การศึกษานี้ประเมินการทำงานของระบบประสาทซิมพาเทติกโดยการตรวจเลือดวัดระดับ normetanephrine และการตรวจความผันแปรของชีพจร (heart rate variability) ทั้งยังประเมินคุณภาพชีวิตด้วย SF-36 ก่อนและหลังเข้าร่วมการศึกษา

ผลการศึกษา: มีผู้เข้าร่วมการศึกษากลุ่มละ 15 ราย หลังจากปฏิบัติธรรมเป็นระยะเวลา 6 เดือน พบว่าระดับ normetanephrine ลดลงแต่ไม่มีนัยสำคัญทางสถิติ ($p = 0.28$) เช่นเดียวกับในกลุ่มควบคุม ($p = 0.11$) การตรวจความผันแปรของชีพจร (heart rate variability) ซึ่งทำการตรวจเฉพาะกลุ่มธรรมปฏิบัติพบว่าดีขึ้น ทั้งค่าตัวแปรด้านระยะเวลา (time domain) และค่าตัวแปรด้านความถี่ (frequency domain) ส่วนผลการประเมินคุณภาพชีวิตพบว่าดีขึ้นทั้งองค์ประกอบทางด้านกายภาพและจิตใจ (physical and mental components) อย่างมีนัยสำคัญทางสถิติ โดยในกลุ่มธรรมปฏิบัติมีคะแนนด้านกายภาพเพิ่มขึ้นจาก 21.4 (5.0-50.2) เป็น 62.2 (51.8-88.4) คะแนน ($p<0.01$) และคะแนนด้านจิตใจเพิ่มขึ้นจาก 16.9 (4.4-46.0) เป็น 72.4 (45.1-81.6) คะแนน ($p<0.01$) อย่างไรก็ตามพบว่าคะแนนทั้งด้านกายภาพและจิตใจก็เพิ่มขึ้นในกลุ่มควบคุมเช่นกันโดยด้านกายภาพเพิ่มจาก 19.4 (10.4-49.2) เป็น 55.4 (36.4-83.4) คะแนน ($p<0.01$) และด้านจิตใจเพิ่มจาก 13.9 (7.7-44.2) เป็น 45.0 (29.8-77.6) คะแนน ($p<0.01$) ตามลำดับ โดยคะแนนคุณภาพชีวิตในกลุ่มธรรมปฏิบัติเพิ่มขึ้นมากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ

สรุป: ในผู้ป่วยโรคไตอักเสบลูปัสที่มีภาวะไตวายเรื้อรังพบว่า ธรรมปฏิบัติทำให้คุณภาพชีวิตดีขึ้นกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ ความผันแปรของชีพจร (heart rate variability) ดีขึ้นในกลุ่มธรรมปฏิบัติ ส่วนระดับ normetanephrine ในเลือดมีแนวโน้มลดลงทั้งสองกลุ่ม การศึกษานี้สนับสนุนบทบาทของธรรมปฏิบัติเพื่อเป็นการรักษาร่วมสำหรับผู้ป่วยโรคไตอักเสบลูปัสที่มีภาวะไตวายเรื้อรัง