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I don't want you to be only
a doctor but I also want you
to be a man
A quotation by His Royal Highness Prince Mahidol of Songkla

the clinical academia

Aim and Scope

Our journal is an opened access international journal devoted to peer-reviewed contributions dealing with clinical medicine and medical education from experimental to clinical aspects. Our journal publishes only high quality research, review and other types of original articles, technical and clinical reports every two months. Reviews of various global and Asian aspects will be solicited. Innovation or epidemiological aspects as well as health system research will be addressed. Rigorous systematic review and neglected tropical diseases are our priority

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message from the editor

Dear readers,

This is the second issue of volume 45. In this issue, we hope that you, our beloved reader, would benefit from reading our interesting studies including the study regarding diagnostic performances of different cut-off points of urine protein to creatinine ratio for detection of significant proteinuria in suspected preeclamptic women. Another study is about the intervention to enhance adherence of the continuous positive airway pressure machine users using the cloud-based tracking system with telemonitoring. The last but not least study in this issue is the use of topical herbal medicine to relieve pruritus in patients with end-stage renal disease. We do hope you found these interesting as always.

Enjoy!

Thammasorn Jeeraaumponwat, M.D., Ph.D.
Editor-in-Chief of The Clinical Academia

submission

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Our issues of each volume will be published online
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All accepted articles are classified into two main categories;
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Contents

1. General Principles

The text of articles reporting original research is usually divided into Introduction, Methods, Results, and Discussion sections. This so-called "IMRAD" structure is not an arbitrary publication format but a reflection of the process of scientific discovery. Articles often need subheadings within these sections to further organize their content. Other types of articles, such as meta-analyses, may require different formats, while case reports, narrative reviews, and editorials may have less structured or unstructured formats.

Electronic formats have created opportunities for adding details or sections, layering information, cross-linking, or extracting portions of articles in electronic versions. Supplementary electronic-only material should be submitted and sent for peer review simultaneously with the primary manuscript.

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Reporting guidelines have been developed for different study designs; examples include CONSORT for randomized trials, STROBE for observational studies, PRISMA for systematic reviews and meta-analyses, and STARD for studies of diagnostic accuracy. Journals are encouraged to ask authors to follow these guidelines because they help authors describe the study in enough detail for it to be evaluated by editors, reviewers, readers, and other researchers evaluating the medical literature. Authors of review manuscripts are encouraged to describe the methods used for locating, select¬ing, extracting, and synthesizing data; this is mandatory for systematic reviews. Good sources for reporting guidelines are the EQUATOR Network and the NLM's Research Reporting Guidelines and Initiatives.

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The following are general requirements for reporting within sections of all study designs and manuscript formats.

a. Title Page

General information about an article and its authors is presented on a manuscript title page and usually includes the article title, author information, any disclaimers, sources of support, word count, and sometimes the number of tables and figures.

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Word count. A word count for the paper's text, excluding its abstract, acknowledgments, tables, figure legends, and references, allows editors and reviewers to assess whether the information contained in the paper warrants the paper's length, and whether the submitted manuscript fits within the journal's formats and word limits. A separate word count for the Abstract is useful for the same reason.

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Original research, systematic reviews, and meta-analyses require structured abstracts. The abstract should provide the context or background for the study and should state the study's purpose, basic procedures (selection of study participants, settings, measurements, analytical methods), main findings (giving specific effect sizes and their statistical and clinical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations, note important limitations, and not over-interpret findings. Clinical trial abstracts should include items that the CONSORT group has identified as essential. Funding sources should be listed separately after the Abstract to facilitate proper display and indexing for search retrieval by MEDLINE.

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c. Introduction

Provide a context or background for the study (that is, the nature of the problem and its significance). State the specific purpose or research objective of, or hypothesis tested by, the study or observation. Cite only directly pertinent references, and do not include data or conclusions from the work being reported.

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Specify the study's main and secondary objectives–usually identified as primary and secondary outcomes. Identify methods, equipment (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow others to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and brief descriptions for methods that have been published but are not well-known; describe new or substantially modified methods, give the reasons for using them, and evaluate their limitations. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration. Identify appropriate scientific names and gene names.

iii. Statistics

Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to judge its appropriateness for the study and to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size and precision of estimates. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. Specify the statistical software package(s) and versions used. Distinguish prespecified from exploratory analyses, including subgroup analyses.

e. Results

Present your results in logical sequence in the text, tables, and figures, giving the main or most important findings first. Do not repeat all the data in the tables or figures in the text; emphasize or summarize only the most important observations. Provide data on all primary and secondary outcomes identified in the Methods Section. Extra or supplementary materials and technical details can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.

Give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical significance attached to them, if any. Restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. Avoid nontechnical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlations," and "sample."

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Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, distinguish between clinical and statistical significance, and avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses when warranted, but label them clearly.

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References should follow the standards summarized in the NLM's International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals: Sample References webpage and detailed in the

NLM's Citing Medicine, 2nd edition. These resources are regularly updated as new media develop, and currently include guidance for print documents; unpublished material; audio and visual media; material on CD-ROM, DVD, or disk; and material on the Internet.

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Tables capture information concisely and display it efficiently; they also provide information at any desired level of detail and precision. Including data in tables rather than text frequently makes it possible to reduce the length of the text.

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Diagnostic performances of different cut-off points of urine protein to creatinine ratio for detection of significant proteinuria in suspected preeclamptic women

ORIGINAL ARTICLE BY

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ABSTRACT

OBJECTIVE

To determine the diagnostic performances of different urine protein to creatinine ratio (UPCR) cut-off points for diagnosis of significant proteinuria compared with the standard 24-hour urine protein (UP-24) in suspected preeclampsia (PE) women.

METHODS

This cross-sectional diagnostic study was conducted in suspected PE pregnant women with gestational age above 20 weeks from April to October 2019, at Roi-Et Hospital, Thailand. Their random urine samples for UPCR and UP-24 collection were examined. The diagnostic performances of different UPCR cut-off points were later compared.

RESULTS

A total of 116 pregnant women were included in the present study. The prevalence of significant proteinuria (UP-24≥300 mg) was 62.9% (95% confidence interval (CI), 59.7 to 77.2). The UPCR cut-off point at ≥0.30 mg/g had the best diagnostic performance when compared with other cut-off points with the sensitivity, specificity, positive and negative predictive value, accuracy and Youden index at 87.7%, 86.1%, 91.4%, 80.4%, 87.1%, and 73.8, respectively. Area under the receiver operating characteristic curve of the UPCR was 91.3% (95% CI, 85.9 to 96.6). The borderline group (UPCR between 0.20 to 0.29), 30.8% had significant proteinuria (UP-24>300 mg).

CONCLUSION

The UPCR cut-off point at 0.30 mg/g had the best diagnostic performance index, however the borderline UPCR between 0.20 to 0.29 mg/g had a high rate of significant proteinuria.

INTRODUCTION

Preeclampsia (PE) is one of the major causes of serious maternal and fetal complications.[1-3] The others include eclampsia, maternal mortality, HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome, placental insufficiency, fetal distress or death and preterm birth.[3-4] The prevalence of PE has been reported to be 1.8% to 16.7%.[5-6] The disease is diagnosed by new onset of hypertension and the presence of significant proteinuria.[4, 7] Therefore, lower case proteinuria is a main component of the diagnosis and severity criteria of PE.[8] Twenty- four- hour urine protein measurement (UP-24) is the standard diagnostic method for the qualification of proteinuria. Significant proteinuria in pregnancy is defined as proteinuria ≥300 mg/day.[9] However, the benefit of UP-24 is limited due to inconvenience and time consumption. Waiting time for urine collection can cause delayed diagnosis and management in this emergency condition.[3,8,10-12] Several studies reported a spot urine protein to creatinine ratio (UPCR) as a simple alternative option that has advantages in terms of more rapidity and convenience.[10,12-18] The commonly used cut-off point for significant proteinuria is 0.30 mg/g.[4,7] Several studies reported other UPCR cut-off points has been proposed showing the higher rates of significant proteinuria prediction varying between 0.20 and 0.35.[8,11,12,14,19,20] Based upon this inconclusive information, the objective of this study was to determine the diagnostic performance of different UPCR cut-off points compared with the gold standard UP-24 in the prediction of significant proteinuria.

METHODS

STUDY DESIGN AND OVERSIGHT

This cross-sectional diagnostic test study was conducted with pregnant women over 18 years of age with a gestational age above 20 weeks from April to October 2019. The study was conducted at Roi-Et Hospital, Thailand. This study protocol was approved by the Research Ethics Committee of Roi-Et Hospital (RE 032/2562). The written informed consent was obtained from all participants before enrolling in this study.

PARTICIPANTS

The inclusion criteria were pregnant women with new onset of hypertension (blood pressure ≥140/90 mmHg) and were suspected of having PE from their clinical appearance such as proteinuria, severe headache and changes in version. Patients with chronic hypertension, diabetes mellitus, kidney diseases and having emergency conditions for termination of pregnancy (i.e., eclampsia or fetal distress) were excluded.

DATA COLLECTION

Characteristics, including age, parity, gestational age were recorded. All participants were admitted for blood pressure monitoring. The methods of urine sample collection were explained to all participants. Urine specimens were collected two times: the first sample was a random spot UPCR (mid-stream urine), and the second specimen was 24 hour urine collection to measure UP-24. All specimens were analyzed using the COBAS®8000 C502 automatic analyzer machine (Roche Diagnostic, Thailand). Urine protein was measured using turbidimetric assays and urine creatinine by an enzyme assay. Both tests were controlled for precision, using within-run and between run coefficient of variation (CV%). Urine creatinine of less than 0.6 mg/24 hours was considered insufficient and excluded from this study.[19]

STATISTICAL ANALYSIS

Statistical analysis was performed using STATA program version 13 (Stata Corp, College Station, TX, USA). The baseline characteristics were described in

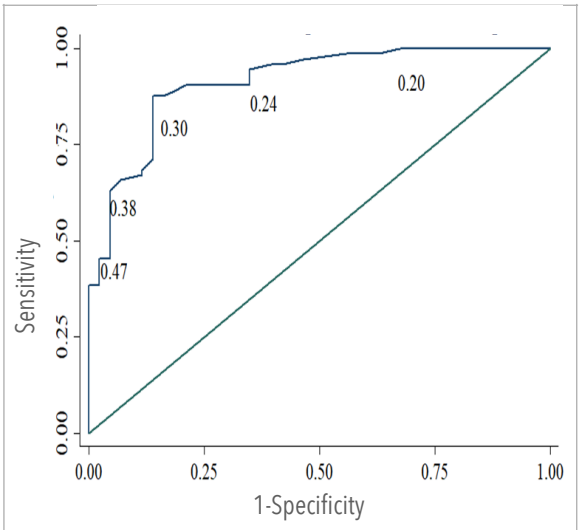

Figure 1. Receiver operating characteristic curve of UPCR for predicting significant proteinuria.

terms of frequency and percentage for categorical data. Mean, standard deviation and range or median and interquartile range were used for continuous data, depending on the normality of data distribution. The normality test was done by skewness and kurtosis test. UP-24 value ≥300 mg/day was used as the standard for significant proteinuria diagnosis.

The diagnostic performance of UPCR was assessed by receiver operator characteristic (ROC) curve. The sensitivity, specificity, positive and negative predictive value and accuracy and Youden index (sensitivity+specificity-100) of UPCR at various cut-off points from previous literatures were calculated. P<0.05 was considered statistically significant.

The borderline UPCR result was defined as a UPCR result between 0.20 to 0.29 mg/g. The false negative UPCR group was defined as UPCR<0.30 mg/g and UP-24≥300 mg. The clinical characteristics of both borderline and false negative groups were also collected. Sample size was calculated by the formula for the diagnostic test study. The estimated sensitivity of 88.5% with 0.06 acceptable error and 5% significance were used. The calculated sample size was 110, then a 5% dropout rate was added. The total sample size was 116.[12, 21]

RESULTS

In the present study, one hundred and sixteen women with suspected PE completed the study and were included in the analyses. Their mean age was 29.6 years and 60 (51.7%) women were nulliparous (Table1). The median gestational age was 35 weeks. Their characteristics and laboratory data are presented in Table 1.

The prevalence of significant proteinuria (UP-24≥300 mg) was 62.9% (95% CI; 59.7 to 77.2). The median 24-hours urine protein concentration was 420 mg, IQR 200 to 680 mg. UPCR was positive in 60.3% (cut-off point ≥0.30 mg/g). (Table 2) The median spot urine protein was 23.0 mg, IQR 9.1 to 47.8 mg, the median spot urine creatinine was 52.4 g and IQR 32.4 to 97.9 g. The diagnostic performance of UPCR using 0.30 mg/g and other cut-off points[1-3,12,14,19,22] are presented in Table 3. The ROC of UPCR to detect significant proteinuria (UP-24≥300 mg) was 91.3% (95% CI; 85.9 to 96.6). (Figure 1)

The cut-off point at 0.30 mg/g showed the best diagnostic performance, when compared with other cut-off points, with sensitivity, specificity, positive and negative predictive value, accuracy and Youden index were 87.7%, 86.1%, 91.4%, 80.4%, 86.2% and 73.8, respectively. (Table 3). Using this 0.3 mg/g cut-off point, the false positive ate of UPCR was 13.9% and false negative was 12.3%.

Table 1. Characteristics of the participants

Characteristic	N=116
Age–yr	29.6±6.9
Age <20 years–no. (%)	11 (10.2)
Age >35 years–no. (%)	26 (24.1)
BMI–kg/m^2	24.7±6.7
Gestational age–week	
Median	31.2
Interquartile range	33-37
Gestational age<34 weeks–no. (%)	31 (26.7)
Gestational age ≥37 weeks–no. (%)	39 (33.6)
Nulliparity–no. (%)	60 (51.7)
Systolic blood pressure–mmHg	
Median	154
Interquartile range	142-169
Diastolic blood pressure–mmHg	
Median	99.5
Interquartile range	90.0-108.5
Presentation of severe disease–no. (%)	34 (29.0)
Headache	25 (21.9)
Blurred vision	12 (10.3)
Epigastric pain	15 (12.9)
Others	2 (1.7)
Time period of urine collection for urine protein to creatinine ratio–no. (%)	
06.00-12.00 am	35 (31.3)
12.00-06.00 pm	41 (36.6)
06.00-12.00 pm	36 (32.1)

* Plus-minus values are means ±SD.

Table 2. Laboratory results and diagnostic of urine protein to creatinine ratio cut-off point at 0.30mg/g

Test	Median (Interquartile range)	Range
24-hour urine protein–mg	420 (200-680)	20-720
24-hour creatinine–g	0.88 (1.06-1.50)	0.60-124.50
24-hour urine volume–ml	2,410 (1,840-3,225)	750-5,500
Spot urine protein to creatinine ratio–mg/g	0.35 (0.17-0.90)	0.02-11.30
Spot urine protein–mg	23 (9.1-47.8)	4-635
Spot urine creatinine–g	52.4 (32.4-97.9)	0.12-243.00

In the false negative group, the median UPCR was 0.18 mg (IQR 0.15 to 0.20, range 0.12 to 0.26). The mean urine protein in this group was 22.9 mg (±SD17.1) which is higher than the median 0.13 mg (IQR 0.10 to 0.17, range 0.01 to 0.29) of the true negative group. In the borderline UPCR group (UPCR 0.20 to 0.29 mg/g), 30.8% of participants had a UP-24 result≥300 mg compared with 15.1% of the UPCR<0.20 mg/g group.

DISCUSSION

Significant proteinuria is the main component to diagnose PE along with hypertension.[4,7,23,24] UP-24 is the gold standard test for detecting this condition but it is limited by its inconvenience and time constraints. Many centers use UPCR as an alternative to UP-24 due to its rapidity and convenience.[2,8,12,14,19] Many optimal UPCR cut-off points were suggested in previous studies ranging from 0.20 to 0.35 mg/g[1-3,8,11-12,14,19,20,22] with estimates of sensitivity and specificity ranging from 65% to 89% and 63% to 87%, respectively.

Data from this study were concordant with Sanchez-Ramos L, et al, Cote AM, et al and Pariyaeksut P, et al studies[14,19-20] which reported a UPCR cut-off point at 0.30 mg/g, a commonly used cut-off point, had the best diagnostic performance with highest Youden index and high area under the ROC curve. This cut-off point, however, still has a high false positive and false negative rate (13.9%, 12.3%). A confirmation test is still necessary, especially in the borderline group (UPCR 0.2 to 0.29 mg/g) which thirty percent of cases were false negative. In emergency situations, the management of suspected PE cases, such as seizure prophylaxis, should be concerned with this information.

The prevalence of significant proteinuria from UP-24 was found in only 62.9% of suspected PE women. This might be due to the exclusion of PE women with severe conditions, which needed termination of their pregnancy before UP-24 could be completed. Women with chronic hypertension,

Table 3. Comparison of diagnostic performance of difference cut-off points of urine protein to creatinine ratio against 24-hour urine protein

Urine protein to creatinine ratio–mg/g	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy	Youden index
0.20[1-3]	93.2	65.1	81.9	84.9	82.8	58.3
0.24[22]	90.4	79.1	88.0	82.9	86.2	69.5
0.26[12]	89.0	81.4	88.0	82.9	86.2	70.4
0.30[14,19,20]	87.7	86.1	91.4	80.4	87.1	73.8
0.32	83.6	86.1	90.1	67.3	84.5	69.7
0.34	75.3	86.1	90.1	67.3	79.3	61.4

diabetes and renal disease, which can cause proteinuria, were also excluded from this study. However, many studies found an increase in maternal and neonatal risks from hypertension alone without significant proteinuria patients.[25]

The strength of the present study is its prospective enrollment of participants, in which the patients who had chronic hypertension, renal diseases, and diabetes, in whom persistent proteinuria were excluded. The limitation of this study is the sample size of the false negative and borderline UPCR cases was limited to accurate demonstration of diagnostic performance in this group.

The UPCR cut-off point at 0.30 mg/g had the best diagnostic performance, however the borderline UPCR between 0.20 to 0.29 mg/g had a high rate of significant proteinuria, therefore, a confirmation test is necessary in this borderline group and the management should be similar to PE where an emergency condition in suspected cases.

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Effects of cloud-based tracking system with telemonitoring on continuous positive airway pressure adherence in obstructive sleep apnea

ORIGINAL ARTICLE

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ABSTRACT

OBJECTIVE

To evaluate the effects of a cloud-based tracking system with telemonitoring on continuous positive airway pressure (CPAP) adherence compared to the standard usual care of patients with obstructive sleep apnea (OSA).

METHODS

This is a prospective open-label single-center randomized controlled trial of newly diagnosed OSA patients who received initial treatment with CPAP at Chiangrai Prachanukroh Hospital, Thailand from January 2019 to November 2020. The patients were allocated to either the telemedicine intervention using a cloud-based tracking system (CB group) for 90 days with monthly telephone-linked communication or the standard usual care (SD group). The primary outcome was the percentage of nights with good adherence to CPAP measured using the information given from CPAP machines. The secondary outcomes included percentage of CPAP usage time, sleep time, residual apnea-hypopnea index (AHI), AHI reduction, the CPAP leakage, Epworth sleepiness scale (ESS) reduction and sleep quality improvement.

RESULTS

A total of 83 patients were enrolled in the study; 41 in the CB group and 42 in the SD group. The CB group had better adherence than SD group. In CB group and SD group, the percent of nights with good adherence to the CPAP were 86, 72 respectively with statistical significance ($P<0.001$) and the percent of time with CPAP use were 93, 78.5 respectively with statistical significance ($P<0.001$). After adjusted of age, gender, body weight, ESS, AHI, mean oxygen saturation overnight and CPAP pressure, there were significant improvement in percent of nights with good adherence of the CPAP (adjusted difference, 11.89; 95% CI, 8.00 to 15.78; $P<0.001$) and percent of time with CPAP use (adjusted difference, 11.95; 95% CI, 7.32 to 16.58; $P<0.001$).

CONCLUSION

This study demonstrated that OSA patients with CB tracking systems with telemonitoring for initial CPAP use had promising results in relation to good adherence with effective treatment outcome at 90 days.

INTRODUCTION

Obstructive sleep apnea (OSA) is one of the most common sleep-related breathing disorders characterized by upper airways collapse during sleep.[1] There is a high prevalence of effect these conditions especially in the male gender, advanced aged, and obese population.[1,2] The overall population prevalence ranges from 9 to 38%.[2] The mean prevalence of OSA is 27.3% in males (range 9 to 86%) and 22.5% in females (range 3.7 to 63.7%).[3] OSA is a major health problem with high morbidity and mortality.[3,4] The problem is that there are a high prevalence and presence in various clinical settings which was under-recognition.[5] The clinical symptoms of OSA are variable presentation including loud snoring, interruptions in breathing while sleeping, excessive daytime sleepiness, morning headache, and also cardiovascular conditions.[6] This disorder diagnosed the presence of obstructive respiratory events including apnea and hypopnea events during sleep as apnea-hypopnea index (AHI).[3] Polysomnography (PSG) is the gold standard used for the diagnosis of OSA.[4,7] The presence of AHI more than five events per hour with associated clinical symptoms, comorbidities or AHI more than 15 events per hour.[8] The treatment of OSA aims to resolve associated clinical symptoms, comorbidities, and normalized obstructive respiratory events.[5,6] Continuous positive airways pressure (CPAP) is the effective treatment of choice of OSA to eliminate upper airway collapse and obstructive respiratory events during sleep.[5,6] The benefit of treating OSA is to improve quality of life, decrease cardiovascular complications, and morbidity.[9] Adherence to CPAP treatment is essential for the treatment outcomes of OSA.[8,9] Initiation treatment with CPAP is quite cumbersome.[1,3,10] The major problem with using CPAP is the side effects of applying positive pressure including unfamiliar, air mask leakage, aerophagia, nasal congestion, inappropriate pressure, and disrupted sleep which made CPAP poor adherence.[10] CPAP adherence is still suboptimal and difficult in multi-factorial factors.[11,12]

Closed monitoring in initial CPAP treatment is beneficial for improved adherence and effective treatment. Intervention to improve adherence and accurate monitoring use of objective data for evaluating consistent treatment is essential.[3,13,14] Currently, data on telemonitoring for CPAP usage was inconsistent.[11] The study of telemonitoring with face to face consultation show improvement of CPAP adherence and decreased frequency of outpatient visits.[15] Varies studies demonstrated that telemonitoring of CPAP did not improve adherence of OSA patients.[16] Initiation of CPAP management with closed follow-up for good adherence and effective treatment is warranted. Cloud-based tracking system obtained current objective data of CPAP information usage including daily hours of use, residual obstructive respiratory event, current CPAP pressure, and also mask leakage.

Telemonitoring is a telemedicine intervention to obtain information about health service and care. The cloud-based tracking system with telemonitoring could improve CPAP adherence for OSA patients.[12] This study aimed to evaluate CPAP adherence using a cloud-based tracking system with telemonitoring compared to standard usual care of OSA patients. We conducted the study of CPAP adherence follow-up of telemedicine intervention using a cloud-based tracking system in 90 days with monthly telephone-linked communication compared to standard usual care.

METHODS

STUDY DESIGN AND OVERSIGHT

This is a prospective, open-label, single-center, randomized controlled trial to evaluate the efficacy of the cloud-based tracking system with telemonitoring (CB group) compared with the standard usual care (SD group). Our study was conducted at the internal medicine department, Chiangrai Prachanukroh Hospital, Thailand between January 2019 and November 2020. Our study protocol was approved by the Ethics Committee of Chiangrai Prachanukroh Hospital, and was carried out in accordance with the Declaration of Helsinki. All patients were informed about the study and signed on the approved consent forms.

PARTICIPANTS

We included the patients who were newly diagnosed OSA patients with age>18 years who required CPAP treatment; AHI more than 15 events per hour or AHI more than 5 events per hour with one of the following symptoms of excessive daytime sleepiness, morning headache, fatigue, hypertension, or any cardiovascular disease.[17-20] Newly diagnosed OSA patients defined by patients who had AHI more than 15 events per hour or more than five events per hour with associated clinical symptoms or co-morbidity diagnosed by PSG criteria using American Academy Sleep Medicine (AASM) version 2.4-2.6.[21] Patients who previously received treatment with CPAP or unable to provide informed consent were excluded from the study.

The sample size calculation was based on the assumption that achieved good adherence from a cloud-based program tracking system group as regularly CPAP used more than 70 percent of total sleep time with at least 4 hours per night[13] would be 20% difference between that of the CB (83%) and SD (63%) groups from the pilot study.[22] Thus, with 90% of power and 5% alpha error, the required sample would be at least 32 in both groups. The study protocol was approved by the Ethics Committee in Human Research Chiangrai Pachanukroh Hospital (EC CHR 056/62 In).

INTERVENTIONS

We randomized the patients with a ratio of 1:1 to either cloud-based tracking system group (CB) with telemonitoring or standard usual care group (SD). The patients in both CB and SD groups visited an out-patient sleep clinic for being prescribed with the CPAP machines. All patients were oriented to CPAP education for initial usage at the clinic. The CPAP machines from the various manufacturing companies were selected by patient preferences including Fisher&Paykel; Sleep Style Auto CPAP, Philips Respironics; DreamStation auto, BMC; RESmart G2 AUTO CPAP, Hoffrichter; Point 2 Auto CPAP, and Resmed; Airsense 10 Autoset. Patients enrolled in the study had informed consent and were eligible for the study protocols regarding the criteria mentioned above. Patients were randomized to CB with the telemonitoring or SB groups. All patients were scheduled to follow up at an interval of 90 days after initiating CPAP treatment. In the CB group, there was an information assessment of CPAP adherence every month with telephone-linked communication. Regular telephone session including assessment of CPAP usage, feedback, and counseling. In monthly adherence assessment of CB group using telemedicine, a part of cloud-based tracking system, we checked for achieved good adherence. Achieved good adherence defined as regular CPAP used more than 70 percent of total sleep time with at least 4 hours per night.[13] In case the goal of adherence was not achieved, we, the researchers, would encourage the patients to improve the usage and correct the side effects of CPAP treatment. During the study period, all the patients who

Table 1. Comparison of baseline characteristics between two groups

Characteristic	Cloud-Based System (N=41)	Standard usual care System	P Value
Ag–yr	48±18	52±18	0.37
Male–no. (%)	31 (76)	28 (67)	0.47
Weight–kg			0.024
Median	92	80	
Interquartile range	72.0-137.5	71.0-96.7	
Height–cm			0.093
Median	168	163.5	
Interquartile range	159.0-174.5	157-167.3	
Body mass index–kg/m^2			0.051
Median	35.3	30.5	
Interquartile range	26.8-51.9	24.9-35.8	
Epworth sleepiness scale			0.020
Median	12	10	
Interquartile range	8-15	5-14	
Apnea-hypopnea index–events/hr.			0.001
Median	45.7	20.8	
Interquartile range	30.0-56.8	11.1-34.0	
Mean oxygen saturation overnight–%			0.008
Median	91	92.5	
Interquartile range	88.5-92.0	90-95	
Minimum oxygen saturation–%			0.002
Median	74	79	
Interquartile range	62-80	72-87	
Continuous positive airway pressure–cmH_2O			0.004
Median	9	7.3	
Interquartile range	7.0-11.8	5-8	

Table 2. Clinical outcome of sleep results after CPAP treatment at 90 days

Outcome	Cloud-Based System (N=41)	Standard usual care System (N=42)	P Value
% of nights with good adherence to the CPAP			<0.001
Median	86	72	
Interquartile range	80-92	67.3-80	
% of time with CPAP use			<0.001
Median	93	78.5	
Interquartile range	83.5-97.0	71.5-84.0	
Sleep time-minutes*			<0.001
Median	379	326	
Interquartile range	348-431	297.0-363.3	
Residual apnea-hypopnea-events/hr*			0.42
Median	2.4	2	
Interquartile range	1.0-6.2	1.4-4.6	
Apnea-hypopnea index reduction-events/hr*			<0.001
Median	-43.3	-17.8	
Interquartile range	-54.1 to -25	-30.3 to -8.3	
CPAP leakage-lite/min*			0.072
Median	26	25	
Interquartile range	24-34	22-30	
Epworth sleepiness scale reduction			<0.01
Median	-6	-2.5	
Interquartile range	-8 to -2	-5 to -1	
Sleep quality improvement			0.05
Median	2	1	
Interquartile range	1-3	0-3	

* The outcomes were presented in terms of the means given by the machines of each individual during the study period of 90 days.

enrolled in the study were allowed to visit the hospital if there were any problems.

OUTCOMES

At 90 days of follow-up after initial treatment with CPAP at an outpatient sleep clinic, we checked for objective data of CPAP information. Our primary outcome was the percentage of nights with good adherence to CPAP measured using the information given from CPAP machines. Our secondary outcomes included (i) percentage of CPAP usage time, (ii) sleep time, (iii) residual AHI (event/hour), (iv) AHI reduction (event per hour), (v) the CPAP leakage (litre/minute). The first five of our secondary outcomes were measured using the information given from the CPAP machines. For parameters ii to v, they were presented in terms of the means of those outcomes given by the machines of each individual during the study period of 90 days. We also checked for subjective data in sleepiness using (vi) Epworth sleepiness scale (ESS) reduction using the eight structured with the choice of 0 to 3 for each question[23] and (vii) sleep quality improvement using the visual analogue scale (0-10) rated by the patients themselves.

STATISTICAL ANALYSIS

Descriptive statistics were used. These data were presented by frequency, percentage, mean, median, standard deviation (SD), The baseline characteristics were compared using exact probability tests for categorical variables; student's t-test or Wilcoxon rank-sum test was used to compare the mean difference of continuous variables. Univariable and multivariable regression analyses were used to evaluate the effects of CPAP adherence between intervention group interpreting using 95% confidence interval (CI), and P. All statistical analyses were two-tailed. A $P<0.05$ was considered statistically significant.

RESULTS

In the present study, a total of 83 individuals from January 2019 to November 2020 were enrolled; 41 in the CB group and 42 in the SD group. Complete details of their baseline characteristics were shown in Table 1. Comparing between those in CB and SD groups; the former tended to have higher weight ($P<0.24$); higher BMI ($P=0.051$), higher ESS ($P=0.02$), higher AHI ($P=0.001$), higher CPAP pressure ($P=0.004$), but less mean oxygen saturation overnight ($P=0.002$) and minimum oxygen saturation ($P<0.008$).

Comparing the treatment outcomes in the CB group with that of the SD group, the former had higher percentage of nights with good adherence to the CPAP (median, 86% vs. 72%, respectively; $P<0.001$), higher percentage of time with CPAP use (median, 93.0% vs. 78.5%, respectively; $P<0.001$), longer sleep time (median, 379 minutes vs. 326 minutes, respectively; $P<0.001$), more AHI reduction (median, -43.3 events/hour vs. -17.8 events/hour, respectively; $P\leq0.001$), and higher ESS reduction (-6.0 vs. -2.5, respectively; $P<0.01$) (Table 2). However, there were no statistically significant difference between the CB and SD groups in terms of residual apnea-hypopnea, CPAP leakage, and sleep quality improvement over 90 days.

From the multivariable regression, after adjustment for age, gender, body weight, ESS, AHI, mean saturation and CPAP pressure of the effect of cloud-based tracking system and telemonitoring on good adherence, there was significant improvement in CPAP adherence (adjusted difference, 11.89; 95% CI, 8.00 to 15.78; $P<0.01$). There was a significantly increased percent of total CPAP time usage (adjusted difference, 11.95; 95% CI, 7.32 to 16.58; $P<0.01$). And sleep duration (adjusted difference, 52.64; 95% CI, 25.95 to 79.33; $P<0.01$) (Table 3).

Table 3. Effect of cloud-based tracking system and telemonitoring on clinical outcome and sleep results after CPAP treatment at 90 days.

Outcome	Unadjusted Difference* (95% confidence interval)	Adjusted Difference* (95% confidence interval)
% of nights with good adherence of the CPAP	11.69 (8.21 to 15.18)	11.89 (8.00 to 15.78)
% of time with CPAP use	11.57 (7.41 to 15.73)	11.95 (7.32 to 16.58)
Sleep time-minutes†	47.23 (22.92 to 71.54)	52.64 (25.95 to 79.33)
Residual apnea-hypopnea index-events/hr.†	0.49 (-0.73 to 1.71)	-0.24 (-1.37 to 0.88)
Apnea-hypopnea index reduction-events/hr.†	-15.86 (-27.74 to -3.98)	-.244 (-1.37 to -0.88)
Epworth sleepiness scale reduction	-3.04 (-4.71 to -1.37)	-1.56 (-2.44 to -0.68)
Sleep quality improvement	0.63 (-0.13 to 1.39)	0.34 (-0.05 to 1.19)

* Adjusted for age, gender, body weight, ESS, AHI, mean saturation and CPAP pressure; regression.
† The outcomes were presented in terms of the means given by the machines of each individual during the study period of 90 days.

DISCUSSION

This study demonstrated that the initiation of CPAP treatment in newly diagnosed OSA patients with a cloud-based tracking system and telemonitoring were beneficial in various aspects. CB groups were beneficial in improving good adherence with higher percent of CPAP time usage and longer sleep duration. Furthermore, CB groups had more AHI reduction and ESS improvement than SB groups. Nevertheless, the residual AHI and the sleep quality were similar results in both groups. These demonstrated that CPAP was the most effective treatment for all OSA patients to achieve targeted therapy to normalized AHI. These results suggested that closed monitors by cloud-based tracking systems with telemonitoring using telephone call monthly notification were more effective in CPAP adherence with effective treatment outcome than standard usual care. Web-based monitoring and telemonitoring systems were used to improve patient compliance with CPAP but currently, the data was inconsistent. Previous studies showed that telemonitoring did not improve CPAP adherence. The use of telematics techniques was made via video conferencing to evaluate CPAP compliance.[24]. At 6 Months follow-up in a very small group of 16 patients, adherence was not different between the groups: 85% for the face-to-face consultation and 75% for the teleconsultation group. A telemetrically triggered intervention in the first month of treatment did not improve daily hours of CPAP use in 6 months in OSA patients, which did not differ significantly between the control group (5.6 hour vs. 4.8 hours, respectively; P=0.663).[25] The other studies had demonstrated some efficacy of education interventions for improving adherence to continuous positive airway pressure from telemonitoring. The study of telephone-linked communications for CPAP (TLC-CPAP) resulted in improved CPAP adherence and functional status [25]

compared between an attention placebo controlled for 12 months. The TLC-CPAP intervention was associated with a 30% higher rate of CPAP use (44.7% of the intervention group using CPAP 4 hours per night vs. 34.5% of the control group). The pilot study revealed that telemetry-triggered interventions have a significant impact on adherence rate in early CPAP treatment in the first 30 days of treatment. [27]

As our study was to start monitoring early at the initial treatment of CPAP, this would be beneficial for increased adherence. The closed monitoring could be beneficial in correcting the problem of CPAP usage immediately for an effective outcome. Frequent motivation and simulation for CPAP using the result in increased adherence. We found that greater adherence to CPAP usage was associated with a greater reduction in sleepiness using ESS. The greater CPAP adherence was no relationship between residual AHI and quality of life using visual analog scale quality of life. The sleep quality was similar in both groups; this may be reflected from CPAP function, not from the intervention of treatment. Although differences were in the same expected direction, CPAP treatment was associated with improvement in reduced AHI and quality of life. The use of a web-based telemedicine system at the initiation of treatment improved CPAP adherence.[10] The mean PAP adherence was significantly greater in the telemedicine arm vs. the standard arm (191 vs. 105 minute per day, respectively; mean difference, 87 min; 95% CI, 25 to 148 min, P= 0.006). Another study of first initiated CPAP use demonstrated that compliance at 3 months was significantly better in the tele-monitoring group compared to usual care (5.7±1.6 vs. 4.2±1.9 hours per night, respectively; P=0.018).[28] This early activation of troubleshooting was associated with better compliance.

The strength of this study was adherence. The study showed very good adherence in both intervention groups. This may be because all the participants received CPAP education clearly at the initial at the clinic. The patients understand the benefit of CPAP treatment. Another possibility was that prompt attention to problem-solving at any time at an out-patient clinic was made to good adherence. There were some limitations of this study. The timing for the follow-up may be too short to explain the good adherence. If further follow-up for more duration would provide more information for the CPAP adherence. There was some bias of the patient generalizability, from the CB group; some of these patients were morbid obesity who will be undergoing bariatric surgery. Thus, these groups had more body weight and higher AHI at the beginning of the study. The preoperative evaluation for adequate CPAP usage must be done before the operation. Thus, these groups seem to have more adherences to CPAP than others. Further study for good randomization enrolled and generalizability with more patient data collection with longer duration would be beneficial to demonstrate the treatment outcome and information. This study suggested that a cloud-based tracking system with telemonitoring for CPAP adherence was beneficial for the treatment outcome of OSA patients. This option could be the treatment of choice for standard guidelines for OSA patients using a CPAP machine. Implementing a telemonitoring system for CPAP management is a promising solution benefit for OSA patients and also the physicians. As intensive early intervention could improve long-term CPAP adherence for improved patient care.

In conclusion, this study demonstrates that OSA patients with CB tracking systems with telemonitoring for initial CPAP use were promising results in good adherence with effective treatment outcome at 90 days. Encouraging using a CB system with telemonitoring for improved quality of OSA patient's care with maximum benefit would be warranted.

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Effect of topical *Andrographis paniculata* extracted in end-stage renal disease pruritus: a randomized controlled trial

ORIGINAL ARTICLE

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ABSTRACT

OBJECTIVE

To assess the itching problem in end-stage renal disease (ESRD pruritus) is a common problem for patients and one of the pathogenesis of ESRD pruritus is an inflammation. Many studies support the anti-inflammatory effects of *Andrographis paniculata*. The research aims to assess the effect of *Andrographis paniculata* extract in topical form for the treatment of ESRD pruritus.

METHODS

The double-blind randomized controlled trial was conducted. Participants were 44 hemodialytic patients who had ESRD pruritus that were followed up at Chiangrai Prachanukroh Hospital, Thailand from July 1, 2020 to December 31, 2020. The patients were randomized into either *Andrographis paniculata* extract treatment or placebo. The treatment outcomes were measured by the Dynamic Pruritus Score (DPS) and the Dermatology Quality of Life Index (DLQI) which were assessed after the first and fourth weeks of treatment.

RESULTS

We found that at the end of the 4th week, the *Andrographis paniculata* extract group had a mean DPS of 7.3±0.8 and a mean DLQI of 0.9±0.9, which was significantly different from the placebo treatment group which had a mean DPS of 5.9±1.1; $P<0.01$ and a mean DLQI of 3.9±4.4; $P=0.03$. An adjusted difference of the DPS at the end of the 4th week was 1.50; 95% CI, 0.72–2.28; $P<0.01$. Patients had neither adverse drug reactions nor dropped out from the study.

CONCLUSION

Andrographis paniculata extract cream could be used to treat ESRD pruritus with low side effects.

INTRODUCTION

The itching problem in end-stage renal disease (ESRD pruritus) is a common problem that presents in approximately a half of ESRD patients. ESRD pruritus can occur in ESRD patients at any age. It can greatly affect the quality of life of a patient. ESRD pruritus was also associated with a higher mortality rate in ESRD patients.[1-3] The pathogenesis of ESRD pruritus can be associated with dry skin, hyperparathyroidism, iron deficiency anemia, hyperphosphatemia, an increase in blood histamine, or an increase in the inflammatory cytokine such as C-reactive protein, interleukin-6 (IL-6), and interleukin-2 (IL-2) but the mechanism is still unclear.[1,2,4-6] There are many studies conducted for the treatment of ESRD pruritus such as gabapentin or pregabalin, mast cell stabilizers, phototherapy, montelukast, ondansetron, primrose oil, cholestyramine, thalidomide, capsaicin cream, tacrolimus ointment. However, there is no definite treatment. [7,8]

Andrographis paniculata is an annual plant. It contains active substances in the Lactone group such as andrographolide, neoandrographolide, 14-deoxyandrographolide, 14-deoxy-11, didehydroandrographolide, or diterpene. These substances have many pharmacological effects such as: stimulate immunity, inhibition of the growth of cancer cells, prevention of liver toxicity, antibacterial, antivirals, lower blood pressure, reduced blood sugar, and decreased coagulation of platelets. It can reduce fever and has an anti-inflammation effect due to the inhibitory effect of tumor necrotic factor-α (TNF-α), Interleukin-1β (IL-1β), IL-6 as well as other inflammatory-related substances.[9-13] Several studies show the anti-inflammatory effect of *Andrographis paniculata*, for instance, oral intake of *Andrographis paniculata* extract significantly reduce inflammation of pelvic inflammatory disease and joint inflammation in rats.[14,15] In human, oral intake of *Andrographis paniculata* extract relieves sore throat in common cold patients and rheumatoid arthritis symptoms.[16,17] It is currently listed on the Thailand National List of Essential Medicine. It is indicated for fever, sore throat, and non-infectious diarrhea.[18] The possible side effects are drug allergies; its use should be avoided in people that have low blood pressure, abnormal coagulation conditions, and pregnant or women that are breastfeeding.[18] Studies in dermatology using *Andrographis paniculata* extract in topical form for skin inflammation is still lacking. There is evidence that *Andrographis paniculata* extract significantly enhanced rate of wound healing and decrease inflammatory cells in rats wound.[19] However, as the above information shows *Andrographis paniculata* extract can be used to reduce inflammation. It is also possible to be developed as a combination therapy to improve the effectiveness of the treatment of inflammatory skin conditions. The aim of the research was to assess the effect of *Andrographis paniculata* extract in topical form for the treatment of ESRD pruritus.

METHODS

STUDY DESIGN AND STUDY SITE

This is a randomized double-blind placebo controlled trial, to determine the effect of *Andrographis paniculata* extract in topical form for the treatment of ESRD pruritus. This study was conducted in End-stage renal disease (ESRD) patients receiving hemodialysis therapy at Chiangrai Prachanukroh Hospital, Thailand. Data were collected from July 1, 2020 to December 31, 2020. The study protocol was approved by the Ethics Committee in Human Research Chiangrai Pachanukroh Hospital.

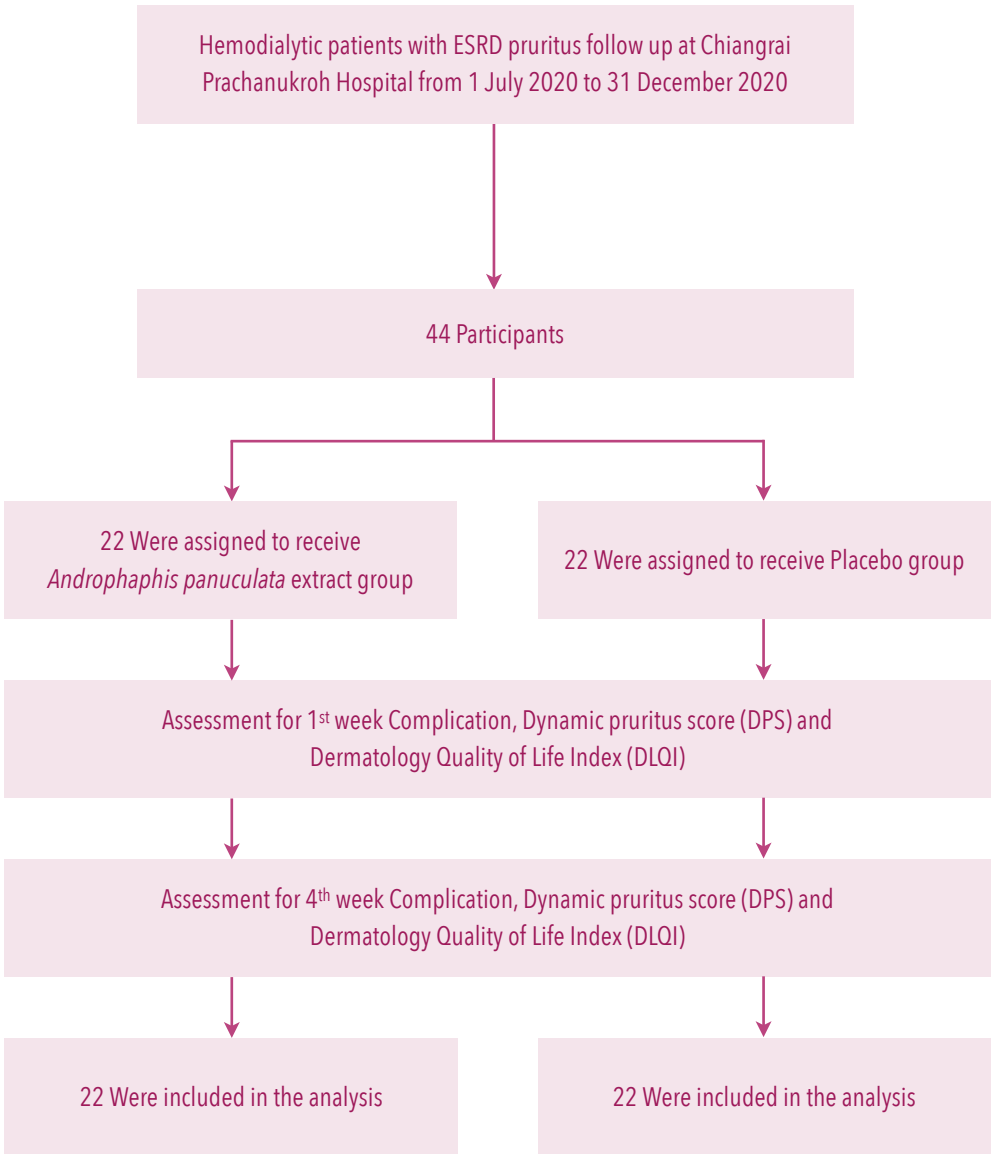

Figure 1. Study flow chart

PARTICIPANTS

Our inclusion criteria included hemodialytic patients, older than 18 years old, and suffering from ESRD pruritus. The exclusion criteria were allergy to *Andrographis paniculata*, use of topical corticosteroids within two weeks, pregnancy or breastfeeding, abnormal blood coagulation, or had chronic infectious skin lesions. The calculation of the sample size was made from a pilot study using *Andrographis paniculata* extract cream or a placebo cream in conjunction with the standard treatment of 13 patients. The mean Dynamic pruritus score

Table 1. Comparison of baseline characteristics between two groups

Characteristic	*Andrographis paniculata* extract Group (N=22)	Placebo Group (N=22)	P Value
Age–yr	61.9±11.7	57.2±15.6	0.27
Male–no. (%)	16 (72.7)	11 (50.0)	0.22
Hypertension–no. (%)	21 (95.4)	21 (95.4)	1.00
Diabetes–no. (%)	5 (22.7)	4 (18.2)	1.00
Hyperlipidemia–no. (%)	4 (18.2)	1 (4.6)	0.34
Inadequate dialysis–no. (%)	1(5.6)	4(20.0)	0.34
Serum BUN level–mg/dl	60.2±24.6	57.7±18.7	0.71
Serum phosphate level–mg/dl	4.0±1.2	4.2 ±1.3	0.32
Serum ferritin level–mg/ dl	416.6 (236.6-801.5)	362.1 (217-717.1)	0.64
Serum iPTH level–pg/ dl	184.2 (116.6-313.7)	331.1 (143.7-645.9)	0.16
Serum albumin level–g/dl	3.8±0.4	3.8±0.5	0.90
DLQI*	8.1±4.6	6.1±4.8	0.16

* Plus-minus values are means ±SD.

(DPS) at the end of the 4th week was used to calculate the sample size. With 90% of power and 5% alpha error, the required sample would be at least 18 in both groups.

INTERVENTIONS

Enrolled patients were randomly assigned in a 1:1 ratio to have 4% *Andrographis paniculata* extract cream (SBU Andrographis Cream®; SBU Corporation Company limited) or a matched placebo (moisturizing cream) applied to itching area over body except around eyes twice daily for four weeks. Randomization was stratified with block randomization. Patients, and investigators giving treatments and assessing outcomes were masked to treatment allocation.

DATA COLLECTION

The data were collected by using the patient record form developed by the researcher. Patient baseline information including age, sex, underlying diseases, adequacy of dialysis, baseline serum blood urea nitrogen (BUN), serum phosphate, serum ferritin, serum intact parathyroid hormone

Table 2. DPS and DLQI at 1 and 4 weeks after treatment

Laboratory result	*Andrographis paniculata* extract Group (N=22)	Placebo Group (N=22)	P Value	Adjusted difference † (95% CI)	P Value
Dynamic pruritus score at 1st week	6.0±1.0	5.4±1.0	0.09	0.66 (-0.65 to 1.39)	0.07
Dynamic pruritus score at 4th week	7.3±0.8	5.9±1.1	<0.01	1.50 (0.72 to 2.28)	<0.01
Dermatology Quality of Life Index at 1st week	3.3±1.9	3.8±3.4	0.59	1.46 (-0.75 to 3.68)	0.20
Dermatology Quality of Life Index at 4th week	0.9±0.9	3.9±4.4	<0.01	-0.64 (-3.08 to 1.81)	0.61

* Plus-minus values are means ±SD.

† Adjusted for age, sex, underlying medical conditions (hypertension, diabetes mellitus, and hyperlipidemia), adequacy of dialysis, serum BUN level, serum phosphate level, serum ferritin level, serum iPTH level, and serum albumin level

(iPTH) level, serum albumin, and quality of life assessment with Dermatology Quality of Life Index (DLQI) would be recorded on the research record form for the first time involved in the trial. Patients were followed for 4 weeks to assess itching with the Dynamic Pruritus Score (DPS)[20] and quality of life assessment with the Dermatology Quality of Life Index (DLQI).[21-23]

OUTCOMES

The primary outcome was DPS at 4th week. The secondary outcomes were DPS at 1st week, DLQI at 1st, and 4th weeks.

STATISTICAL ANALYSIS

Descriptive statistics were used. These data were presented by frequency, percentage, mean, median, standard deviation (SD), The baseline characteristics were compared using exact probability tests for categorical variables; Student's t-test or Wilcoxon rank-sum test was used to compare the mean difference of continuous variables. Multivariable regression analyses were used to evaluate the effects of age, sex, underlying medical conditions (hypertension, diabetes mellitus, and hyperlipidemia), adequacy of dialysis, serum BUN level, serum phosphate level, serum ferritin level, serum iPTH level, and serum albumin level between intervention group and placebo group; interpreting using 95% confidence interval (CI), and P. All statistical analyses were two-tailed. P<0.05 was considered statistically significant.

RESULTS

In a total of 44 hemodialytic patients, 61.4% were male. The mean age of patients was 59.5±13.8 years, 95.4% had hypertension, 20.4% had diabetes, 11.4% had hyperlipidemia, and 13.2% had inadequate dialysis. The baseline serum Phosphate level was 5.0±5.7 mg/dl. Baseline iPTH serum level was 391.5±407.8 pg/dl. The patients had neither adverse drug reactions nor dropped

out from the study. The baseline characteristics of the *Andrographis paniculata* extract treatment group and the placebo treatment group were not different (Table 1).

During the follow-up period of 4 weeks, at the end of the 1st week, the *Andrographis paniculata* extract treatment group had a mean of DPS 6.0±1.0 and a mean of DLQI 3.3±1.9 which was not significantly different from the placebo treatment groups which had a mean of DPS 5.4±1.0; P=0.09 and a mean of DLQI 3.8±3.4; P=0.59. At the end of the 4th week, the *Andrographis paniculata* extract treatment group had a mean of DPS 7.3±0.8 and a mean of DLQI 0.9±0.9, which was significantly different from the placebo treatment groups which had a mean of DPS 5.9±1.1; P<0.01 and a mean of DLQI 3.9±4.4; P<0.01 (Table 2). There was no adverse event in both groups.

After adjusting for age, sex, underlying medical conditions (hypertension, diabetes mellitus, and hyperlipidemia), adequacy of dialysis, serum BUN level, serum phosphate level, serum ferritin level, serum iPTH level, and serum albumin level, treatment of patients with *Andrographis paniculata* extract creams also had a statistically significant effect on the DPS at the end of the 4th week (adjusted difference 1.50; 95% CI, 0.72 to 2.28; P<0.01), but there was no effect on the DPS at the end of the 1st week and no effect on the DLQI at the end of the 1st week and 4th week (Table 3).

DISCUSSION

This study is the first study to evaluate the treatment effect of *Andrographis paniculata* extract cream on ESRD pruritus. We found that the *Andrographis paniculata* extract cream could reduce itching in hemodialytic patients, and improved quality of life after used for four weeks. It signified a more than 75% reduction in itching which was statistically significantly better than the placebo. The quality of life after applying *Andrographis paniculata* extract cream improve from moderate effect on patient's life at the initiation of treatment to no effect at all on patient's life, which was also statistically significantly better than the placebo. After adjusting for other factors, treatment of patients with *Andrographis paniculata* extract creams also had a statistically significant effect on the DPS at the end of the 4th week means that an *Andrographis paniculata* extract cream could be used to effectively treat ESRD pruritus with low side effects. There is no study about *Andrographis paniculata* extract cream for skin inflammation before, but the data from previous study of *Andrographis paniculata* extract on rat wound that reduce inflammatory cell and studies of anti-inflammatory effect of *Andrographis paniculata* by reducing TNF-α, IL-1β, IL-6 show the similar trend as observed in this study.[11-13,19]

In this study, there were some limitations because one of the pathogenesis of ESRD pruritus was dry skin and the placebo was a moisturizing agent that had a therapeutic effect. As a result, the difference between the treatment group and the placebo group was less likely to differ. That might be from the moisturizing agent that was a composition in both types of cream. However, it can be seen that the cream containing *Andrographis paniculata* extract has a better effect on treating itching than conventional moisturizers. These results could be from anti-inflammatory effects, and may be applied to itching in other diseases associated with inflammation of the skin as well. However, a further study on the topic are needed before recommendations can be made.

In conclusion, the present findings suggested that *Andrographis paniculata* extract cream could be used to treat ESRD pruritus. Larger randomized controlled trial should be conducted for more precise estimation of its effects.

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COMPETING INTERESTS: This study has no competing on interest.

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"I shall either find a way or make one"

-Hannibal Barca


I don't want you to be only
a doctor but I also want you
to be a man