Chula Med J Vol. 56 No. 3 May - June 2012

Efficacy and safety of diacerein in the treatment of patients with painful knee osteoarthritis: A modified regimen

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Yuktanandana P, Suravech W. Efficacy and safety of diacerein in the treatment of patients with painful knee osteoarthritis: A modified regimen. Chula Med J 2012 May – Jun; 56(3): 275 - 87

Background : *Recent systematic meta-analyses provide evidence for the efficacy of diacerein 100 mg/day in the treatment of knee and hip osteoarthritis (OA). However, as diacerein may cause acceleration in intestinal transit time during the first 2 weeks of treatment, it is recommended to start with 50 mg/day for 4 weeks then increase the dose to 100 mg/day. However, no study has been performed on the treatment regimen. This study was conducted in order to assess the efficacy of diacerein according to the recommended regimen.*

Objective : *To assess the efficacy and safety of diacerein in reducing pain and functional impairment in patients with painful tibiofemoral osteoarthritis of the knee over a six-month period.*

Design : *Prospective study*

Setting : *Orthopedics Clinic, King Chulalongkorn Memorial Hospital.*

Methods : *Thirty patients between 50 and 65 years old with painful knee osteoarthritis (grade I to III severity on Kellgren - Lawrence radiological scale) were recruited into the study. After a 1-week NSAIDs washout period, the subjects received diacerein 50 mg/day for 1 month then increased to 100 mg/day until the end of the study. No other OA and/or pain-killer*

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medication was allowed during the study except ibuprofen at the maximum dose of 1,600 mg/day when pain was unbearable; and, the number of tablets taken per day was recorded. The efficacy parameters were pain on walking (VAS), Lequesne index for function, intake of ibuprofen and overall efficacy were evaluated by the investigators and patients. These parameters were assessed at baseline (Day 0), Day 28, 56, 84, and 168. Routine hematology, urinalysis and clinical chemistry examinations were carried out at baseline and the end of study. The occurrence of adverse event was recorded at each visit.

Results : *There was a significant reduction of pain from baseline (mean value: 59.9 mm VAS) to the last visit (mean value: 27.7 mm VAS), ($p < 0.001$). The Lequesne index also showed a significant decrease from a baseline value of 12.5 to 5.8 on Day 168 ($p < 0.001$). At the end of the study, about 80% of the subjects and investigators evaluated treatment efficacy as moderate to very effective. There was significant decrease in ibuprofen consumption from 678.7 mg/day at baseline to 207.6 mg/day at the end of the study. Three mild to moderate severity adverse events related to diacerein were observed which were flatulence, GI upset and diarrhea. There were no variations in the laboratory parameters measured.*

Conclusion : *The results of this study exhibited efficacy and safety of diacerein in the recommended regimen in the treatment of knee osteoarthritis over a six-month period.*

Keywords : *Diacerein, knee osteoarthritis, pain.*

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Received for publication. June 15, 2011.

พงศ์ศักดิ์ ยุกตะนันทน์, วรวิทย์ ซื่อสัตย์เวช. ประสิทธิผลและความปลอดภัยของไดอะเซอรีนในผู้ป่วยข้อเข่าเสื่อมที่มีอาการปวด ในแผนการใช้ยาแบบที่ปรับปรุงใหม่. จุฬาลงกรณ์เวชสาร 2555 พ.ค. – มิ.ย.; 56(3): 275 – 87

ภูมิหลัง : *จากหลักฐานการวิเคราะห์ข้อมูลโดยรวบรวมผลการศึกษาทางคลินิกอย่างเป็นระบบของยาไดอะเซอรีน (Systemic meta-analysis) แสดงให้เห็นถึงประสิทธิภาพของยาในขนาด100 มิลลิกรัมต่อวัน ในการรักษาโรคข้อเข่าและข้อสะโพกเสื่อม แต่เนื่องจากยาไดอะเซอรีนอาจมีผลเพิ่มการเคลื่อนไหวของระบบทางเดินอาหารในช่วง 2 สัปดาห์ แรกของการเริ่มการรักษา ดังนั้นจึงแนะนำให้เริ่มใช้ยาในขนาด 50 มิลลิกรัมต่อวันเป็น ระยะเวลา 4 สัปดาห์ จากนั้นค่อยปรับเพิ่มขนาดยาเป็น 100 มิลลิกรัมต่อวัน อย่างไรก็ตามยังไม่มีการศึกษาที่ยืนยันถึงประสิทธิผลของยาในขนาดแนะนำดังกล่าว การศึกษานี้จึงเกิดขึ้น*

วัตถุประสงค์ : *เพื่อศึกษาถึงประสิทธิผลและความปลอดภัยของการใช้ยาไดอะเซอรีนในขนาดแนะนำในผู้ป่วยข้อเข่าเสื่อมชาวไทยที่มีอาการปวดโดยติดตามผลเป็นระยะเวลานาน 6 เดือน*

รูปแบบการวิจัย : *การศึกษาแบบไปข้างหน้า*

สถานที่ทำการศึกษา : *คลินิกออร์โธปิดิกส์ โรงพยาบาลจุฬาลงกรณ์*

วัสดุและวิธีการ : *อาสาสมัครข้อเข่าเสื่อมอายุระหว่าง 50 - 65 ปี และมีความรุนแรงของโรคระดับ 1 ถึง 3 ตามเกณฑ์ประเมินของเคลเกนลอเรนซ์ (Kellgren-Lawrence grade I-III) ถูกคัดเลือก เข้ามาทำการศึกษาทั้งหมด 30 ราย ผู้เข้าร่วมโครงการทุกรายต้องหยุดการใช้ยาแก้ปวด ลดการอักเสบเป็นระยะเวลาอย่างน้อย 1 สัปดาห์ก่อนเข้าร่วมการศึกษา โดยอาสาสมัครทุกรายจะได้รับยาไดอะเซอรีนในขนาด 50 มิลลิกรัมต่อวัน เป็นเวลา 4 สัปดาห์ จากนั้นเพิ่มขนาดเป็น 100 มิลลิกรัมต่อวันต่อเนื่องจนจบการศึกษา โดยในระหว่างการศึกษา อนุญาตให้ใช้ยาไอบูโปรเฟนในขนาดไม่เกิน1,600 มิลลิกรัมต่อวันเพื่อบรรเทาอาการปวดในกรณีที่จำเป็นเท่านั้น ประสิทธิภาพในการรักษาประเมินโดยอาการปวดในขณะเดิน (Pain on walking-Visual Analog Score; VAS) และเกณฑ์ประเมินเลอ เควนซ์ (Lequesne index) สำหรับการประเมินการทำงานของข้อรวมทั้งพิจารณาจากปริมาณไอบูโปรเฟนที่ใช้และจากแบบประเมินประสิทธิภาพโดยรวมจากความเห็นของ ผู้ทำ*

การวิจัยและอาสาสมัครโดยทำการประเมินผลเหล่านี้ ณ วันแรกที่เข้าโครงการ, วันที่ 28, 56, 84, และ 168 รวมทั้งมีการตรวจวิเคราะห์ผลเลือด, ปัสสาวะ และการวินิจฉัยทางห้องปฏิบัติการ ณ วันแรกที่เข้าร่วมโครงการและวันที่สิ้นสุดการศึกษา และในแต่ละครั้งที่อาสาสมัครมาพบผู้ทำการวิจัยจะได้รับการสอบถามถึงอาการไม่พึงประสงค์ที่เกิดขึ้น

ผลการศึกษา : *ค่าการประเมินอาการปวดแสดงให้เห็นอาการปวดที่ลดลงอย่างมีนัยสำคัญจาก ณ วันแรกที่เข้าโครงการ (ค่าเฉลี่ยของ VAS เท่ากับ 59.9 มม.) จนกระทั่ง ณ วันที่สิ้นสุดการศึกษา (ค่าเฉลี่ยของ VAS เท่ากับ 27.7 มม.) ($p < 0.001$) เช่นเดียวกับผลการประเมิน การทำงานของข้อที่พบว่าการทำงานของข้อดีขึ้นอย่างมีนัยสำคัญโดยค่าเลอเควนซ์ ลดลงจาก 12.5 ณ วันแรกที่เข้าโครงการเหลือ 5.8 ณ วันสิ้นสุดการศึกษาในวันที่168 ($p < 0.001$) รวมทั้งร้อยละ 80 ของผู้ทำการวิจัยและผู้เข้าร่วมโครงการประเมินว่ายาไดอะเซอรีนมีประสิทธิภาพปานกลางถึงมาก และการใช้ไอบูโปรเฟนบรรเทาปวดมี ปริมาณลดลงอย่างมีนัยสำคัญ จากวันละ 678.7 มิลลิกรัมเหลือเพียงวันละ 207.6 มิลลิกรัม ณ วันสิ้นสุดการศึกษา พบรายงานการเกิดอาการไม่พึงประสงค์ที่อาจเกี่ยวข้องกับการใช้ยาไดอะเซอรีน 3 รายงาน ได้แก่ อาการท้องอืด, อาการไม่สบายท้องและการถ่ายเหลวซึ่งไม่รุนแรง และไม่พบความผิดปกติอื่นในค่าทางห้องปฏิบัติการ ณ เดือนที่ 6 เปรียบเทียบกับวันแรกที่เข้าร่วมโครงการ*

สรุป : *การศึกษานี้แสดงถึงประสิทธิผลและความปลอดภัยของการใช้ยาไดอะเซอรีนในขนาดแนะนำ โดยพบว่ายามีประสิทธิภาพในการรักษาผู้ป่วยโรคข้อเข่าเสื่อมยาวนาน 6 เดือน*

คำสำคัญ : *ไดอะเซอรีน, ข้อเข่าเสื่อม, อาการปวด.*

Osteoarthritis (OA) is the most prevalent joint disease especially in elderly population. OA is becoming more important as a public health problem due to the increasing number of the elderly around the world. The management of OA is mainly focused on reducing symptoms by using analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) including the cyclooxygenase (COX) inhibitors. However, these drugs cannot slow down the progression of the disease and some NSAIDs have even been shown to accelerate cartilage degradation.[1] It is now well accepted that interleukin 1β (IL-1β) has a major role in OA progression in terms of inducing cartilage destruction and joint inflammation.[2] Thus inhibition of IL-1 or its activity should have benefits for OA treatment.

Diacerein, an IL-1β inhibitor[3,4] has been shown to be effective in improving the symptoms and slowing disease progression in many studies.[5-10] Recent systematic meta-analyses provide evidence for diacerein 100 mg/day in the treatment of knee and hip OA.[11-12] Even though the dosage regimen in most studies is 100 mg/day, it is recommended to start the treatment with 50 mg/day for 4 weeks and then increase to 100 mg/day because diacerein may cause acceleration in intestinal transit time during the first 2 weeks of treatment. However, there has not been any clinical study performed on this recommended regimen. Therefore, this study was conducted in order to assess the efficacy and safety of diacerein using the recommended regimen.

Material and Method

This is a prospective, open-labeled, one group pretest-posttest study which has been reviewed and approved by the Institional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University.

Thirty knee osteoarthritis patients were enrolled and followed-up at the Orthopedics Clinic of King Chulalongkorn Memorial Hospital during July 2005 and May 2007. All subjects were asked to provide informed consent before their enrollment. The inclusion criteria were; male or female patients; aged between 50 and 65 years old, with primary knee OA of the tibio-femoral joint; pain on walking 15 meters $\geq$ 30 mm using 100 mm visual analogue scale (VAS); pain present for at least 15 days in the month prior to the start, radiological staging ascertained grade I, II or III severity of knee OA on the Kellgren-Lawrence criteria, and Body Mass Index (BMI) $\leq$ 30 kg/m^2. Woman of childbearing age were required to use adequate contraceptive method during the study. Exercise program, hydrotherapy, acupuncture, physiotherapy or others should not be started during the study. If the patient is involved in any of these treatments before the start of the study, no changes may be made in the regimen for the entire duration of participation in the study. The exclusion criteria were secondary OA; accompanying osteoarthritis of the hip of sufficient severity to interfere with the functional assessment of the knee; intra-articular treatment with any products (e.g., corticosteroid in last 2 months, or glycosaminoglycans or hyaluronic acid during the 6 months prior to the study), or history of joint lavage and arthroscopic procedure within 6 months before the start of the study; using oral SYSADOA treatment (chondroitin sulfate, glucosamine sulfate, piascledin, diacerein) within 4 months before recruitment to the study; current treatment with anti-depressants,

tranquilizers, antacids; poor general health or other conditions which would make regular hospital attendance difficult; primary inflammatory painful conditions of the knee; painful knee conditions other than osteoarthritis; rapid destructive arthritis; evolving arthritis requires surgery within the coming year; necrosis of one of the femur condyles; persistent diarrhoea (> 3 stools /24 h) or laxative use (any laxative use is to be stopped before inclusion in the trial); severe gastrointestinal disorders, indications or history of severe gastrointestinal disorders (e.g. gastric or duodenal ulcers, ulcerative colitis, Crohn's syndrome, diverticulitis, recurrent pancreatitis); severe renal insufficiency (serum creatinine $\geq$ 1.8 mg/dl or proteinuria of 2+ in more than one test); hepatic disease (transaminases >2.5 x normal values); severe parenchymal organ disease; pregnancy, lactation; participation in a drug clinical trial within 3 months before the start of the study; and ascertained hypersensitivity to diacerein and/or similar compounds, paracetamol and ibuprofen use.

There was a wash-out period (7 days) for all pain-killer medications before starting the study drug. During the wash-out period, patients were not allowed to take any other pain-controlled medications except paracetamol with the maximal dose of 3 g/day. After the wash-out period, all patients received one capsule of 50 mg Diacerein once daily with the evening meal for 4 weeks then increased to two times daily with breakfast and dinner for 5 months until the end of study. Pain-killers or other osteoarthritis medications were not allowed throughout the study except ibuprofen (with maximal dose of 1,600 mg/day) when pain was unbearable and the number of tablet used per day was recorded in patient diary. The patients were instructed to bring remaining tablets and empty blister at next visit to recheck the amount taken with the number recorded in patient diary.

The efficacy parameters were Visual Analogue Scale (VAS) of pain on walking 15 metres (0 to 100 mm; 0 = no pain and 100 = extreme pain), Lequesne Functional Index (0 - 24 score on total 10 questionnaire in which lower scores mean less functional impairment), ibuprofen intake (mg), global efficacy and tolerability assessment by investigators and patients. These parameters were assessed at baseline (Day 0), week 4, 8, 12, and 24 (visit 2 - 6). The occurrence of adverse event was recorded at every visit together with the date of occurrence, seriousness, severity, onset, duration, imputability, medical intervention and outcome. Routine hematology, urinalysis and clinical chemistry examinations were carried out at baseline and also at the end of study.

Statistical analysis

Characteristics of the patients such as age, gender, weight, height, body mass index (BMI), previous and current medications, and laboratory tests were analyzed by using descriptive statistics. The pain visual analogue scale (VAS) and the Lequesne impairment index values at visit 2 were considered as the baseline values and compared with other values from visit 3, 4, 5, and 6 using parametric statistics, Repeated Measure ANOVA. The amount of ibuprofen (mg) used between each visit was compared using nonparametric statistics for repeated measure of interval scale data with no normal distribution, using Friedman test. Subject and investigator global efficacy and tolerability

assessments were assessed at visit 3 and compared with values from visit 4, 5, and 6 by nonparametric statistics for repeat measures of ordinal scale, using Friedman test. The occurrences of adverse event from baseline visit until visit 6 were compared by using Cochrane Q test.

Results

Patient characteristics

Baseline characteristic of patients are summarized in Table 1. There are 30 subjects in this study, with a mean age of 62.03 years, and 93.3% were female. The mean body mass index from weight and height calculation is 24.41 kg/m^2, which is higher than the standard normal BMI of Asian people (less than 23 kg/m^2). Of the subjects included, 30 % were classified as Kellgren-Lawrence grade I, 50 % as grade II, and 20% as grade III. A total of 28 patients completed the study (response rate of 93.3 %). One patient dropped out at visit 4 follow-up due to GI irritation from Ibuprofen and another patient dropped out at visit 5 due to personal reason. The ITT analysis was carried out on all (30) patients.

Table 1. Demographic and baseline clinical characteristics of the subjects (n = 30).

Characteristics	**Mean (S.D.) or %**
Percentage woman	93.3%
Age (year)	62.03 (4.95)
Height (meter)	1.54 (0.04))
Weight (kg)	57.92 (7.05)
Body mass index, BMI (kg/m^2)	24.41 (2.66)
Medical history and current affections	56.7%
Cardiovascular diseases (eg. stroke, hypertension)	30.0%
Respiratory diseases (eg. acute pharyngitis)	6.7%
Others (eg. metabolic syndrome as Diabetes)	20.0%
Percent previous OA	63.3%
Percent right index knee	46.7%
Finding Physical Examination	
Cardiovascular	6.7%
Gastrointestinal	6.7%
Metabolic/Endocrinologic	3.3%
Urogenital	3.3%
Peripheral vascular	3.3%
Kellgren-Lawrence Grade	
Grade I	30.0%
Grade II	50.0%
Grade III	20.0%

VAS pain on walking 15 metres and Lequesne impairment index

Two efficacy variables, pain (VAS) and Lequesne impairment index were evaluated 5 times for six months from the baseline visit or visit 2 (week 0) to visit 6 (week 24). Repeated measure ANOVA showed a significant reduction of pain (VAS) from the baseline visit to visit 6: the values were 59.97, 47.27, 41.80, 38.67 and 27.67 mm, respectively (p <0.001) as shown in Table 2. When compared with the baseline visit, there are significant reductions of pain at each visit, except between visit 4 and visit 5 (Table 3). The Lequense index also decreased gradually from the baseline value of 12.48 to 5.83 in visit 6 (p <0.001). During each visit, the multiple comparison by Bonferroni (Table 3) showed a significant decrease of total score in the Lequense index, p <0.05. The decreasing trend of pain and functional impairment are reported and shown in Figure 1.

Table 2. Change of efficacy parameters of knee of a 100-mm VAS pain scale and 24-score of Lequesne index for ITT population over visit 2 and visit 6; Mean (Standard Deviation).

Visit	Mean (SD)	
	VAS pain scale (mm)	Lequesne index (score)
Visit 1 (screening)- week -1	-	-
Visit 2 -baseline	59.97 (17.19)	12.48 (3.68)
Visit 3 - week 4	47.27 (17.21)	10.58 (3.43)
Visit 4 - week 8	41.80 (17.71)	8.67 (3.37)
Visit 5 - week 12	38.67 (19.83)	7.47 (3.83)
Visit 6 - week 24	27.67 (20.43)	5.83 (3.68)
P value*	<0.001	<0.001

* Test with Repeated Measure ANOVA

Table 3. Change from baseline and following visit in a 100-mm VAS pain scale and 24-score of Lequesne index at 6 visits; Mean difference.

Visit	Mean difference**			
	VAS Pain (mm)	p value	Lequesne index (score)	p value
Visit 2 - baseline	0	-	0	-
Visit 3 - week 4	12.70	<0.001	1.90	<0.001
Visit 4 - week 8	18.17	0.019	3.82	<0.001
Visit 5 - week 12	21.30	0.338	5.02	0.002
Visit 6 - week 24	32.30	0.005	6.65	0.002

* The mean difference is significant at the .05 level.

** Adjustment for multiple comparisons: Bonferroni.

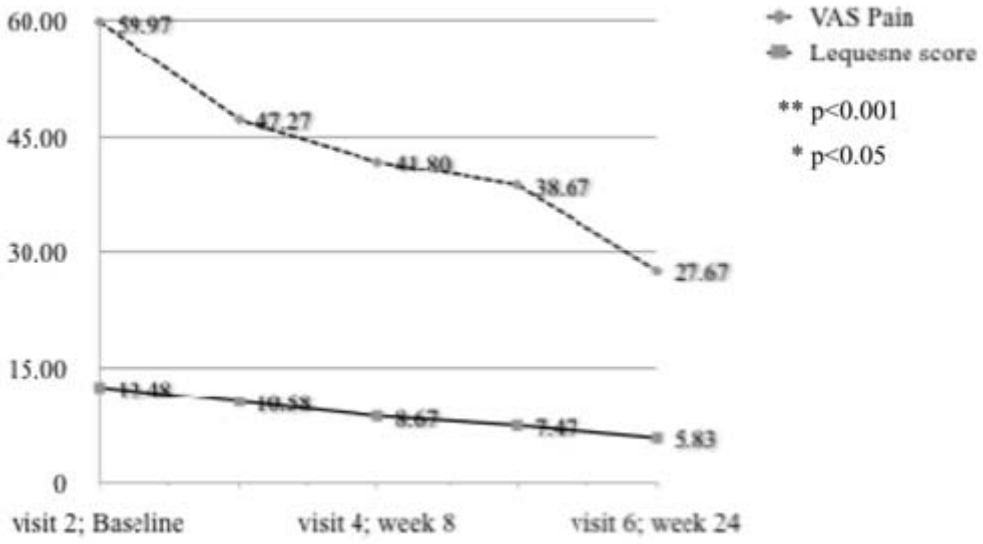

Figure 1. Plot of the efficacy parameters: pain (on 100 mm VAS) and the Lequesne Index (0-24 points) at each assessment visit.

Global assessment of efficacy and tolerability

A global evaluation of treatment efficacy was made by the patients and the investigator from visit 3 until visit 6, using 4-point scale which range from not effective (0) to very effective (3). Significant differences in global evaluation of treatment efficacy by the subjects and investigators at visit 6 compared to baseline levels were found (p <0.001) (Figure 2). In terms of global evaluation of treatment tolerability by the subjects and investigators, both the subjects and investigators were asked whether how well the OA subjects tolerated the treatment, assessed on a 5-level scale ranking from nil (0), poor (1), moderate (2), good (3) to very good (4). Significantly improvement of the treatment tolerability was found in both subjects and investigators evaluation, (p <0.001). These results are shown in Figure 2.

Ibuprofen consumption

Ibuprofen tablets were allowed as rescue medication in case of severe pain with a maximal dose of 1,600 mg/day. It was found that after taking diacerein, patients gradually decreased ibuprofen consumption from 678.67 mg/day at visit 3 to 207.59 mg/day at visit 6 (p = 0.001) (Figure 3).

Safety

As for the four adverse events were found. One subject experienced severe GI irritation from Ibuprofen and discontinued from the study. One reported the flatulence after taking the medication that lasting for a day, and one reported GI upset that last for two days. These two adverse events were considered by the subjects as mild, and resolved spontaneously without treatment or drug discontinuation. One subject reported diarrhea of moderate severity after taking the medication. The subject chose to take turmeric capsule (Curcuma longa, two capsules, three times a day for four to five day) to relieve this symptom which could be resolved

without stopping diacerein treatment. There was no difference in the occurrence of adverse events from visit 3 until visit 6. Tables 4 and 5 show the safety aspect of diacerein treatment.

Concerning the routine hematology, clinical chemistry examinations and urinalysis, there were no variations in laboratory parameters measured at baseline and at the end of the study.

Discussion

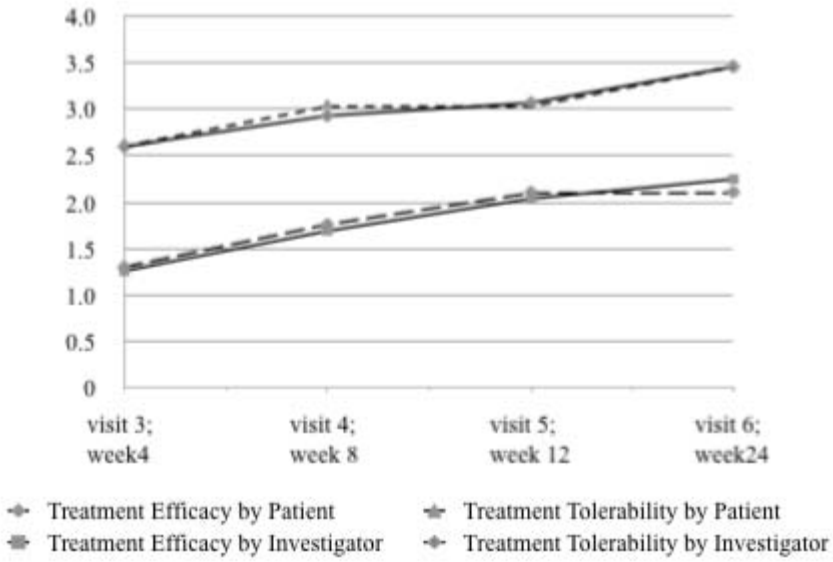

Figure 2. Plot of mean global evaluation of treatment efficacy and tolerability by subjects and investigators at each assessment visit.

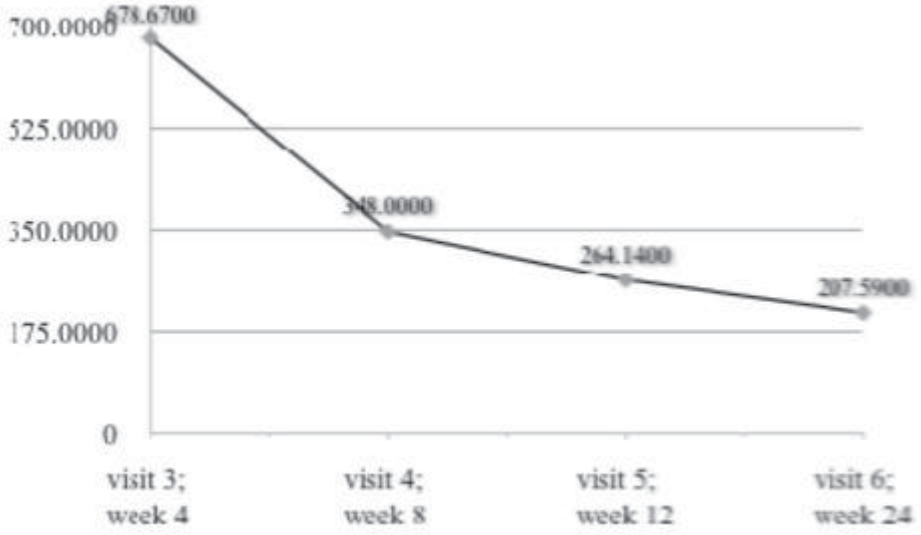

Figure 3. Plot of mean ibuprofen tablet consumption (mg) at each assessment visit.

Table 4. Overview of adverse events reported in the study patients (n = 30).

Adverse event	Frequency
No. of adverse events, n (%)	4 (13.3)
Mild (Flatulence, GI upset)	2 (6.7)
Moderate (Diarrhea)	1 (3.3)
Severe (GI Irritation from Ibuprofen)	1 (3.3)

Table 5. Number of adverse events reported as related to the drug in the study patients.

Visit	Frequency of AE
Visit 1 (screening)- week -1	-
Visit 2 (1st diacerein dispense)- baseline	0
Visit 3 (2nd diacerein dispense)- week 4	1 (Flatulence)
Visit 4 (3rd diacerein dispense)- week 8	2 (GI upset/Diarrhea)
Visit 5 (4th diacerein dispense) - week 12	0
Visit 6 (Follow up) - week 24	0
p value*	0.223

*Test with Cochran Q test

Discussion

Due to the drug-class adverse events of diacerein, which may cause acceleration in intestinal transit time during the first 2 weeks of treatment. It is recommended to start treatment with 50 mg/day for 4 weeks and then increase to 100 mg/day. However, there is no study that confirms the effectiveness of diacerein in the recommended dosage regimen. Most clinical studies on diacerein in the treatment of osteoarthritis were conducted with a diacerein dosage of 100 mg/day.[5-6, 8-10] The dose-finding study by Pelletier *et al.*, in 2000, compared efficacy and safety of diacerein 50 mg, 100 mg, and 150 mg/day in symptomatic knee OA patients, showed that the 150 mg/day dose exhibited the most effectiveness but with a high incidence of known adverse events (gastro-intestinal system disorders).[7] The authors then concluded that the appropriate daily dose of diacerein was 100 mg/day. However, the results from this study showed that diacerein 50 mg/day is also effective in treatment of knee osteoarthritis in term of pain reduction and functional improvement over 16 weeks.

The findings from our study support the results of the Pelletier study and also confirm the effectiveness of diacerein in the recommended dosage regimen. We found that pain (VAS) and the Lequesne Index scores decreased significantly (<0.001) after 1 month of treatment with diacerein 50 mg/day. This improvement increased when the diacerein dose was increased to 100 mg/day. Compared to baseline values, the mean decrease in pain (VAS) at the end of the study (week 24) was 32.30

mm VAS while the decrease in the Lequesne Index for functional impairment at week 24, compared to baseline values, was 6.65 points. Moreover, the global evaluation of treatment efficacy and tolerability by the subjects and investigators also exhibited a significant improvement from visit 3 to visit 5 which persisted until the last visit (visit 6).

In terms of ibuprofen consumption as rescue medication, the subjects gradually took fewer ibuprofen tablets from visit 3, i.e., 4 weeks after the start of diacerein treatment, until the end of study. These parameters demonstrated the efficacy of diacerein, in the recommended dose regimen, in patients with painful osteoarthritis of the knee.

We also found that fewer drug-class adverse events occurred in this study than in a previous one done in Thailand which started diacerein treatment with the 100 mg/day[8] dose. For example, diarrhea was observed in 3.3% of the patients in our study compared to 36.0% in the previous study in Thailand. This lower incidence of adverse events was due to the fact that we started treatment with a lower dose of diacerein (i.e. 50 mg/day) for 4 weeks which allowed the patients to get accustomed to the drug. Once the patients got accustomed to the medication, the known adverse events with the medication occurred less frequently even when the dose of diacerein was increased to 100 mg/day.

Conclusion

This study has shown that painful knee osteoarthritis patients who were treated with diacerein, starting with a dose of 50 mg/day for 4 weeks which was increased to 100 mg/day until the end of the study, had significant improvements in pain and function compared to baseline values. Significant improvements in these parameters, compared to baseline values, were already evident after one month of treatment with the lower diacerein dose (50 mg/day). Greater improvements with fewer adverse events were evident when the dose was increased to 100 mg/day up to the end of the study. Moreover, the consumption of ibuprofen was also decreased throughout the study. Only three adverse events related to diacerein which were mild to moderate severity occurred and they could be resolved. Therefore, the treatment of painful knee osteoarthritis patients with diacerein at the recommended dose regimen was safe, with a lower incidence of known adverse events, and effective in improving symptoms and decreasing pain-control medications over a six-month period.

Disclosures

This research was partially supported by TRB Chemedica. The authors did not have any conflict of interest.

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