Cost-Utility Analysis and Economic Burden of Knee Osteoarthritis Treatment: The Analysis from the Real Clinical Practice

Thanat Turajane MD*,
Ukrit Chaweevanakorn MD*, Pawaris Sungkhun MD*,
Viroj Larbphiboonpong MD*, Rungsee Wongbunnak MD**

* Department of Orthopedic Surgery, Police General Hospital, Bangkok, Thailand
** Department of Pharmacy, Police General Hospital, Bangkok, Thailand

Background: Non-steroidal anti-inflammatory drug (tNSAIDs) or selective COX-II inhibitor (COXIBs) are generally used as the first-line intervention of knee osteoarthritis (OA). Total knee arthroplasty (TKA) is suggested for those who dissatisfy from non-surgical treatment. However, the long-term usage of tNSAIDs may lead to articular cartilage and resulted in higher rate of TKA. The evaluation of real clinical practice needs to be scrutinized as the inappropriate treatment will be socially burden.

Objective: To evaluate cost-utility of selective COX-II inhibitors (COXIBs) compared to traditional NSAIDs in patients with knee osteoarthritis (OA) and to estimate health and economic burden of disease of knee OA.

Material and Method: The present study is an economic evaluation alongside a prospective observational study. The data of cost and treatment outcomes were collected from real clinical practice. EQ-5D questionnaire was employed to calculate utility values at baseline and 6 months after treatment.

Results: Total 939 patients were prescribed tNSAIDs and 380 patients received celecoxib. Eleven cases (1.17%) of all tNSAIDs usages and 3 cases (0.79%); p = 0.56 of celecoxib usages were detected GI complication. Two cases of tNSAIDs group were dead from severe GI bleeding. TKA was markedly reported with 12.99% of tNSAIDs and 9.80% of celecoxib; p = 0.06. QALYs gained from 6 months was 0.34 (± 0.11) for tNSAIDs and 0.36 (± 0.11) for celecoxib; p = 0.004. Average direct medical expenses per patient were comparable with 17,468.97 THB for tNSAIDs and 17,495.07 THB for celecoxib. Cost of TKA was a key element in both groups with 90% and 67% of total expenses in tNSAIDs and celecoxib groups, respectively. Incremental cost-effectiveness ratio (ICER) per Quality-adjusted life years (QALY) gained comparing celecoxib and tNSAIDs was 1,382.70 THB.

Conclusion: The finding from our study can be a concrete evidence to support the appropriate future decision of clinical judgment and health care provider.

Keywords: Cost-Utility Analysis, coxib, NSAIDs and TKA

Osteoarthritis (OA) is the most common musculoskeletal disorder affecting the peripheral joint sites(1,2). Its prevalence and incidence rates are generally higher among elderly(3). OA can occur at any joint site, particularly the knee and hip, but lifetime risk of developing knee OA tends to be higher(4,5). Treatment of OA may start from weight control, routine activity adjustment and pharmacological treatment(6). Traditional Non-Steroidal Inflammatory Drugs (tNSAIDs) are considered effective to OA and are widely used as the first-line therapy for OA patients, who have low risk of GI complication; whereas selective COX-2 inhibitors (COXIBs) are usually prescribed for those who cannot tolerate GI side-effect, including high risk patients(2). Uncontrolled pain or pharmacologic treatment failure are consequently required for surgical intervention, total knee arthroplasty (TKA) being the most common surgical intervention(7). It was reported that OA was the fourth most common cause of hospitalization among US citizens. OA progression frequently leads to severe pain, limitation of daily activities and disability(6). The symptom has substantial direct impact to the quality of life and patient economy as well as
indirect burden to society(8). Workers with OA stated the productivity lost and interference of their daily work is markedly disproportionate to workers without OA(8). The evaluation of real clinical practice needs to be scrutinized because the unappropriate treatment will be social burden eventually.

Study Objectives

The authors’ primary objective was to evaluate cost-utility of selective COX-II inhibitors (COXIBs) compared to traditional NSAIDs in patients with knee OA. The second objective was to estimate health and economic burden of disease of knee OA.

Material and Method

Study Design

This is an economic evaluation alongside a prospective observational hospital-based study conducted in the tertiary care center at Police General Hospital, Bangkok, Thailand, June 2010 to June 2011. The present study was approved accordingly by the Ethics Review Committee of Police General Hospital. The inclusion criteria was male or female, new OA patients aged 55 years or above, who had symptomatic and radiographic verified OA in either knee, with a pain severity score at least 40 from 100 of visual analog scale (VAS). The diagnosis was made according to the American College of Rheumatology (ACR) criteria. All patients received either tNSAIDs (diclofenac, piroxicam, indomethacin, sulindac, diflunisal, loxoprofen, meloxicam, nimesulide and naproxen) or celecoxib as a treatment for their OA symptom. The authors used celecoxib to represent COXIBs in the present study because, from the authors’ experience, celecoxib is commonly prescribed in elderly OA cases. The authors assumed that the outcomes attributable from each tNSAIDs are comparable. On the one hand, patients were excluded from the analysis if they had been contraindicated on other medication which may interfere the outcomes assessment of their knee OA e.g. glucosamine, Disease Modifying Osteoarthritis Drugs (DMOAD). Nevertheless, patients who were concomitantly prescribed gastric protective agents were included. All clinical outcomes and procedures were confirmed by ICD-10 and ICD-9CM, respectively. Subjects were recruited at the orthopedic clinic of Police General Hospital during regular visits. Consent was obtained from indentified and eligible patients before data was collected. EQ-5D questionnaire was employed for the utility score assessment and interviewed during baseline and 6 month follow-up visit. Nonetheless the assignment of any therapy throughout the present study was carried out according to the actual practice with no intervention from clinical investigators. The present study was analyzed under healthcare provider perspective. Hence all direct medical costs related to OA were captured in the analysis. The authors assumed the hospital charge as the cost due to the fact that the Police General Hospital is government hospital so the hospital charge is not significantly different to the cost of treatment.

Statistical analysis

Descriptive analysis was carried out to report demographic data and outcomes measurement. T-test was performed to calculate the significant level of utility outcomes from both groups. Fisher’s exact test was applied to explore the significance of GI events and TKA between both groups. At the p-value, a < 0.05 was considered statistically significant.

Results

Total of 1,319 OA patients were recruited for this analysis. Among these, 939 patients were prescribed tNSAIDs and 380 patients received celecoxib. Patients’ characteristics in both groups were comparable (Table 1). Mean (± SD) age of tNSAIDs and celecoxib groups were 64.73 (± 10.10) and 62.27 (± 9.39), respectively. Mean (± SD) of body weight as well as body mass index (BMI) were also similar with 64.79 (± 3.82) and 25.28 (± 2.08) for tNSAIDs group; 64.07 (± 3.78) and 24.74 (± 2.11) for celecoxib group, respectively.

During 6 months period of study, adverse events related to GI were reported in the present study. Total of 11 cases or 1.17% of all tNSAIDs usages and 3 cases or 0.79% of celecoxib usages were detected GI complication; p = 0.56. Among 11 cases from tNSAIDs, six of them (54.55%) were diagnosed as gastroduodenal hemorrhage, three (27.27%) were symptomatic ulcer and two (18.18%) were dead from severe GI bleeding; whereas, one cases out of those 3 GI events (33.33%) in celecoxib group were gastroduodenal hemorrhage and 2 (66.66%) were symptomatic ulcer. There was no dead case reported in the celecoxib group. In addition, we observed that patients underwent TKA in tNSAIDs group were substantially higher than celecoxib group. Total 122 cases (12.99%) were underwent TKA comparing to 35 cases (9.80%) in celecoxib group; p = 0.06 (Table 2).

EQ-5D scores were weighted by the Thai population-based preference scores for EQ-5D health states10 and interpreted to utility values specific to Thai
population. At baseline, mean (± SD) utility values were -0.08 (± 0.19) for tNSAIDs group and -0.11 (± 0.19) for celecoxib group. Six months after treatment, utility values vastly improved to 0.60 (± 0.12) for both groups. Compared average of utility gained in 6 months between tNSAIDs and celecoxib were found significantly different with mean (± SD) of 0.67 (± 0.21) and 0.71 (± 0.22) respectively (p = 0.004). Mean (± SD) QALY gained were 0.34 (± 0.11) in tNSAIDs and 0.37 (± 0.11) in celecoxib; (p = 0.004).

Average direct medical expenses per patient were comparable with 17,468.97 THB for tNSAIDs and 17,495.07 THB for celecoxib (Table 3). When reviewing the proportion of expenses types, it was obviously shown that TKA expenses were the major contribution in both groups. 90% and 67% of total cost in tNSAIDs and celecoxib were driven by TKA expenses, respectively. Drug cost and GI related expenses were responsible for 2% and 8% of total expenditure of tNSAIDs group; while drug and GI related cost were 23% and 10% of celecoxib group, respectively (Fig. 1). Cost-utility analysis was evaluated to present the worthiness of the interventions. As a result, ICER per QALY gained of celecoxib comparing with tNSAIDs was 1,382.70 THB (Table 3).

Discussion

Knee OA is the leading cause of pain and disability among elderly population in community. Patients who are intolerable to the symptoms and dissatisfied with the pharmacological treatment are usually referred to surgical intervention. The report of TKA cases is rising every year(11). Though there are several factors that worsen OA symptom, articular cartilage breakdown is one of the most important causes. Several evidences have shown the negative effect to knee cartilage after the long-term usage of tNSAIDs(12-14). On the contrary, some research suggested the advantageous or neutral effect of COXIBs on articular cartilage(15-17). In the present study, substantial cases of TKA were observed in both groups, majority contributed by tNSAIDs users. In all TKA cases, approximate three-fourths patients received tNSAIDs and one-fourths received celecoxib. Although our results cannot confirm the causal relationship between tNSAIDs and deterioration of articular cartilage or the association of celecoxib and its effect on cartilage, it creates the awareness of the impact from long-term usage of NSAIDs. Additionally, pharmacological treatment, especially for elderly patients, should be specific to individual condition. Physicians should have more options to select the most appropriate intervention for each patient.

Several evidences have shown that COXIBs have significant lower risk of GI adverse events comparing to tNSAIDs(18-20). Furthermore the recent randomized controlled trial has shown that celecoxib has statistically significant inferior events of NSAIDs induced GI complication comparing to diclofenac plus omeprazole(21). In the present study, total 14 cases or approximate 1% of all subjects were detected GI adverse events and 2 cases from tNSAIDs group died from...
Table 2. Total cases of GI complication and TKA in tNSAIDs and Celecoxib

<table>
<thead>
<tr>
<th></th>
<th>tNSAIDs (n = 939)</th>
<th>Celecoxib (n = 380)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI complication events (%)</td>
<td>11 (1.17%)</td>
<td>3 (0.7%)</td>
</tr>
<tr>
<td>Gastroduodenal Hemorrhage</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Systematic ulcer</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Severe GI bleeding (death)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total knee arthroplasty cases (TKA) (%)</td>
<td>122 (12.99%)</td>
<td>35 (9.8%)</td>
</tr>
</tbody>
</table>

Table 3. Cost and Utility of tNSAIDs and Celecoxib

<table>
<thead>
<tr>
<th></th>
<th>tNSAIDs (n = 939)</th>
<th>Celecoxib (n = 380)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost (Thai Baht, year 2011)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total drug costs</td>
<td>314,554.25</td>
<td>1,504,689.00</td>
</tr>
<tr>
<td>Total GI complication costs</td>
<td>1,340,562.00</td>
<td>668,827.00</td>
</tr>
<tr>
<td>Total TKA cost</td>
<td>14,748,249.00</td>
<td>4,474,610.00</td>
</tr>
<tr>
<td>Total Cost</td>
<td>16,403,365.25</td>
<td>6,648,126.00</td>
</tr>
<tr>
<td>Average cost per patient (Thai Baht)</td>
<td>17,468.97</td>
<td>17,495.07</td>
</tr>
<tr>
<td>Baseline utility values, mean (SD)</td>
<td>-0.079 (0.19)</td>
<td>-0.110 (0.18)</td>
</tr>
<tr>
<td>After 6 months utility values, mean (SD)</td>
<td>0.595 (0.12)</td>
<td>0.602 (0.12)</td>
</tr>
<tr>
<td>Average QALYs per patient at 6 months</td>
<td>0.337</td>
<td>0.356</td>
</tr>
<tr>
<td>Incremental Cost (Celecoxib-NSAID)</td>
<td>26.10</td>
<td></td>
</tr>
<tr>
<td>Incremental QALY (Celecoxib-NSAID)</td>
<td>0.019</td>
<td></td>
</tr>
<tr>
<td>Cost per QALY gained</td>
<td>1,373.47</td>
<td></td>
</tr>
</tbody>
</table>

Severe GI bleeding. The insignificant difference of GI events in both groups and the low incidence of GI when comparing with 40% in other report can be explained by the increasing awareness of GI complication in tNSAIDs group. Gastro-protective agents are concomitantly prescribed together with tNSAIDs. In addition, the authors could not detect asymptomatic GI adverse event but solely severe or symptomatic GI events were included in the present report.

Seemingly, knee OA has major financial impact to society. For one patient, approximate 17,000 THB was required for a 6 month treatment. Furthermore when considering the entire expenses, it is interesting that TKA became the key element of total expenditures. Although the cost of celecoxib is relatively higher than conventional NSAIDs, the average of expenses was comparable eventually. Considering the health related quality of life, OA symptoms appear to have direct impact to quality of life as shown from the remarkable increase of utility values in both groups. As a result, the ICER per QALY gained comparing between celecoxib and tNSAIDs was 1,382.7 THB per QALY. Regarding the WHO recommendation of ICER threshold for developing countries, celecoxib is considered very cost-effective.

It is worthwhile to address the limitation of our research. Firstly, the present study included solely one COXIB into the analysis. Therefore, the outcomes reported here was specific to the drug itself and may not be able to be referred as the treatment outcomes from other COXIBs. The results from other agents may be various. Moreover our 6 months monitoring period may be too early to observe the final outcomes. The clinical manifestation of GI events as well as cartilage damage may require longer time to develop and reveal. Lastly, the authors could only monitor patient-reported symptomatic GI adverse events. Chronic blood loss from GI bleeding or other asymptomatic GI events was not able to observe because we do not routinely perform hematocrit monitoring in every patient. Therefore the GI adverse event may be underestimated.

Conclusion

The authors results demonstrate the effectiveness and economic burden of disease under the real circumstance to public and it can be a concrete evidence for clinical judgment and health care providers.
to adjust the most appropriate allocation of resources for future treatment.

Acknowledgement
This research was financially supported by Arthritis Foundation, Thailand under patronage of HRH Princess Mahajakri Siridhorn.

Potential conflicts of interest
None.

References


การวิเคราะห์ต้นทุน–ประสิทธิภาพและภาวะทางเศรษฐศาสตร์ของการรักษาโรคข้อเข่าเสื่อมโดยการวิเคราะห์จากมุมมองจากเวชปฏิบัติ

ธนา ธรรมเจน, อุกฤษฏ์ จริยธรรมภัทร, ประภัส สันติยา, วิชัย สาทิพย์พงษ์, ธัญชัย วงศ์บุญหนัก

กลุ่มตัวอย่าง: ผู้ป่วยที่ได้รับยาต้านการอักเสบแบบตั้งต้นไม่ได้สมบัติให้รักษาตามวิธีการรักษาตั้งต้นไม่ได้สมบัติ เปลี่ยนแปลงทางพฤติกรรมการรักษาและเพิ่มความสามารถในการทำงานของกลุ่มในปัจจุบัน การใช้ยาตามการรักษาเพื่อรักษาข้อเข่า เสื่อมเป็นที่ยอมรับในเวชปฏิบัติ เมื่อจากมีผลกระทบต่อการเจริญ พฤติกรรมทางใจ ในระบบทางเดินอาหารและสมองเสื่อม แต่ยังไม่มีการเปรียบเทียบผลของการรักษาโดยใช้ยาต้านการอักเสบในระยะยาว ซึ่งจะน่าจะไปสู่การตัดสินใจที่ถูกต้อง เมื่อจากผลการวิจัยในเรื่องการรักษาลู่ปัจจุบันในกลุ่มนี้ และจะมีการเปรียบเทียบของผลการรักษาในระยะยาวต่างกันมาก

วัตถุประสงค์: เพื่อศึกษาผลต้นทุน–ประสิทธิภาพและการทางเศรษฐศาสตร์ของการรักษาโรคข้อเข่าเสื่อมโดยการรักษาแบบมาตรฐานและแบบดีกรีเฉพาะเจาะจงในจำนวนผู้ป่วยที่เสียชีวิตจากอาการเลือดออกในทางเดินอาหาร รวมถึงผลการรักษาโดยใช้ยาซีรีคอกซิบ

วัตถุประสงค์การศึกษา: ศึกษาผลต้นทุน–ประสิทธิภาพของการรักษาผู้ป่วยโรคข้อเข่าเสื่อมโดยใช้ยาซีรีคอกซิบเป็นยาต้านการอักเสบแบบมาตรฐาน ซึ่งมีการติดตามผลโดยการวิเคราะห์ต้นทุน–ประสิทธิภาพโดยการจัดการศึกษาค่าประสิทธิภาพที่ต้องการในกลุ่มที่ได้รับการรักษาโดยใช้ยาซีรีคอกซิบติดตามผลการรักษาโดยใช้ยาซีรีคอกซิบเป็นยาต้านการอักเสบแบบมาตรฐาน และการรักษาแบบการศึกษาค่าประสิทธิภาพ

วิธีการ: กลุ่มที่ได้รับการรักษาผู้ป่วยจากกลุ่มที่ได้รับการรักษาโดยใช้ยาซีรีคอกซิบเป็นยาต้านการอักเสบแบบมาตรฐาน

ผลการศึกษา: กลุ่มจดหมาย 939 ราย ได้รับการติดตามผลการใช้ยาต้านการอักเสบแบบมาตรฐานและ 380 ราย ได้รับการติดตามผลการใช้ยาซีรีคอกซิบ 90.3% ของกลุ่มที่ได้รับยาซีรีคอกซิบ ซึ่งเป็นกลุ่มที่ได้รับการรักษาผู้ป่วยจากกลุ่มที่ได้รับยาซีรีคอกซิบ 90.3% ของกลุ่มที่ได้รับยาซีรีคอกซิบ

ผลการศึกษา: กลุ่มที่ได้รับยาซีรีคอกซิบ 90.3% ของกลุ่มที่ได้รับยาซีรีคอกซิบ ซึ่งเป็นกลุ่มที่ได้รับการรักษาผู้ป่วยจากกลุ่มที่ได้รับยาซีรีคอกซิบ 90.3% ของกลุ่มที่ได้รับยาซีรีคอกซิบ