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Evidence for Success in Hospital Formulary Consideration of Knee Osteoarthritis Treatment: Budget Impact Analysis of Glucosamine

หลักฐานเพื่อความสำเร็จของการพิจารณายารักษาโรคข้อเข่าเสื่อมเข้าสู่บัญชียาโรงพยาบาล: การศึกษาผลกระทบเชิงงบประมาณของการใช้กลูโคซามีน

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This study was aimed to examine the financial impact of adding glucosamine to hospital formulary. A budget impact model using probabilistic analysis (Monte Carlo Simulation) was applied to capture the changes of drug budget of knee osteoarthritis treatment before and after the available of glucosamine (between budget year 2004 vs 2005-2009). The study was conducted from provider perspective based on Petchabun hospital data. Six available drugs used for knee osteoarthritis were included in the analysis. Result analyses showed that the estimated drug budgets of knee osteoarthritis in 2007-2009 were 14.2, 14.7, and 14.9 million baht respectively. The average increasing amount was 430,000 Baht each year after the introduction of glucosamine to hospital formulary. This modest incremental drug budget gave the impression to support the inclusion of glucosamine to formulary as it yet falls under the regular annual growth of drug budget in years before the availability of glucosamine in the hospital formulary. However, the further examination and monitoring of data estimations are recommended to minimize uncertainty of the result analyses.

Keywords : Glucosamine, knee osteoarthritis, budget impact analysis.

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การศึกษานี้มีวัตถุประสงค์เพื่อประเมินผลกระทบเชิงงบประมาณก่อนและหลังการบรรจุยากลูโคซามีนเข้าสู่บัญชียาโรงพยาบาลเพชรบูรณ์ในช่วงปีงบประมาณ 2004 เปรียบเทียบกับปีงบประมาณ 2005-2009 รวมทั้งพิจารณาผลกระทบเชิงงบประมาณต่อยารักษาข้อเข่าเสื่อมอีก 6 ชนิด โดยใช้แบบจำลองและการวิเคราะห์แบบ probabilistic ด้วยวิธี Monte Carlo Simulation และอาศัยมุมมองจากโรงพยาบาล ผลการวิเคราะห์ แสดงให้เห็นว่างบประมาณด้านยาเพื่อรักษาข้อเข่าเสื่อมในปีงบประมาณ 2007-2009 หลังจากมีการบรรจุกลูโคซามีนเข้าสู่บัญชียาโรงพยาบาล จะมีมูลค่าประมาณ 14.2, 14.7, และ 14.9 ล้านบาทตามลำดับ ซึ่งโดยเฉลี่ยแล้วมีการเพิ่มขึ้นของงบประมาณด้านยาปีละ 430,000 บาท ผลกระทบเชิงงบประมาณในจำนวนนี้จึงนับว่าไม่มากเมื่อเทียบกับอัตราการเพิ่มขึ้นของงบประมาณในช่วงปีที่ผ่านๆมา และอาจใช้เป็นข้อสนับสนุนในการบรรจุยานี้เข้าสู่บัญชียาโรงพยาบาลได้ อย่างไรก็ตาม โรงพยาบาลเองจะต้องมีการตรวจสอบค่าของตัวแปรต่างๆที่ใช้ในการคำนวณ เพื่อลดความไม่แน่นอนของผลลัพธ์การวิเคราะห์และติดตามผลกระทบเชิงงบประมาณที่เกิดขึ้นจริงด้วย

คำสำคัญ : กลูโคซามีน ข้อเข่าเสื่อม ผลกระทบเชิงงบประมาณ

Introduction

In OA (osteoarthritis), the cartilage, that protects the ends of the bones breaks down, is not completely understood in its etiology. OA affects many joints, with diverse clinical patterns. The knee is a dominantly affected site.[1] Major clinical manifestation of OA of the knee is pain, which is usually related to activity, and around the joint that is typically worse with weight-bearing.[2] The symptoms are highly varied across population, and might be static, relapsing, or progressive.[3] OA progresses slowly over years and is rarely predictable since its symptoms correlate poorly with clinical and radiological signs. Diagnosis then rests on the clinical recognition of the common patterns and the exclusion of alternatives.

Conventional goals of treatment are to control pain and improvement in function and health-related quality of life, with avoidance, if possible, of toxic effects of therapy.[4] Delaying progression of disease is an additional advanced treatment objective.[5] These objectives have laid the groundwork for the second rationale in choosing OA. Glucosamine, which is considered as effective particularly in delaying progression, becomes a challenging illustration once it is introduced to the formulary.

Evidences supporting the new perspective in the management of osteoarthritis which is structure modification in knee thus become a focal point of current OA treatment. The dietary

supplement of glucosamine has been advocated as safe and effective option for the OA management in this case. It acts as a chondroprotective agent in osteoarthritis. A meta-analysis of studies evaluating the efficacy of glucosamine for osteoarthritis suggested potential benefit from this agent but raised questions about the scientific quality of the studies.[6] Two long-term studies already included in this meta-analysis, showed the significant improvement of the joint space narrowing in patients taking glucosamine comparing to placebo group. It is therefore proposed that this agent might be effective in delaying disease progression eventually.[7,8] However, recently, the large multi-centre, well designed, controlled study of glucosamine and chondroitin sulfate, which is another chondroprotective agent, reported their substantial effects only in the patients with moderate-to-severe pain.[9] The authors emphasized that the continuing research is needed to establish the potential efficacy and increase the understanding of biology, pharmacology, and pharmacokinetics of these agents.

Even there are conflicting results of using glucosamine in osteoarthritis, the study on financial impact of glucosamine as an alternative is still of interest and considered as of value since current OA treatments have many serious adverse events especially in the elderly patients.

As a result of uncertain evidence of using glucosamine in long-term OA treatment, the cost-effectiveness analysis might not be an only helpful substantiation to aid the decision making. In addition to cost-effectiveness evidence to support the decision whether or not this drug should be used, the issue of affordability became a great concern. Budget impact analysis (BIA) estimates the impact on annual healthcare use and costs for the first, second, and subsequent years after the introduction of the new product for a national or hospital level. It provides an estimate of the financial impact of a drug based on its rate of uptake as well as the magnitude and timing of which on healthcare utilization and costs.[10]

Objective

To examine the financial impact of adding glucosamine to hospital formulary with an intention to illustrate the usefulness of financial implications where the value of money based on economic evaluation of an intervention is still unclear due to limited clinical evidence.

Methods

The model-based probabilistic analysis was used to examine the financial consequences of including glucosamine in hospital formulary. Petchabun hospital was used to be study site. Estimation of budget impact of glucosamine during 2005-2009 comparing to the year before glucosamine was available (2003-2004) was done.

Model Structure Model mainly focuses on the changes in uses of healthcare resources

associated with the disease of interest. These changes are directed toward on drugs and health services that will tentatively be used less often because of the clinical benefit of new drug over current treatments. They are shown as a part of model comparators. The following budget impact model then was developed.

Budget Impact Model

$= (C_p x Q_p) + \sum [\Delta (C_{ki} x Q_{ki})]$

Where

C is the average cost (Baht/patient/year).

Q is the number of drug use (patients/year).

p is the drug proposed for listing in the fomulary

k are the competitive drugs/services.

i = 1,2,3,.....,n

Δ refers to the differences of value of each variable as a result of a comparison of such at before and after the listing.

Competitive drugs and services in the model are those that are currently used to effectively treat knee OA in the setting under study. Hypothetically, all relevant healthcare resources should be determined in BIA model. Nevertheless, in order to address the importance of BIA and also keep model simplistic, only those regarded as representatives for each therapeutic indication are purposively included in the analysis.

Here i = 1-7 referring to competitive drugs and the new drug. To make the model structure more clinically allied, each drug/service was grouped according to its indication: indication-based analysis, resulting in the following equation.

Budget Impact Model

$= (C_p x Q_p) + \sum [\Delta (C_{ki} x Q_{ki})]$

$= (C_p x Q_p) + \Delta$ Cost of delaying progression+Δ Cost of pain-relieving

$= (C_p x Q_p) + [(\Delta C_6 Q_6] + [(\Delta C_1 Q_1) + (\Delta C_2 Q_2) + (\Delta C_3 Q_3) + (\Delta C_4 Q_4) + C_5 Q_5) + (\Delta C_7 Q_7)]$

Where i = 1 = diclofenac sodium tablet

i = 2 = diclofenac sodium and ranitidine tablets

i = 3 = diclofenac sodium and omeprazole tablets

i = 4 = celecoxib tablet

i = 5 = tramadol tablet

i = 6 = hyaluronic acid sodium injection

i = 7 = glucosamine

Model Descriptions As the perspective of hospital was used, only drug acquisition cost, which occurred in the hospital, was included in the model analysis. Target populations were patients with knee osteoarthritis who failed to control pain by acetaminophen.

Model Analyses

1. Estimation the Annual Cost of Drugs Used per Patient (C_p and C_{ki})

1.1 Pain-Relieving Agents: NSAIDs and Its Combination. To quantify the cost of using NSAIDs and its combination to prevent

gastrointestinal complication, the decision-analytic model, cost-consequence, was developed. Cost data were obtained from hospital database whereas the probabilities were estimated from literature review.

1.2 Pain-Relieving Agents: Tramadol. Cost of pain treatment using tramadol was calculated by the drug acquisition cost and the average number of use per patient per year. The future average amount of tramadol use was estimated by Delphi technique through 3 orthopedicians provided the historical dispensing pattern. No additional resource consumed for adverse events of using this drug was included. The future acquisition cost of tramadol was predicted from 3 purchasing pharmacists by modified Delphi technique.

1.3 Delaying Progression Agents: Glucosamine and Hyaluronic Acid Injection. Costs of using these two drugs consisted of only drug costs. Again, the future average number of use of each drug was calculated based on the historical data on dispensing pattern and then multiplied with the purchasing price. The past dispensing pattern that provided to all physicians for the future estimations was used in the budget impact analysis by Delphi technique. The modified Delphi technique was also used to reach the future acquisition cost of glucosamine and hyaluronic acid by 3 purchasing pharmacists.

2. Estimation of Number of Patients Using Each Drug per Year (Q_p and Q_{ki})

2.1 Estimation of Number of Patients with Knee Osteoarthritis. The prevalence of knee osteoarthritis was calculated by using hospital electronic record. To estimate the number of this patient group in the upcoming years, the simple regression analysis was used. Trend lines of the years before and after the introduction of glucosamine into the hospital formulary were estimated. The induced demand effect was also predicted by comparing the slopes of the growth rate before and after the glucosamine introduction. If there were not many differences, the usual trend line was used. In contrary, if a great magnitude of the difference in number of patients with knee osteoarthritis was detected, the induce demand effect was then added onto the regular growth.

2.2 Estimation of Number of Patients Using Each Drug. From the same set of dispensing data of knee osteoarthritis patients, the proportion of patients prescribed each drug was extracted. By using the hospital number (HN) of each patient to trace back their historical dispensing patterns recorded in the pharmacy database, the movements of patients amid all treatment alternatives were revealed. These data were summarized and presented to 3 treating orthopedics as the background data for estimating the expected number of patients using each drug by modified Delphi technique.

3. **Probabilistic Analyses** One year time horizon was applied in each budget impact model and replicated analyses will be done until glucosamine reaches the steady market share in terms of number of users (patients). In probabilistic simulation, each uncertain variable is modeled by a probability distribution. MonteCarlo Simulation was used by involving random sampling of each variable under the specified probability distribution to produce hundreds or thousands of iterations. Each probability distribution is sampled in a way that reproduces the distribution's shape. Hence, the values calculated reflect the probability of the values that might occur.

Table 1 Drug budget before and after inclusion of glucosamine to hospital formulary

Year	Drug Budget of Knee OA (Million Baht)	(Million Baht)	Differences % Growth Rate
2003	11.0		
2004	12.0	1.0	9.1
2005	12.8	0.8	6.7
2006	13.6	0.8	6.2
2007	14.2	0.6	4.4
2008	14.7	0.5	3.5
2009	14.9	0.2	1.4

Results

From Table 1, the growth rate of drug budget in 2003-2004 was the highest rate at 9.1 percent comparing to of 2005-2009. In 2005, the first year of availability of glucosamine, the growth rate of drug budget decreased to be 6.7 percent. Diminished growth rate was seen again in 2006 drug budget.

The forecasted drug budgets in 2007-2009 were about 14.2, 14.7, and 14.9 million baht respectively. Thus, drug budget during these three years was not significantly increased.

The result showed that on average the drug budget would increase by 430,000 Baht each year after the introduction of glucosamine to hospital formulary. There were only 86 from total 1,437 patients with knee osteoarthritis (6 percent) becoming glucosamine users in the 2005 which is the first year of glucosamine listing in hospital formulary. In a year after, number of patients using glucosamine was increased almost two times (157 patients). The proportion of glucosamine users to total patients with knee osteoarthritis in 2006 was 10.8 percent. Based on the forecasted number of glucosamine users in 2009; 368 patients, there will be 368 patients from the estimated 1,534 patients with knee osteoarthritis (24 percent).

Discussions

Market penetration of glucosamine in 2005-2006 was not an immediate type. It was increased from 6 percent coverage of patients

to 10 percent. However, based on the treating physicians' opinions, it was expected to expand its market size with a double penetration rate in 2007; 20 percent patient coverage. The gradual penetration rates were expected to happen in 2008-2009; 2 percent increase each year. However, even the number of patients using glucosamine in 2007 was expected to be two times of 2006, the drug budget was not much increased. Moreover, the expected additional drug budget in 2008 was only 500,000 Baht which was the probable effect from the reduction use of celecoxib.

The introduction of glucosamine brought the dynamic changes in terms of number of patients using each drug (market share) and the quantity of analgesic use to the drug cost spending. Most of effects were observed in the changes of pain-relieving agents. Interestingly, there also was small effect of glucosamine use in the utilization of hyaluronic acid which can be considered as the targeted competitive drug.

As mentioned earlier, the average increased amount was 430,000 Baht each year after glucosamine has been listed. This amount of money roughly equates to the costs of knee replacement in 5 patients. Therefore, considering only this figure and if the long-term use of glucosamine can evidently delay progression i.e. patients can stay in comparable disease stage (mild-to-moderate pain), by given the incremental costs of 430,000 Baht to nearly 400 patients, it might be worthy of note to including glucosamine in hospital formulary. However, before jumping into making conclusion without any specification, to consider the study limitation which might bring a drawback to the study conclusion is imperative.

The first study limitation is related to the long-term outcome of using glucosamine, delaying disease progression, which was not considered in the model analysis. If the cartilage damage can be effectively deferred by glucosamine, there then will be eventually the cost-savings from knee replacement therapies. However, this study, presented only the probable budget associated with using glucosamine to achieve the pain-relieving outcome as a benefit return of investment, not the delaying progression which is a desirable outcome.

The estimation of costs and number of patients, in particularly those of glucosamine use in the model was considered as the second limitation. These variables were estimated based on the historical dispensing pattern together with the physicians' opinions based on many assumptions, so it brought the uncertainties to model analysis and then affected the study conclusions.

Conclusions

The result analyses of budget impact gave the impression to support the inclusion of glucosamine to formulary because of its minor incremental budget (430,000 Baht per year) which falls under the regular annual growth of

drug budget and total budget of knee osteoarthritis in years before the introduction of glucosamine into the hospital formulary. However, due to the study limitations described earlier, the further investigation of data inputs (value, distribution) is required in order to minimize uncertainty of result analysis. Additionally, to monitor the use of glucosamine and its actual financial impacts to the hospital is recommended.

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