Appropriateness of Therapeutic Drug Monitoring for Lithium

Chaveewan Ratanajamit BPharm, PhD*, Suchada Soorapan BPharm, PhD*,
Thitima Doang-ngern BPharm MSc*, Wudtikai Waenwaisart BPharm**,
Laksamee Suwanchavalit BPharm*, Siwaporn Suwansiri BPharm*,
Sopit Jantasaro BPharm*, Itsaree Yanate BPharm*

** Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat Yai, Songkhla*
*** Head of Pharmacy Department, Songkhla Psychiatric Hospital, Songkhla*

Objective: *Evaluate the appropriateness of therapeutic drug monitoring (TDM) for lithium.*
Material and Method: *A retrospective chart review of all patients who received lithium for treatment of psychiatric disorders between January 2004 and October 2005 was done. The present study was investigated in a psychiatric hospital in Thailand. Based on detailed chart review, the appropriateness of TDM utilization comprised of three aspects, i.e., the indication of TDM request, the time of blood sample taking in relation to the medication process, and the clinical applications of the reported serum lithium levels, were evaluated. The Morecambe Bay Shared Care Guideline 2003 was modified and used as criteria for evaluation. Altogether, 91 serum lithium samples were measured among 60 patients.*
Result: *In 66 (72.5%) of requests, clear indications for lithium TDM were recorded i.e., initiation therapy 41.8%, suspected toxicity 15.4%, patient compliance assessment 5.5%, after regimen changes 5.5%, and therapeutic failure 4.4%. Routine tests without specified indications were found in the remainder (27.5%), all were in-patients, which pointed to potentially redundant use. The time of sample taking was recorded in 37 (40.6%) of blood samples, all were taken from in-patients, after steady state had been reached. These data for out-patients were not recorded, except one noted that blood sample was drawn after the patient had not received lithium for four days. Serum lithium levels were reported in 83 (91.2%) samples. Of these, 37 (44.6%) were out of therapeutic range, and only 12 required dosage alterations. The evaluation demonstrated somewhat inappropriate use of reported lithium levels. Dose changes were done in some patients who required dosage adjustment. Among 14 toxicity-suspected patients, nine actually had serum lithium levels exceeding the therapeutic range. Of these, only one patient was subsequently switched to a reduced dose, three patients were discontinued while five patients were prescribed the pre-TDM doses. Similarly, in five toxicity-suspected patients whose serum lithium levels were below therapeutic range, lithium was discontinued in three patients and no dosage alteration, which was considerably acceptable, in two patients. The doses were increased in three out of four inadequately controlled patients whose serum lithium was lower than the therapeutic range. Overall, in only 33 (36.3%) requests was TDM performed appropriately according to the indication, sampling time and subsequent dose adjustment.*
Conclusion: *The findings indicate the need to improve the utilization of TDM for lithium. Education for hospital personnel on appropriateness of serum sample collection, interpretation, and proper use of serum drug levels is encouraged. Development of a request form containing essential data, such as indication for TDM, current drug dosing regimen, time of last dose, patient compliance, test results and interpretations and clinical decision made, can help optimize TDM use and reduce unnecessary costs.*

Keywords: *Therapeutic drug monitoring, TDM, Lithium, Mania, Bipolar disorder*

J Med Assoc Thai 2006; 89 (11): 1954-60
Full text. e-Journal: *http://www.medassocthai.org/journal*

Correspondence to : Soorapan S, Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Songkhla 90110, Thailand. E-mail: suchada.so@ psu.ac.th

Lithium has been approved for the treatment of manic episode of manic-depressive (bipolar) illness[1]. Maintenance therapy prevents or diminishes the frequency and intensity of subsequent manic episodes in bipolar patients with a history of mania. Toxicity caused by lithium is closely related to serum lithium levels and can occur at therapeutic doses, primarily due to inter-individual pharmacokinetic variability. This drug also has narrow therapeutic ranges, and severe toxicities may result in mortality. Serum lithium monitoring is therefore required for lithium therapy. Although TDM is a useful tool to optimize therapy of many medications, a misuse of TDM resulting in improper use of TDM results and unjustifiable cost was documented[2-5]. The authors evaluated the appropriateness of TDM for lithium, a drug that has been largely monitored in the setting, as a prerequisite for developing improvement strategies.

Material and Method

A retrospective chart review of all patients with psychiatric disorders who received lithium between January 2004 and October 2005 was done at a psychiatric hospital in southern Thailand. Based on detailed chart review, the appropriateness of TDM utilization with regard to 3 aspects, i.e., the indication of TDM request, the time of blood sample taking in relation to the medication administration (dosage schedule, a duration between last lithium intake and blood sampling), and the consequences of the reported serum lithium levels for clinical decision making were analyzed. TDM were indicated in several situations including lithium therapy initiation/restarting lithium therapy after discontinuation, suspected toxicity (patients presented with adverse drug reactions including tremor, confusion, diarrhea, lethargy, nausea/vomiting, T-wave depression, seizure, etc), suspected therapeutic failure/ sub-therapeutic concentrations, assessment of patient compliance, assessment following a change in dosage regimen, clinical state alteration of patients, potential drug interactions (thiazide diuretics, angiotensin-converting enzyme inhibitors (ACEIs), non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin II receptor blockers, etc.), and high-risk patients (change in serum sodium, dehydration, vomiting, diarrhea, fever, etc). The sampling time was considered appropriate if it was undertaken after steady state has been attained (approximately 5 half-lives, i.e., $\geq$ 4-5 days in patients with normal renal function, and $\geq$ 7-8 days in patients with impaired renal function) and distribution phase has been terminated ($\geq$ 10-12 hours after the last dose), unless early sample taking was indicated, such as, patients with suspected lithium intoxication. Under circumstances that TDM was requested for identifying the reasons why a patient was not responding to a prescribed regimen or was exhibiting toxic signs or symptoms, these data were taken into account in assessment of appropriateness of utilization of reported serum lithium levels. However, clinical response primarily determined clinical decision. For example, in cases of suspected sub-therapeutic levels, even if blood levels lay in therapeutic range, increased lithium dose was considerably appropriate. Similarly, in patients with potentially toxic lithium concentrations (with an exception in those who did not present toxic symptoms) or those who experienced lithium toxicity, dose reduction was an appropriate action. The Morecambe Bay Shared Care Guideline 2003[6], was modified and used as criteria for evaluation. Descriptive statistics was used for data analysis.

Study Sample

In- and out-patients who were prescribed lithium for at least three consecutive months and requested for a TDM at a psychiatric hospital in southern Thailand between January 2004 and August 2005 were included. In order to estimate a precise proportion for each aspect of appropriate TDM utilization as described earlier, the authors determined a sample size using the following equation.

$$n = (Z / e)^2 (\pi) (1 - \pi)$$

where, Z = standard normal deviation at significant level 0.05

e = precision of the estimate = 0.1

π = a proportion (p) of TDM samples which were considered appropriately performed, we set p = 0.5 in order to get a largest sample size.

We required a sample of approximately 90 TDM requests for our study. The results were presented in frequency distribution tables with number (n) and percent. Mean, range, and standard deviation were calculated in continuous variables.

Results

Characteristics of the present study sample are summarized in Table 1. As some patients requested TDM more than once (ranged 1-9), the authors obtained 91 TDM samples from 60 patients. Half of the patients were diagnosed with bipolar disorder. Only five patients were treated by lithium alone. Medications concurrently used (data not shown) were trihexy-phenidyl (n = 77),

haloperidol (n = 53), chlorpromazine (n = 52), diazepam (n = 9) and thioridazine (n = 7). These medications, however, did not significantly alter lithium pharmacokinetics. In 66 (72.5%) requests, clear indications for lithium TDM were recorded i.e., initiation therapy 41.8%, suspected toxicity 15.4%, patient compliance assessment 5.5%, changes in regimen 5.5%, and therapeutic failure 4.4% (Table 2). Routine tests without clear indications were found in 25 (27.5%) in-patients, which pointed to potentially redundant use of TDM. Overall, the exact time of sample taking was recorded in 37 (40.6%) of blood samples after steady state had been reached, all were in-patients. Appropriateness of the sampling time among the remainder (53 samples) was not fully evaluated since related data, especially patients' compliance with the dosage regimen, were not recorded (Table 3). Assuming that out-patients complied with the lithium regimen, except one out-patient who had not taken the drug for four days, time of sample taking was considerably appropriate as blood samples were drawn at steady state conditions and at least 12 hours following the last lithium dose as patients had not taken the drug in the morning of their visits. Only 83 (91.2%) serum lithium levels were available for analysis (Table 4). Of these, 37 (44.6%) tests were out of therapeutic range (0.6-1.2 mmol/L), only 12 required dosage alterations as clinical decision making was primarily based on clinical response. The evaluation demonstrated somewhat inappropriate utilization of reported lithium levels. Dose changes were done in some patients who required dosage adjustment. Among 14 toxicity-suspected patients,

Table 1. Characteristics of patients

Variable	Summary statistic (n = 60)
Male, n (%)	33 (55.0)
Out-patients:In-patients, n (%)	46 (76.7) :14 (23.3)
Mean age ± SD (range), years	35.7±13.6 (15-79)
Diagnosis, n (%)	
- Bipolar disorder	30 (50.0)
- Psychosis	10 (16.7)
- Schizophrenia	9 (15.0)
- Schizophrenia with bipolar disorder	3 (5.0)
- Others	4 (6.7)
Number of TDM requested, n (%)	
- Once	44 (73.3)
- Twice	7 (11.7)
- Three times	8 (13.3)
- 9 times	1 (1.7)

Table 2. Appropriateness of indication of TDM utilization for lithium

Variable	Frequency, n (%)		
	Out-patients (n = 54)	In-patients (n = 37)	Total (n = 91)
- Appropriate	54 (100)	12 (32.4)	66 (72.5)
• Initiation of therapy/ monitoring every 3-6 months	30 (55.6)	8 (21.6)	38 (41.8)
• Suspected toxicity	13 (24.1)	1 (2.7)	14 (15.4)
• Assessment of patient compliance	4 (7.4)	1 (2.7)	5 (5.5)
• Regimen alteration	4 (7.4)	1 (2.7)	5 (5.5)
• Therapeutic failure	3 (5.6)	1 (2.7)	4 (4.4)
- Inappropriate			
- Routine testing without indications	0 (0)	25 (67.6)	25 (27.5)

Table 3. Appropriateness of sampling time of TDM utilization for lithium

Variable	Frequency, n (%)		
	Out-patients (n = 54)	In-patients (n = 37)	Total (n = 91)
- Appropriate	53 (98.1)	37 (100.0)	90 (98.9)
- Inappropriate	1 (1.8)	0 (0.0)	1 (1.1)

Table 4. Serum lithium levels and clinical response

Variable	Frequency, n (%)		
	Out-patients (n = 47)	In-patients (n = 36)	Total (n = 83)
- Levels lied within therapeutic range (0.6-1.2 mmol/L)	22 (46.8)	24 (66.7)	46 (55.4)
• No change in dosage with good response	21 (44.7)	24 (66.7)	45 (54.2)
• Dosage increased subsequently to therapeutic failure	1 (2.1)	0 (0.0)	1 (1.2)
- Levels below therapeutic range (<0.6 mmol/L)	20 (42.5)	8 (22.2)	28 (33.7)
• No change in dosage			
- Good clinical response	12 (25.5)	8 (22.2)	20 (24.1)
- Toxic response	2 (4.2)	0 (0.0)	2 (2.4)
- Awaiting clinical evaluation after regimen alteration	1 (2.1)	0 (0.0)	1 (1.2)
• Dosage increased because of therapeutic failure	2 (4.2)	0 (0.0)	2 (2.4)
• Discontinued because of toxicities	3 (6.4)	0 (0.0)	3 (3.6)
- Levels exceed therapeutic range (>1.2 mmol/L)	5 (10.6)	4 (11.1)	9 (10.8)
• No change in dosage despite toxic symptoms	1 (2.1)	4 (11.1)	5 (6.0)
• Dosage decreased because of toxicities	1 (2.1)	0 (0.0)	1 (1.2)
• Discontinued because of toxicities	3 (6.4)	0 (0.0)	3 (3.6)

Table 5. Lithium-related toxicities

Toxic symptoms*	Frequency, n (%)		
	Out-patients (n = 54)	In-patients (n = 37)	Total (n = 91)
- Tremor	6 (11.1)	0 (0.0)	6 (6.6)
- Anorexia	3 (5.6)	0 (0.0)	3 (3.3)
- Fatigue	3 (5.6)	0 (0.0)	3 (3.3)
- Nausea/vomiting	1 (1.8)	0 (0.0)	1 (1.1)
- Polyuria	1 (1.8)	0 (0.0)	1 (1.1)
Total	14 (25.9)	0 (0.0)	11 (12.1)

* Some patients experienced > 1 toxic symptom

nine actually had serum lithium levels exceeding the therapeutic range, while five had serum lithium levels below the therapeutic range. Of the nine patients whose serum lithium levels were high (> 1.2 mmol/L), only one patient was subsequently switched to a reduced dose, three patients were discontinued and five patients were prescribed the pre-TDM doses. Similarly, in five toxicity-suspected patients whose serum lithium levels were below the therapeutic range, lithium was discontinued in three patients and no dosage alteration, considerably acceptable, in two patients. TDM results should be used to optimize dosing and to avoid toxicities, i.e., dosage reduction might be more appropriate than discontinuation especially in patients who were still beneficial to lithium treatment. However, four patients whose subtherapeutic lithium levels were suspected, two patients who had low lithium levels were prescribed with an increased dose. One patient who was inadequately controlled by lithium was prescribed a higher dose even though the serum lithium level was in the therapeutic range. Of 25 in-patients whose blood samples were taken without specified indication, 20 had therapeutic serum lithium levels and five had subtherapeutic levels, all received the pre-TDM regimen. Overall, in only 33 (36.3%) of requests was TDM performed appropriately with regard to indication, sampling time and subsequent dose adjustment.

The authors found 11 patients, with a serum concentration range 0.2-1.9 mmol/L, experienced lithium-related toxicities. Some patients experienced ≥

1 toxicity. Common toxicities were those that affected CNS (i.e., tremor, anorexia, fatigue) and gastro-intestinal system (i.e., nausea, vomiting, and diarrhea) (Table 5). Nephrogenic diabetes insipidus was identified in a woman aged 37 years old who had used lithium for seven years.

Discussion

TDM requests among out-patients, were appropriate, while two-thirds of that among in-patients were requested inappropriately. Sampling time was performed appropriately in both in- and out-patients. Utilization of reported serum lithium levels was somewhat appropriate.

Ordering TDM for lithium as routine service without clear indications among in-patients resulted in unnecessary costs. In contrast, the authors did not examine under use of TDM, as in many cases (especially those with preceding dose changes or therapy initiation) additional serum level determinations might have been useful to speed up optimal dosing. Sample taking of lithium has been established at 12 hours after dose, usually in the morning after the evening dose, to ensure that blood collection was done during the elimination phase, avoiding absorption and distribution phases, where inter-subject variability exists. All patients who are planned for TDM must be informed not to take the medication in the morning of the visit. Additionally, doctors should assess compliance with medication to ensure the blood sample is drawn at steady state conditions. All relevant data required for test interpretation including sampling time, time of last dose, length of therapy with the current regimen, dosage form, dose, and dosage administration, etc should be recorded. Other laboratory parameters such as serum sodium, renal function, and thyroid function may be useful in clinical decision making and post-TDM regimen design.

The findings indicated the need of strategies to improve the utilization of TDM for lithium. Improvement of TDM service by education of hospital staff involved in TDM service, including nursing staff, laboratory personnel, physicians and pharmacists, was documented[2,7]. The pharmacy-based clinical pharmacokinetic service also improved the appropriateness of physician utilization of serum drug levels[3]. However, frequent discrepancies were found between the TDM laboratory's recommendations and actual clinical decision making, for example suggested dose changes were followed in only 30%[8]. This disagreement might have resulted from difference in data supporting the decision, i.e., recommendations would not be practical if they were not based on both pharmacokinetic parameters and patients' clinical response. Pharmacists who are knowledgeable of pharmacokinetics and who are aware of the limitations of laboratory findings may contribute to TDM improvement, but a survey in the United Kingdom found that pharmacists collaborated in only 26% of therapeutic drug assay laboratories[9]. Using the consensus guideline developed by TDM expert group will help ensure optimal clinical benefit of TDM in psychopharmacotherapy including lithium[10].

Conclusion

TDM application is still somewhat inappropriate. Education for hospital personnel on appropriateness of serum sample collection, interpretation, and proper use of serum drug levels is encouraged to improve the appropriateness of TDM utilization. Incomplete data recording, a common problem among out-patients, partially limited ability to evaluate the appropriateness of TDM use. Development of a request form containing all essential data can help optimize TDM use, avoid unnecessary tests, and improve cost-effectiveness of this practice.

Acknowledgement

The authors wish to thank the staff at Pharmacy Department of Songkhla Psychiatric Hospital for the provision of the data for this study.

References

1. Farthing K, Jones B, Ferrill MJ, Sweet BV, Generali JA. Drug facts and comparisons. 3rd ed. St. Louis, Missouri: Facts and Comparisons; 2003.
2. Sidwell A, Barclay M, Begg E, Moore G. Digoxin therapeutic drug monitoring: an audit and review. N Z Med J 2003; 116:U708.
3. Michalko KJ, Blain L. An evaluation of a clinical pharmacokinetic service for serum digoxin levels. Ther Drug Monit 1987; 9:311-9.
4. Bussey HI, Hoffman EW. A prospective evaluation of therapeutic drug monitoring. Ther Drug Monit 1983; 5:245-8.
5. Travers EM. Misuse of therapeutic drug monitoring: an analysis of causes and methods for improvement. Clin Lab Med 1987; 7:453-72.
6. Anon. Morecambe Bay Shared Care Guideline: Lithium. http://www.mbpct.nhs.uk/medman/scg/LITHIUM.pdf. 2003. accessed on 27-4-2005.
7. Carroll DJ, Austin GE, Stajich GV, Miyahara RK, Murphy JE, Ward ES. Effect of education on the

appropriateness of serum drug concentration determination. Ther Drug Monit 1992; 14:81-4.
8. Mann K, Hiemke C, Schmidt LG, Bates DW. Appropriateness of therapeutic drug monitoring for antidepressants in routine psychiatric inpatient care. Ther Drug Monit 2006; 28:83-8.
9. Thomson AH, Watson ID, Wilson JF, Sweeney G, Dawkins CE, Smith BL, et al. An audit of therapeutic drug monitoring service provision by laboratories participating in an external quality assessment scheme. Ther Drug Monit 1998; 20:248-52.
10. Baumann P, Hiemke C, Ulrich S, Eckermann G, Gaertner I, Gerlach M, et al. The AGNP-TDM expert group consensus guidelines: therapeutic drug monitoring in psychiatry. Pharmacopsychiatry 2004; 37:243-65.

การประเมินความเหมาะสมการตรวจติดตามระดับยาในเลือดของยา Lithium

ฉวีวรรณ รัตนจามิตร, สุชาดา สูรพันธุ์, ฐิติมา ด้วงเงิน, วุฒิไกร แว่นไวศาสตร์, ลักษมี สุวรรณชวลิต, ศิวพร สุวรรณศิริ, โศภิษฐ์ จันทสโร, อิสรี ยาเนตร

การศึกษานี้ประเมินความเหมาะสมของกระบวนการตรวจติดตามระดับยาในเลือด (Therapeutic drug monitoring, TDM) ของยา lithium เก็บข้อมูลแบบย้อนหลังโดยการทบทวนแฟ้มประวัติผู้ป่วยที่ได้รับการรักษาด้วยยา lithium และมีการสั่งทำ TDM ณ โรงพยาบาลเฉพาะทางโรคจิตเวช ระหว่างมกราคม พ.ศ. 2547 ถึง ตุลาคม พ.ศ. 2548 ประเมินความเหมาะสมของการทำ TDM 3 ประเด็น ได้แก่ (1) ข้อบ่งชี้ในการสั่งทำ (2) เวลาในการเก็บตัวอย่างเลือด และ (3) การนำข้อมูลระดับยามาพิจารณาร่วมกับข้อมูลการตอบสนองทางคลินิกในการตัดสินใจปรับ/เปลี่ยนขนาดยา โดยใช้เกณฑ์ที่ดัดแปลงจาก Morecambe Bay Shared Care Guideline ปี พ.ศ. 2546 จากตัวอย่างจำนวน 60 ราย ผู้ป่วยบางรายได้รับการทำ TDM มากกว่า 1 ครั้ง จึงได้ข้อมูลทั้งหมด 91 ครั้ง พบว่า การเจาะวัดระดับยามีข้อบ่งชี้เหมาะสมเป็นส่วนใหญ่ (72.5%) ได้แก่ วัดเมื่อเริ่มการรักษาหรือติดตามการรักษา (41.8%) สงสัยระดับยาอยู่ในช่วงที่เกิดพิษ 15.4% ประเมินความร่วมมือการใช้ยา 5.5% ประเมินหลังเปลี่ยนรูปแบบการให้ยา 5.5% และการรักษาไม่ได้ผล 4.4% แต่พบการตรวจวัดระดับยาเป็นประจำในผู้ป่วยในโดยไม่มีข้อบ่งชี้ 25 ครั้ง (27.5%) ซึ่งถือว่าไม่เหมาะสมและเกินจำเป็น การประเมินความเหมาะสมของเวลาในการเก็บตัวอย่างในผู้ป่วยนอกไม่มีบันทึกชัดเจนเกี่ยวกับความร่วมมือในการใช้ยา และมี 1 รายที่ขาดยามา 4 วัน ส่วนผู้ป่วยในมีการบันทึกข้อมูลต่าง ๆ อย่างชัดเจน และพบว่าเวลาเก็บตัวอย่างมีความเหมาะสมทั้ง 37 ครั้ง (40.6%) จากข้อมูลทั้งหมด มีการบันทึกระดับยาในเลือด 83 ครั้ง (91.2%) และในจำนวนนี้มีระดับยาอยู่นอกช่วงการรักษา 37 ครั้ง (44.6%) อย่างไรก็ตามเมื่อพิจารณาร่วมกับการตอบสนองทางคลินิกมีเพียง 12 ครั้งเท่านั้นที่ควรปรับรูปแบบการใช้ยา แต่แพทย์ได้ปรับเปลี่ยนขนาดยาในผู้ป่วยบางรายเท่านั้น เช่น ในผู้ป่วยที่ แพทย์สงสัยว่าเกิดอาการพิษเนื่องจากระดับยาสูง 14 ครั้ง มีระดับยาสูงกว่าช่วงการรักษา (> 1.2 mmol/L) 9 ครั้ง แต่แพทย์ได้ปรับลดขนาดยา 1 ครั้ง หยุดยา 3 ครั้ง และจ่ายยาในขนาดเดิม 5 ครั้ง ส่วนที่เหลืออีก 5 ครั้ง ผู้ป่วยมีระดับยาต่ำกว่าช่วงการรักษา (< 0.6 mmol/L) และแพทย์สั่งหยุดยา 3 ครั้ง และจ่ายยาแบบเดิม 2 ครั้ง ส่วนผู้ป่วยที่ผลการ รักษาไม่ดีและแพทย์สงสัยว่าระดับยาต่ำกว่าช่วงการรักษา จำนวน 4 ครั้งนั้น แพทย์ปรับเพิ่มขนาดยา 3 ครั้ง พบว่ามีเพียง 33 ครั้ง (36.3%) เท่านั้นที่การตรวจติดตามระดับยาในเลือดมีความเหมาะสมครบทั้ง 3 ประเด็น (ได้แก่ ข้อบ่งชี้ เวลาในการเก็บตัวอย่าง และการประยุกต์ข้อมูลระดับยาในเลือด) โดยสรุป ข้อบ่งชี้การสั่งตรวจวัดระดับยาในเลือดเหมาะสมเป็นส่วนใหญ่ แต่ควรงดสั่งเจาะเลือดเป็นประจำโดยไม่มีข้อบ่งชี้เพื่อลดค่าใช้จ่าย เนื่องจากบริการนี้มีต้นทุนค่อนข้างสูง การนำข้อมูลระดับยามาประยุกต์ร่วมกับการตอบสนองทางคลินิกเพื่อปรับเปลี่ยนการรักษายังไม่เกิดประโยชน์สูงสุดแก่ผู้ป่วย การสร้างแบบขอใช้บริการตรวจวัดระดับยาที่ระบุข้อบ่งชี้/เหตุผล ในการสั่งทำ บันทึกการใช้ยาของผู้ป่วย การแปลผลและการตัดสินใจทางคลินิกจะเพิ่มคุณภาพของบริการให้ดีขึ้นและลดค่าใช้จ่ายที่ไม่จำเป็น