A System for Drug Utilization Review in Ambulatory Care

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Background. It is more difficult to conduct drug utilization reviews in ambulatory care settings than in inpatient care settings. This is true for several reasons: it is harder to identify outpatients who are receiving specific medications; often there is less evidence on which to base clinical standards for drug use; and it is more difficult to ensure patient compliance with drug therapy.

Methods. This article describes a drug utilization review system designed to operate in ambulatory care clinics. The system consists of (1) a computerized database for efficient identification of patients who receive prescriptions for a specific medication, (2) clinic-wide consensus guidelines, (3) reminders in the medical record, (4) regular chart audits, and (5) feedback to physicians.

Results. Experience in monitoring the use of serum theophylline assays illustrates how this system can be used in an ambulatory care clinic. According to guidelines adopted in our clinic, overuse of assays is not a problem. The system of physician reminders and chart audits can help prevent underuse.

Conclusions. Despite the difficulties in conducting drug utilization reviews in the ambulatory setting, a system based on clinic-wide guidelines is feasible and should be an integral part of quality assurance programs.

Key words. Drug utilization; quality assurance, health care; theophylline. *J Fam Pract 1991; 32:607-612.*

Quality assurance methods were first developed to evaluate the care delivered in hospitals, where the severity of illnesses is greater and the financial expenditures per patient are higher than in ambulatory care. Accreditation and insurance organizations are now increasing the emphasis on assessing the quality of ambulatory care as well.[1] It is evident that quality-improvement programs will be integrated into the practice of medicine in all settings.

Although the principles are the same, conducting quality assurance procedures in ambulatory care is often more difficult than in inpatient care.[2,3] Palmer[1] has summarized a number of respects in which the assessment and assurance of the quality of ambulatory care is more difficult: (1) there is less evidence and expertise on which to base clinical standards; (2) the correction of deficiencies may be difficult if practitioners feel less subject to peer pressure; and (3) patient understanding and compliance are more likely to influence the effectiveness of care. Even identifying those patients who received a specific medication requires more effort when there are no central pharmacy records.

The purpose of this article is to describe a drug utilization review system designed to operate in an ambulatory care clinic. The system consists of (1) a computerized medication database, (2) clinic-wide consensus guidelines, (3) chart reminders, (4) regular chart audits, and (5) feedback to physicians. Our experience in monitoring the use of serum theophylline assays illustrates the operation of the system in a university-based family medicine residency training site where 15 physician faculty and 18 residents practice. Approximately 23,000 patient visits are made each year to the clinic.

Computerized Medication Database

Because it would have been impractical to audit the chart of every clinic patient each time a specific drug utilization review was performed, it was necessary to have a method for identifying those patients who took the medication to be reviewed. Laboratory test records can be used for this purpose when a drug is monitored using serum assays. Few drugs require such laboratory monitoring, however.

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Also, an audit in which a serum assay is the indicator will miss patients who have not been tested. To avoid these problems, a computerized medication database previously established by two of the authors (A.E. and R.S.) was used to record all of the medications prescribed for patients in the clinic.

A copy of every prescription was retained in the clinic. Information from the prescription including the date, patient's name, patient identification number, physician's name, and a specific medication code was entered into the database. The database was developed using the RBase System V (Microrim Inc, Bellevue, Wa) database manager; additional software was added to maximize the system's efficiency and to enhance its report-writing features. The database was stored on an IBM AT-compatible computer, which was located in the Family Medical Center for convenient access. The classification codes used to identify the medications were taken from a modified version of the American Hospital Formulary Service Therapeutic Classification provided by the Iowa Drug Information Service.* When conducting an audit, a list of the patients who received a prescription for the medication of interest during a specified period was produced.

Consensus Guidelines

Quality assurance studies involve comparing patient care data with specifications for the process of care. Remarkably few criteria for drug utilization in ambulatory care have been rigorously tested. For example, a patient who is hospitalized with a pulmonary problem and is receiving theophylline or aminophylline will obviously need to have a serum assay performed; but it is not obvious how frequently a serum assay should be performed for an outpatient who is asymptomatic. No studies of patient outcomes with testing intervals as long as 1 year have been reported.

One solution to the problem of inadequate data on which to base objective clinical guidelines is to conduct studies. Quality assurance programs in ambulatory care centers usually do not have the resources to perform research, however, and almost every drug utilization review would require another study. Instead it is often necessary to rely on clinical judgment to formulate guidelines. Because clinical judgment is based on personal opinion and the interpretation of available data, it is important to reach a consensus among the physicians in the clinic both about the need for guidelines for the particular aspect of care being reviewed and about what those guidelines should be. It is a fundamental principle of continuous quality improvement that physicians participate in the process.[4]

Some guidelines are developed for education and others for cost-effectiveness, such as to discourage the use of a new antibiotic when a less expensive alternative is adequate. Other guidelines are developed as a result of an adverse outcome, such as a patient having an anaphylactic reaction to a medication administered in the clinic. Often, a need for guidelines is apparent from chart audits. The development of guidelines involves the discussion of proposals by medical staff during quality assurance meetings. Relevant patient care data and evidence from the literature (when available) are presented and discussed until an agreement is reached.

Chart Reminders

Although chart reminders are not essential for evaluating drug use, several studies have suggested that they can improve prescribing performance and reduce oversight errors in managing medications.[3] A printed chart reminder is especially helpful for medications like theophylline because the drug dosing and the serum drug levels may be scattered throughout the chart, and the patient may have multiple, complicated medical problems. In such cases, a flow sheet in the patient chart can serve both as a reminder and as a convenient reference to patient data. Additional information such as medication interactions and dosage guidelines can be included on the flow chart.

Feedback to Physicians

Studies of attempts to improve prescribing behavior in primary care have recently been reviewed.[3] Several of these studies suggest that ongoing feedback can be effective in improving compliance with protocols. If a quality-improvement program is to provide education and have the support of participating physicians, the feedback to physicians must be given constructively rather than punitively.[4] Residents are especially interested in medical information relevant to decisions about their patients. If an error is due to oversight, a reminder is sufficient. If an error is due to lack of understanding or knowledge, a physician or pharmacist affiliated with the quality assurance program takes the opportunity to teach the relevant information to the resident in one-to-one encounters that emphasize continuous quality improvement.[4]

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An Example: Use of Serum Theophylline Assays

Background

A number of published studies, many of them in the pharmacy literature, have demonstrated that a large proportion of the theophylline assays ordered for hospitalized patients are either not indicated or incorrectly used.[5–12] There are similar problems in ambulatory settings, where serum theophylline levels are often not monitored correctly.[13–18] In one clinic, only 3 of 22 adult outpatients had a therapeutic serum level taken.[15] In a different study, 42 of 55 ambulatory patients who took theophylline regularly had no record of a serum level measurement taken during the preceding year.[14] Regular monitoring is important because of the narrow therapeutic range of theophylline and the limited usefulness of clinical information in predicting the need for a serum assay.[13,19–21]

These same concerns were raised in our clinic following a small audit of the charts of patients with a diagnosis of either chronic obstructive pulmonary disease or asthma who received theophylline prescriptions regularly. The review demonstrated that 5 of 18 patients adjusted their own dose as needed, and 4 others who received frequent care in the clinic had not had a serum assay performed for a period of 1 year or longer. It is also evident that management of theophylline dosing, monitoring, and potential drug interactions may be less than optimal when patients have multiple medical problems that complicate their care.

Problems with theophylline use may become more common as physicians become less familiar with it. As inflammation is now regarded as the underlying pathologic process in asthma, inhaled sympathomimetics and steroids have replaced the methylxanthines as the treatment of choice, both during acute exacerbations and for chronic maintenance therapy.[22,23] Similarly, for chronic obstructive pulmonary disease, the addition of intravenously administered aminophylline to other standard treatments for acute exacerbations contributed no additional benefits. Instead, inhaled sympathomimetics and anticholinergics are becoming the standard maintenance therapy.[23,24] Nonetheless, theophylline remains useful in the treatment of certain patients.[23–25]

Guidelines for Use of Serum Theophylline Assays

To provide information for physicians in the clinic and to develop clinic guidelines, the literature on theophylline utilization was reviewed. No clinical trials to determine the best interval between tests have been reported, so the optimum frequency for routine monitoring when patients have no acute indication is not known. Trough serum levels without a dose change are reasonably reproducible in observations lasting as long as several months for adults, while a downward trend in levels was observed in a pediatric population monitored at approximately 6- to 12-month intervals.[26,27] In one outpatient clinic and in a number of hospital wards, routine serum assays were judged to be overused.[5–12,28]

Hendeles and Weinberger suggest that in the absence of changes that can affect serum levels (specific concurrent drug therapy, altered smoking or dietary habits, prolonged fever, or variation in liver or cardiac function), a serum assay should be obtained at least once yearly for adults.[20,21] During rapid growth in childhood, more frequent monitoring is advised. Other indications for more frequent monitoring include suspected toxicity, questionable therapeutic response, or a recent dose change. During departmental quality assurance conferences, these recommendations were presented along with the results of a chart review of theophylline utilization. The recommendations of Hendeles and Weinberger were approved as guidelines for the clinic.

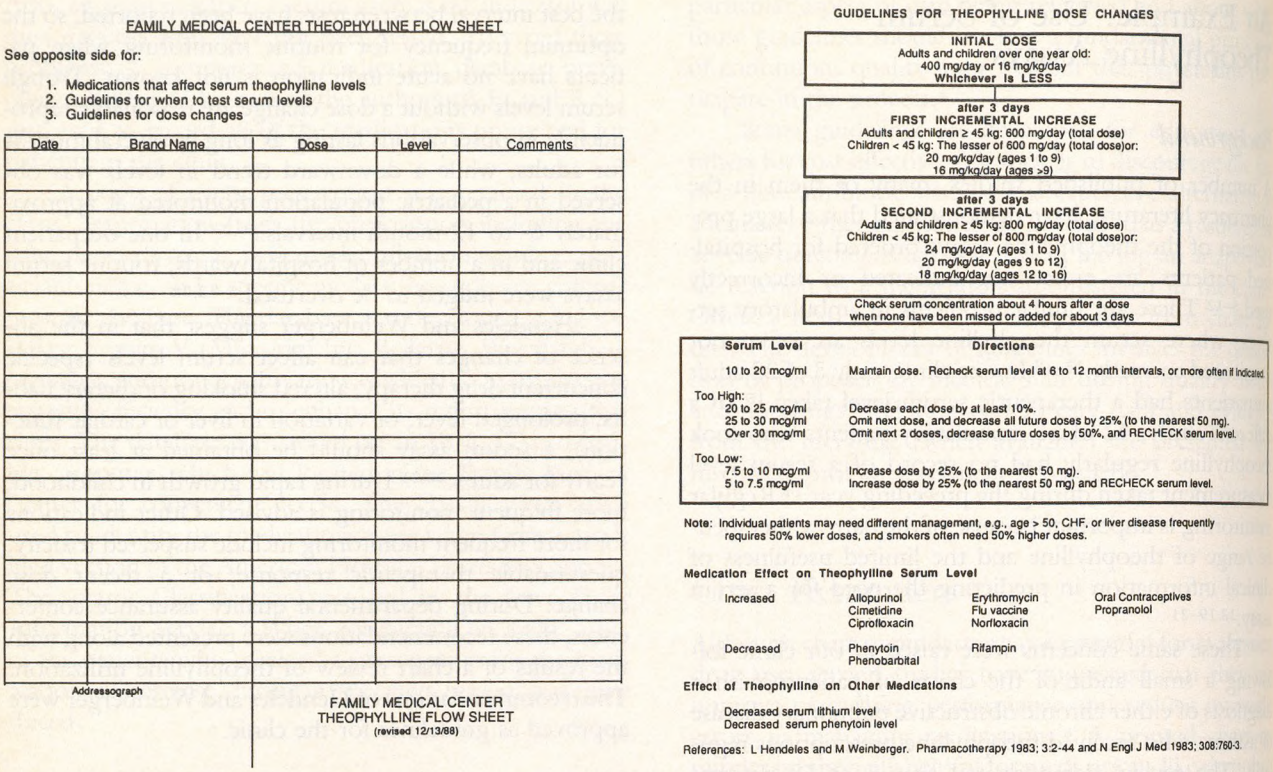
Chart Reminders

The theophylline flow sheet displayed in Figure 1 was designed to help clinicians find serum assay results in the medical record and to serve as an additional reminder of the need for regular monitoring. The protocols of Hendeles and Weinberger for initial doses, dose adjustments, indications for monitoring, and timing of serum assays are listed on the reverse side, along with a list of medications that can affect serum theophylline levels.[20,21]

Audit Results

A plan for continual monitoring and feedback was established. Many patients request theophylline prescription renewals by telephone. These occasions often present opportunities to review the patient's chart and inform the patient if a serum assay is indicated. In our clinic, a pharmacist usually performs this function, but in clinics where there is no pharmacist, a physician or a trained assistant can conduct the chart review using the clinic guidelines as criteria.

The first such review of indications, frequencies, and effects of serum theophylline assays in our clinic was performed in July 1990 for the preceding 12 months of care. The charts of all 29 patients who received prescriptions for theophylline during the first 6 months of 1990



FAMILY MEDICAL CENTER THEOPHYLLINE FLOW SHEET

See opposite side for:

1. Medications that affect serum theophylline levels
2. Guidelines for when to test serum levels
3. Guidelines for dose changes

Date	Brand Name	Dose	Level	Comments

Addressograph

FAMILY MEDICAL CENTER
THEOPHYLLINE FLOW SHEET
(revised 12/13/88)

GUIDELINES FOR THEOPHYLLINE DOSE CHANGES

INITIAL DOSE
Adults and children over one year old:
400 mg/day or 16 mg/kg/day
Whichever is LESS

after 3 days
FIRST INCREMENTAL INCREASE
Adults and children ≥ 45 kg: 600 mg/day (total dose)
Children < 45 kg: The lesser of 600 mg/day (total dose)or:
20 mg/kg/day (ages 1 to 9)
16 mg/kg/day (ages >9)

after 3 days
SECOND INCREMENTAL INCREASE
Adults and children ≥ 45 kg: 800 mg/day (total dose)
Children < 45 kg: The lesser of 800 mg/day (total dose)or:
24 mg/kg/day (ages 1 to 9)
20 mg/kg/day (ages 9 to 12)
18 mg/kg/day (ages 12 to 16)

Check serum concentration about 4 hours after a dose when none have been missed or added for about 3 days

Serum Level	Directions
10 to 20 mcg/ml	Maintain dose. Recheck serum level at 6 to 12 month intervals, or more often if indicated.
Too High:	
20 to 25 mcg/ml	Decrease each dose by at least 10%.
25 to 30 mcg/ml	Omit next dose, and decrease all future doses by 25% (to the nearest 50 mg).
Over 30 mcg/ml	Omit next 2 doses, decrease future doses by 50%, and RECHECK serum level.
Too Low:	
7.5 to 10 mcg/ml	Increase dose by 25% (to the nearest 50 mg).
5 to 7.5 mcg/ml	Increase dose by 25% (to the nearest 50 mg) and RECHECK serum level.

Note: Individual patients may need different management, e.g., age > 50, CHF, or liver disease frequently requires 50% lower doses, and smokers often need 50% higher doses.

Medication Effect on Theophylline Serum Level

Increased	Allopurinol Cimetidine Ciprofloxacin	Erythromycin Flu vaccine Norfloxacin	Oral Contraceptives Propranolol
Decreased	Phenytoin Phenobarbital	Rifampin	

Effect of Theophylline on Other Medications

Decreased serum lithium level
Decreased serum phenytoin level

References: L Hendeles and M Weinberger. Pharmacotherapy 1983; 3:2-44 and N Engl J Med 1983; 308:760-3.

Figure 1. Left: A flow sheet to help clinicians find serum theophylline assay results. Right: On reverse side of flow sheet are the guidelines for theophylline dose changes and monitoring directions. Reprinted, by permission of *The New England Journal of Medicine*, 308: 760–4, 1983.

were reviewed. Four patients were excluded from subsequent analysis because the prescription for theophylline was their first, and they either did not continue the medication or did not require a refill during the audit period.

The distribution of ages of the 25 patients who met the entry criteria ranged from 3 to 88 years, with a mean of 48 years (SD = 21). Of the 25 patients, 20 requested a refill by telephone at least once in 6 months; thus, 5 of the patients' charts were not brought to the attention of a clinical pharmacist. At the time they requested prescription refills by telephone, four patients had not had a serum assay within the previous year; therefore they were advised to return for testing. One of these patients was tested, one did not return to the clinic, and two discontinued the medication before returning to the clinic.

One patient who had received all of his prescription renewals in the clinic did not have a serum assay performed during the audit period. When the physician called the patient, it became apparent that the patient had misunderstood the instructions for taking the medication and had been taking a subtherapeutic dose.

Table 1 displays the frequency of each indication for testing. Of the 25 patients included in the audit, 20 had a record of at least one serum assay. Of the 30 assays performed, 12 (40%) were for routine monitoring. Only one patient had two routine assays performed, and these were 10 months apart. Thus, in our clinic, where discus-

Table 1. Indications for Serum Theophylline Assays (N = 30) Ordered for Each Patient During 12-Month Audit Period

		Indication for Assay			
Number of Assays per Patient	Number of Patients	Routine Monitor	Suspect Toxicity	Worse Symptoms	Dose Change
0	5	—	—	—	—
1	13	7	1	3	2
2	4	2	0	3	3
3	3	3	0	3	3
Totals	25	12	1	9	8

sion of the costs of medical care is increasingly common, overuse was not judged to be a problem.

Of the 12 serum levels obtained for routine monitoring, one was less than 27.5 μmol/L (5.0 mg/L), four were between 27.5 and 55 μmol/L (5.0 to 10.0 mg/L), four were in the commonly accepted therapeutic range of 55 to 110 μmol/L (10.0 to 20.0 mg/L), and three were between 110 and 121 μmol/L (20.0 to 22.0 mg/L).

Actions taken as a result of the 30 serum levels were also audited. Dose changes were recommended for both of the patients with serum theophylline levels of less then 27.5 μmol/L (5.0 mg/L), for two of the nine with levels between 27.5 and 55 μmol/L (5.0 to 10.0 mg/L), and for one of the four with levels between 110 and 121 μmol/L (20.0 to 22.0 mg/L). No dose changes were recommended for the 15 patients with levels in the therapeutic range of 55 to 110 μmol/L (10.0 to 20.0 mg/L). Others have noted that dose changes are made less often for patients with a low serum level than for those with a high serum level.[18] There is debate about whether the acceptable therapeutic limit of 55 μmol/L (10 mg/L) should be lowered to 27.5 μmol/L (5 mg/L).[16,28] Hendeles and Weinberger recommend increasing the dose if the serum theophylline level is lower than 55 μmol/L (10 mg/L).[20,21] Lower levels have the potential benefit of reduced side effects, but they also have the potential risk of suboptimal therapy.

Discussion

Drug therapy is the most common treatment prescribed by physicians, so it is reasonable for every quality assurance program to include a system for periodic audits of medication use.[3] The drug-utilization review system described here is designed to operate in ambulatory care clinics. The clinic medication database facilitates efficient retrieval of patient data, and the procedures for establishing clinic-wide consensus guidelines make use of what limited evidence is available.

Unfortunately, evidence on which to base clinical standards in ambulatory care is limited, and quality assurance programs usually do not have resources to perform research on clinical effectiveness. The example of a utilization review of theophylline assays described here illustrates that in our family practice clinic, which has 23,000 patient visits per year, the number of patients taking theophylline is too small to conduct a definitive study of patient outcomes including controls. Yet, problems with theophylline use have been reported previously, including those recently receiving national publicity, and they may occur more frequently in the future as physicians have less experience prescribing the drug.[13–18,29]

The quality assurance needs of individual clinics can differ. The theophylline serum assay reviews in our clinic and those of at least one other clinic demonstrated underuse of testing.[14] In another clinic, where larger numbers of patients take theophylline, overuse of testing was documented.[28] These differences illustrate the importance of establishing guidelines that meet the needs of the clinic where they will be applied.

It is also important to emphasize that guidelines are not rules or standards. Physicians are free to use their judgment in the management of individual patients. The participatory process of reviewing the available evidence and reaching a consensus on guidelines is intended to assist physicians in making decisions, not to make the choices for them. It is expected, however, that the physician's reasons for not following accepted guidelines will be summarized in the patient chart to facilitate the quality assurance process.

The fundamental principles used in designing the drug utilization review system described here are to link quality assurance with continuing education and to conduct the program with the explicit objective of continuous quality improvement, rather than the punitive approach of "quality by inspection."[4]

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