Polypharmacy: A Case Report and New Protocol for Management

R. David Lee, MD

Background: Polypharmacy is an important issue in primary care, yet few data are available concerning its prevalence, complications, and management in clinical medicine. The following case illustrates the clinical perils of polypharmacy and serves as a point for critical discussion.

Methods: MEDLINE was searched, using the key word “polypharmacy,” from 1994 to the present. A case report of polypharmacy is described, and a novel protocol for the management of polypharmacy is proposed.

Results: Polypharmacy can lead to unnecessary expense, wasted time, and embarrassment on the part of the patient and confusion and mismanagement on the part of the physician. The literature reveals controversy surrounding the definition of polypharmacy and reflects the considerable morbidity and expense associated with polypharmacy. Finally, the SAIL protocol shows that physicians need to keep in mind simplicity, adverse effects, indications, and a precise list of all medications to manage appropriately a patient's drug regimen.

Conclusions: Polypharmacy is associated with morbidity and iatrogenic complications. The SAIL protocol can be a useful tool in the management of this entity. More research needs to be done on the prevalence, complications, and management of polypharmacy.

Polypharmacy is a major problem in clinical practice, yet clinically relevant data regarding its prevalence, complications, and treatment are scarce. Even the definition of polypharmacy is controversial and varies from study to study, which further complicates the translation of research results into useful information for the practicing primary care physician.

Methods
Using the key word “polypharmacy,” the medical literature was searched through MEDLINE for reports of polypharmacy and to review definitions, possible complications, and interventions. A case report describes a patient in whom polypharmacy led to misdiagnosis, unnecessary testing, and inappropriate treatment. Finally, a protocol for appropriate prescribing based on the SAIL acronym is proposed.

Case Report
A 67-year-old woman attended a family practice office for treatment of refractory hypertension. She had a medical history of high blood pressure, enlarged heart, and gout. Records from her previous physician did not further clarify her history. Her medications included digoxin 0.25 mg daily, furosemide 40 mg daily, potassium chloride 10 mEq twice daily, isosorbide dinitrate 40 mg daily, isradipine 2.5 mg daily, and allopurinol 300 mg as needed for gout.

She had no physical complaints and no unusual findings when questioned. Her last exacerbation of gout had been several years earlier. She was a retired nurses’ aide, had never smoked, and did not drink alcohol. Her family history was notable only for hypertension in her mother.

During a complete physical examination, her blood pressure was 154/94 mmHg, pulse 80 beats per minute, respiratory rate 22/min, and temperature of 36.2°C. Head and neck examination revealed A-V nicking on fundoscopy. Findings of the remainder of the physical examination were normal. Trichomonas infection was found incidentally on Papanicolaou smear and treated with a single 2-g dose of metronidazole.

Chemistry values included sodium 144 mEq/L, potassium 3.7 mEq/L, blood urea nitrogen 15 mg/dL, creatinine 1.0 mg/dL, glucose 420 mg/dL, and uric acid 7.9 mg/dL. Her cholesterol level was 188 mg/dL with a low-density lipoprotein level of
118 mg/dL and a high-density lipoprotein level of 35 mg/dL. Complete blood count, thyroid function, and hepatic function were normal. Digoxin level was 0.8 μg/L. Electrocardiographic findings were normal.

Diabetes mellitus was diagnosed and treated with metformin 500 mg twice daily and glyburide 5 mg twice daily with normoglycemic results.

Further work-up for secondary causes of hypertension, including a renal scan using captopril, urine screening for pheochromocytoma, and an echocardiogram, was negative. A cardiologist and a nephrologist were consulted, but their recommendations did not result in improved control of her hypertension. Several more antihypertensive medications were added to her previous medication regimen and titrated to the following doses: isradipine 5 mg twice daily, captopril 25 mg three times daily, lisinopril 10 mg twice daily, clonidine 0.4 mg in the mornings and 0.2 mg in the evenings, metoprolol 50 mg twice daily, doxazosin 4 mg daily, and sustained-release verapamil 240 mg daily. The clonidine was eventually withdrawn gradually and discontinued because of untoward side effects.

The patient’s blood pressure varied markedly between office visits, ranging from 130/80 mmHg to 194/118 mmHg. This lability was noted by various examiners and did not depend on whether the patient was examined in the office or at her home by a home health nurse or a neighbor. Also of interest was that although her blood glucose levels obtained in the office were between 80 and 100 mg/dL, her glycohemoglobin level was consistently between 8.0 and 9.0 percent. When questioned about medication compliance on several occasions, the patient always appeared to be sincere in her efforts to manage her health and, in fact, missed only 2 of 38 appointments during this time. She was insured through Medicare and Medicaid, and it was assumed that her prescriptions were covered services.

After nearly 3 years of evaluation and treatment for refractory hypertension, she confided to a physician that her prescriptions cost more than $400 a month, and her sole source of monthly income was a Social Security check for $600! Prescription costs were not covered by her insurance carriers. She admitted tearfully that she was embarrassed about not being able to pay for her medications and would rotate them so that she would take one pill for several days in a row, then switch to another. In this way, she would be able to take all of her prescriptions while making each last longer. For example, on the days leading up to a scheduled blood glucose check, she would faithfully take her hypoglycemic agents but afterward would start taking another medication. Switching medications accounted for her normal blood glucose but elevated glycohemoglobin levels during office visits and her fluctuating blood pressure readings.

All medications except glyburide 5 mg once daily were discontinued, and her antihypertensive medications were then resumed after obtaining a baseline blood pressure of 150/98 mmHg. The patient’s blood pressure was finally stabilized on a daily combination of 5 mg of amlodipine/10 mg of benzapril and 4 mg of doxazosin. Upjohn is currently supplying this patient with glyburide (Micronase®), Ciba is supplying her with amldopine/benazepril (Lotrel 5/10®), and Pfizer is supplying her with doxazosin (Cardura®) through their respective indigent programs. The patient’s diabetes and hypertension both appear to be well-controlled. Her most recent blood pressure was 122/80 mmHg, and her glycohemoglobin was 7.2 percent.

Discussion
Although the above case is extreme, it illustrates several issues that the primary care physician must consider when prescribing multiple medications for a patient (Table 1). Polypharmacy is an iatrogenic condition, and because of a delayed diagnosis, this patient had to deal not only with the expense of superfluous medications but also the time lost to her appointments, tests, and referrals, in addition to undue embarrassment and guilt about her financial situation. Additionally, her complex regimen led to two physician-prescribing errors, which were later discovered and documented in the chart. There were also multiple errors made when transcribing her medication list from visit to visit, which were not noticed by the prescribing physicians. In summary, this case illustrates how polypharmacy placed an unwarranted social burden on a patient who was trying to be responsible for her health and how it also led to mismanagement of her care by physicians.

Polypharmacy in its strictest sense is the concomitant use of many drugs. In clinical practice,
Table 1. Clinical Profile of Patient Before and After Diagnosis of Polypharmacy.

<table>
<thead>
<tr>
<th>Clinical Markers</th>
<th>Clinical Profile Before Diagnosis</th>
<th>Clinical Profile After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medications</td>
<td>Allopurinol 300 mg as needed</td>
<td>Amlodipine 5 mg/benazepril 10 mg qd</td>
</tr>
<tr>
<td></td>
<td>Captopril 25 mg tid</td>
<td>Doxazosin 4 mg qd</td>
</tr>
<tr>
<td></td>
<td>Clonidine 0.4 mg each morning, 0.2 mg every evening*</td>
<td>Glyburide 5 mg qd</td>
</tr>
<tr>
<td></td>
<td>Digoxin 0.25 mg qd</td>
<td></td>
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<tr>
<td></td>
<td>Doxazosin 4 mg qd</td>
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<tr>
<td></td>
<td>Furosemide 40 mg qd</td>
<td></td>
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<tr>
<td></td>
<td>Glyburide 5 mg bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Isosorbide dinitrate 40 mg qd</td>
<td></td>
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<tr>
<td></td>
<td>Isradipine 5 mg bid</td>
<td></td>
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<td></td>
<td>Lisinopril 10 mg bid</td>
<td></td>
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<tr>
<td></td>
<td>Metformin 500 mg bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metoprolol 50 mg bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Potassium chloride 10 mEq bid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Verapamil 240 mg qd</td>
<td></td>
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<tr>
<td>Mean blood pressure</td>
<td>Systolic, 149 mmHg</td>
<td>Systolic, 130 mmHg</td>
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<tr>
<td></td>
<td>Diastolic, 95 mmHg</td>
<td>Diastolic, 82 mmHg</td>
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<tr>
<td>Referrals</td>
<td>Cardiologist</td>
<td>Annual ophthalmologic screening</td>
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<td></td>
<td>Nephrologist</td>
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<td>Laboratory studies</td>
<td>Comprehensive chemistry panel</td>
<td>Routine health maintenance only</td>
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<tr>
<td></td>
<td>Complete blood count</td>
<td></td>
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<tr>
<td></td>
<td>Thyroid function panel</td>
<td></td>
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<tr>
<td></td>
<td>Digoxin level</td>
<td></td>
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<tr>
<td></td>
<td>Glycohemoglobin</td>
<td></td>
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<tr>
<td></td>
<td>Urine pheochromocytoma screening</td>
<td></td>
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<tr>
<td>Other studies</td>
<td>Electrocardiogram</td>
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<td></td>
<td>Echocardiogram</td>
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<tr>
<td></td>
<td>Captopril renal scan</td>
<td></td>
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<tr>
<td>Average frequency of appointments</td>
<td>Every 21.6 d for 3 y plus multiple physician-initiated home nursing visits</td>
<td>Scheduled for every 3-6 mo</td>
</tr>
</tbody>
</table>

*Discontinued because of side effects.

however, polypharmacy implies the prescribing of excessive medication. There are two definitions for polypharmacy in the literature in terms of what is excessive in one's drug regimen.

One definition focuses only on the number of drugs the patient is taking. The authors disagree, however, on the number of drugs and whether to include as-needed medications, over-the-counter drugs, or herbal and alternative medications. Polypharmacy has been variously defined as the concomitant use of more than 2 drugs, 4 drugs, 5 drugs, 6 drugs and 10 drugs.

The other way to define polypharmacy is to focus only on the clinical indications and effects of a given drug regimen, regardless of the number of drugs used. Polypharmacy would therefore mean that more medications are used or prescribed than are clinically indicated. This broader definition, while making outcomes research on polypharmacy logistically more difficult, allows for an individualized approach to a patient's drug regimen. For example, a patient who has suffered a myocardial infarction might be discharged from the hospital with prescriptions for aspirin, a nitrate, a β-blocker, an angiotensin-converting enzyme (ACE) inhibitor, and a lipid-lowering agent. Although the patient is taking five medications, this regimen would not be considered polypharmacy because each drug is clinically necessary, and the regimen is associated with improved survival. Cancer, congestive heart failure, diabetes mellitus, and the acquired immune deficiency syndrome are
Table 2. Reported Complications of Polypharmacy.

- Increased total medical expenses
- Increased incidence of adverse drug effects
- Decreased patient compliance
- Decreased social activity
- Increased incidence of depression
- Diminished cognition
- Increased incidence of eventual nursing home placement
- Increased prescribing errors

diseases for which prescribing multiple drugs concomitantly is associated with decreased morbidity and mortality. On the other hand, a patient who takes only digoxin would be considered to have polypharmacy if there were no indication for this prescription.

Polypharmacy led to serious complications in the patient described and has been associated with an increase in morbidity as well (Table 2). Hamdy et al. concluded that polypharmacy was associated with an increase in a patient's total medical expense, a decrease in patient compliance, and an increase in the incidence of adverse drug effects. Burns et al. found decreased social activity, increased incidence of depression, and decreased cognition in patients with polypharmacy. Satish et al. concluded that polypharmacy in the elderly is an independent risk factor for eventual nursing home placement. Carlson reported an increased incidence of prescribing errors on the part of the clinicians whose patients had polypharmacy.

SAIL: A New Protocol for the Management of Polypharmacy

Polypharmacy is associated with adverse complications and is frequently iatrogenic. The precise number of drugs the patient is taking appears to be less important than the clinician's ability to relate the use of each drug to the patient's medical, social, and economic circumstances. It is imperative that physicians recognize and manage polypharmacy aggressively.

It is with the above in mind that I have developed the SAIL protocol for appropriate prescribing (Table 3). This mnemonic is intended to help physicians minimize polypharmacy in their clinical practice. Simple drug regimens can usually be achieved by prescribing drugs that can be taken once daily and by changing to a single combination pill when adding a second drug. Although the direct cost of such a regimen might be higher in the short-term, the potential costs of long-term polypharmacy must be weighed when considering the economics of a particular regimen. The physician must also possess a thorough knowledge of the adverse effects of all drugs the patient is taking, including the side effects of a drug as well as its interactions with other drugs. The indication for each drug the patient is taking must be clearly understood. Each drug should have a well-defined therapeutic goal and must achieve the desired goal or be eliminated from the patient's medication list. Finally, the physician and the patient both should have an accurate and current list of the medications. This list must include all prescriptions, over-the-counter medications, as-needed medications, and herbs and other alternative medicines.

Although the SAIL protocol has not yet been tested in clinical practice, its application in this particular case shows how it can be effective in managing polypharmacy. The patient's regimen was simplified by structuring her drug regimen to include only medicines that are taken once daily. Additionally, prescribing a combination drug amlopidine/benzapril rather than a calcium channel blocker plus an ACE inhibitor decreases the total number of pills the patient has to take. Drugs with adverse effects, such as clonidine, and drugs with potential adverse effects, such as digoxin and allopurinol, were discontinued. Several drugs that had no indication, such as digoxin, allopurinol, and isosorbide dinitrate, were discontinued. Fi-
nally, prescribing errors occurred because clinicians had not maintained an accurate, up-to-date list of this patient's medications, as evidenced by the patient taking two ACE inhibitors simultaneously. Reducing the list of medicines to three pills a day has made her drug regimen more manageable both for the patient and her physicians. In this patient, the SAIL protocol managed polypharmacy effectively and reduced its complications, morbidity, and cost.

Conclusion
Polypharmacy can be defined as the administration of pharmacological agents for which there is no indication. Such medication misuse is prevalent in clinical practice and is associated with high morbidity and high economic costs. The SAIL protocol can help physicians reduce polypharmacy in their own practice. More research is needed in the areas of prevalence, complications, and treatment of this problem.

References

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