Guidelines for Hospitalization for Chemotherapy

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ABSTRACT
Administration of cancer chemotherapeutic agents has shifted from the hospital to outpatient settings, usually the oncologist’s office. Hospitalization for chemotherapy is now limited to specific situations, reflecting the need for prolonged direct observation, prevention or treatment of anticipated or real side effects, the use of special facilities and the minimization of certain treatment risks which cannot be effectively dealt with in an outpatient setting. New financial guidelines also have a significant impact on the location of chemotherapy administration. Outpatient chemotherapy has the advantages of allowing safe, easy drug administration, respecting the patient’s wish to avoid hospitalization and providing a familiar facility, which enhances the patient’s physical comfort and psychological well-being. The oncologist has direct and immediate control of drug administration, assistance is immediately available if problems arise, care is less expensive than inpatient care and overnight stay can be avoided. It also facilitates monitoring and control of treatment costs and allows treatment to be administered at the patient’s convenience. Specific circumstances which justify hospitalization for chemotherapy, as detailed in Table 1, include: higher dosage cisplatin, special procedure chemotherapy, induction therapy for acute leukemia, high-dosage chemotherapy with or without stem cell/bone marrow transplantation, severely emetogenic chemotherapy, ifosfamide therapy, combination radiation therapy plus chemotherapy programs, coexistent medical problems (comorbidities), complex chemotherapy programs, the initial dose of chemotherapy while hospitalized for diagnosis of cancer, a scheduled dose of chemotherapy occurring during hospitalization for an unrelated problem, special measures required to prevent significant side effects, high-dose methotrexate protocols, intraperitoneal chemotherapy, certain investigational treatment protocols, and if chemotherapy administration is mandatory despite comorbidities that would ordinarily delay or contraindicate chemotherapy.

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GUIDELINES FOR HOSPITALIZATION FOR CHEMOTHERAPY
In the past, chemotherapy was typically administered in a hospital, even for relatively simple and straightforward treatment programs devoid of major immediate risks and side effects. Today, however, treatment has shifted to outpatient settings, usually the oncologist’s office, but sometimes also to hospital outpatient facilities or the home. Now, hospital admission for chemotherapy administration is limited to specific circumstances delineated by widely accepted practice guidelines which evolved out of this important and necessary change in practice setting. These guidelines currently exist as the “conventional wisdom” of practicing oncologists, but have not been delineated in a standardized written format.

These practice guidelines for hospitalization reflect such clinical parameters as the need for prolonged direct observation, prevention/treatment of anticipated or real side effects, or the use of facilities and the minimization of certain treatment risks which cannot be effectively dealt with in an outpatient setting. A new element has been introduced into the practice guidelines by managed care organizations: the usually significantly higher cost of such chemotherapy administration in the hospital compared to an outpatient facility. Thus, these guidelines reflect not only clinical and pharmacologic parameters, but also financial ones. The choice of an outpatient setting for chemotherapy administration is closely related to rates of drug reimbursement and the associated need for authorization from third-party payers.

Although practice guidelines primarily ensure delivery of effective quality care, they also have a financial component. Health care payers are reluctant to authorize or pay for chemotherapy treatments given in the hospital that could have been given in an outpatient setting.

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<th>CIRCUMSTANCE AND RATIONALE:</th>
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<tr>
<td><strong>1 Higher-dosage cisplatin</strong> (75 mg/m² or more). The higher dosages require prolonged i.v. fluids, as well as extended monitoring of intake and output. Additional medications such as i.v. furosemide may be needed, as well as frequent laboratory studies. Lower dosages can be given in an outpatient setting, since the amount of required pre- and post-treatment hydration can be accomplished over four to six hours.</td>
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<td><strong>2 “Special procedure” chemotherapy.</strong> This includes intra-arterial chemotherapy and chemo-embolization (usually via the hepatic artery). Such procedures require several days’ close and continuous observation.</td>
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<td><strong>3 Induction therapy for acute leukemia.</strong> Such patients are generally quite ill, require multiple i.v. chemotherapeutic agents, become more ill during and after treatment, require multiple transfusions of blood products, as well as i.v. antibiotics and other agents, and require prolonged continuous observation.</td>
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<td><strong>4 Stem cell/bone marrow transplantation with high-dose chemotherapy.</strong> Hospitalization requirement is usually stated in the protocol. A newer trend in some centers is to administer such chemotherapy as an outpatient, and then admit the patient during the period of blood count nadirs or during periods of complications.</td>
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<td><strong>5 “High-dosage chemotherapy,”</strong> without bone marrow or stem cell support. In some cases, chemotherapy dosages are significantly increased (for example, high-dosage cyclophosphamide in breast cancer or sarcomas). These patients may require close and prolonged observation.</td>
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<td><strong>6 Severely emetogenic chemotherapy.</strong> Outpatient antiemetic therapy was ineffective on a prior occasion in treating severe chemotherapy-related nausea and vomiting. Subsequent treatment should be given in the hospital where frequent doses of multiple i.v. antinausea medications and i.v. fluids can be administered for 24 hours or longer to prevent resulting dehydration. Sometimes combination chemotherapy programs include agents which given individually are not problematic, but which may cause severe nausea if given together. Severe nausea also occurs with certain single agents, such as dacarbazine, nitrogen mustard or streptozocin, and hospitalization is needed in cases where prior outpatient use of antinausea drugs has been unsuccessful in preventing this side effect.</td>
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<td><strong>7 Ifosfamide therapy.</strong> This anticancer drug produces severe bladder toxicity unless a uroprotective agent, Mesna®, is given simultaneously. Both drugs are intravenous, but the half-life of Ifosfamide is much longer than the half-life of Mesna®, which needs to be continued for perhaps 12 hours after the Ifosfamide ends. Although some oncologists give patients Mesna® to self-administer at home 6 and 12 hours later via an indwelling venous access line, in some cases hospitalization is required to be sure the Mesna® is given at the appropriate time, perhaps with i.v. fluids and nausea medications as well.</td>
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<td><strong>8 Combination radiation therapy + chemotherapy programs</strong> in which unusual circumstances apply. Examples would be severe nausea and vomiting, need for continuous i.v. hydration and significant immobility due to weakness and/or pain.</td>
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<td><strong>9 Coexistent medical problems (comorbidities) requiring separate and continuous observation, evaluation and treatment.</strong> Examples would include pulmonary or cardiac disease, diabetes and metabolic problems.</td>
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<td><strong>10 Complex chemotherapy programs</strong> requiring more than 6 hours of continuous observation and drug administration. An example would be the “eight drugs in one day” protocol for brain tumors.</td>
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<td><strong>11 Initial dose of chemotherapy while hospitalized.</strong> When cancer has just been diagnosed, it may be important to begin therapy immediately. The initial dose of conventional chemotherapy (otherwise usually given in the office) may be administered shortly before the last day of hospitalization.</td>
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Conforming with guidelines will tend to stabilize the personal income of the oncologist, but even more important, can satisfy the concerns of managed health care organizations about the cost and quality of care provided. Given the global changes occurring in our country’s medical care patterns, the actual impact of chemotherapy practice guidelines on overall quality and cost of cancer care is yet to be seen. This article provides a perspective on changing patterns in the location of chemotherapy administration.

ADVANTAGES OF OUTPATIENT CHEMOTHERAPY

- Allows safe, easy drug administration;
- Respects patient’s wish to avoid hospitalization;
- Familiar and “safe” facility enhances patient’s physical comfort and psychological well-being;
- Oncologist has direct and immediate control of drug administration;
- Assistance immediately available if problems arise;
- Less expensive than inpatient care;
- Overnight stay avoided (anti-nausea medications and other agents such as Mesna® can be given at home via central catheters);
- Facilitates “tracking” and control of treatment costs; and
- Treatment can be administered at patient’s convenience.

Examples of chemotherapy programs formerly requiring hospitalization, but for which hospitalization is ordinarily not required, include:

- Five-day infusions of 5-FU. These are now given by infusion pump devices via an indwelling central venous catheter;
- Cisplatin in dosages of 75 mg/m² or less;
- Prolonged i.v. infusions of chemotherapy drugs not requiring special observations or precautions. These are managed with indwelling venous access devices and daily office visits to change the cartridge/syringe.

Although this list appears to be up to date and accurate at this time, evolution of care patterns and standards of care will occur continually as newer drugs and treatment programs evolve. Some items will be changed and others will be added. Equally important will be the legal, fiscal and contractual guidelines for chemotherapy administration. Lists similar to the above are in widespread use by third-party payers, and are used by reviewing physicians (often retrospectively) to determine whether inpatient chemotherapy is/was appropriate.

THEN AND NOW

Before medical oncology emerged as a major specialty and payment systems changed, chemotherapy generally was...
administered in the hospital. More complex or toxic programs were given on an inpatient basis, with simpler drug programs administered in outpatient clinics. Certain relatively nontoxic agents, such as 5-fluorouracil (5-FU), were administered in the physician’s office, often by a nurse, but sometimes by the physician. Hospital inpatient oncology units became treatment facilities of choice, and drug administration protocols and standing orders came into common use.

All this changed when administration of complex chemotherapy programs in physicians’ offices or other outpatient facilities became possible. Under close supervision, highly skilled oncology nurses can administer most chemotherapy programs over no more than several hours. Development of indwelling and central venous access catheters was a key component in this transition. “Searching” for a vein is a thing of the past; access is almost guaranteed and patients can give themselves antiemetics or other medications at home before or after chemotherapy. Complications and problems are few and easily solved. In fact, in this setting, unlike inpatient hospital facilities, a supervising oncologist is immediately available to answer questions, change antinausea medications, discuss side effects or handle untoward reactions. Regimens once given on an outpatient basis and now available for office administration include five-day infusions of 5-FU delivered by infusion pump and indwelling central venous catheter, cisplatin in dosages of 75 mg/m² or less, and prolonged i.v. infusions of chemotherapy drugs that do not require unusual observation or precautions requiring overnight hospitalization. Such programs are managed with indwelling venous access devices and daily office visits to change the cartridge/syringe containing chemotherapy.

Many oncologists have created elaborate and impressive outpatient chemotherapy facilities, including drug-mixing stations (usually with vacuum hoods to protect personnel and fulfill legal requirements), comfortable drug-administration chairs, partitions to increase privacy, and distractions such as television, music and educational video programs. Oncology nurses expertly manage these facilities and teach patients about their illness and treatment.

**OTHER TREATMENT SETTINGS**

Chemotherapy can also be given in the patient’s home, according to standardized protocols and procedures, by oncology nurses under the direction of the attending oncologist. This setting is useful for treating patients who find it difficult to travel to the office.

In academic centers, patterns of chemotherapy administration should be similar to those seen in private oncologists’ offices. However, the ways in which third-party payers judge these facilities often are different. Third-party payers tend to apply the same set of standards to academic oncology centers with established standards of excellence but are less vigorous about reviewing them. In academic centers, some aspects of patient management are delegated to oncology fellows, making their outpatient treatment clinics conceptually analogous to the oncologist’s private office treatment area. Allowing fellows to observe or participate in managed care treatment negotiations is especially vital these days, because they will be in our shoes 10 and 20 years from now. Some academic centers have become leaders in the new reimbursement and treatment environment, for example, converting most of the in-hospital days connected with stem cell transplantation associated with high-dose chemotherapy to outpatient days and reserving the in-hospital time for blood count nadirs and complications.

**PAYMENT PATTERNS**

Superimposed on these developments has been a profound change in payment patterns. Third-party payers and medical review organizations have created their own guidelines for chemotherapy administration. Oncologists must adhere to diverse payers’ and review organizations’ guidelines or risk adversely affecting their reimbursement. These guidelines for reimbursement are continually changing, as with paclitaxel, for example, and may differ with different payers. We need to be continuously aware of such changing guidelines. Medicare regulations for diagnosis-related groups also specify certain requirements for inpatient chemotherapy, providing only a relatively small number of payment patterns regardless of the regimen’s duration and complexity. Managed care programs have profoundly affected health care delivery systems, requiring the practicing oncologist to promote cost efficiency by providing quality care at an “affordable” cost. Indeed, the cost of chemotherapy must conform to certain guidelines that either already exist or need to be planned and formulated by the oncologist, who usually has only scant financial drug usage/actuarial information on which to base decisions.

Clearly, the oncologist has more direct and effective control of chemotherapy if it is given in the office instead of the hospital, whether inpatient or outpatient. Deciding how and where to administer chemotherapy is even more significant in light of capitation, under which reimbursement for oncology care is specified by contract. The oncologist is paid a certain rate for each individual covered, not each one who becomes ill and needs care. Unlike the former fee for service pattern, this system puts the oncologist at financial risk for all care given under the capitated contract.
CONCLUSION

Many new factors influence cancer care delivery, especially planning and formulation of contracts and facilities. All of us have participated and need to continue to participate in this “revolution” in chemotherapy delivery. Managed care organizations’ guidelines sometimes call for only standard or “single-course” programs for neoplasms that do not respond well to treatment, such as pancreatic, gastric, non-small cell lung and even colon cancer. When the results anticipated are similar, an oncologist may be obliged to choose the least expensive of several suitable treatment protocols with widely differing costs.

Excessive or inappropriate use of new products such as colony-stimulating factors and expensive antinausea medications will have a profound impact on the cost of cancer care. Under a capitated program, for example, such excess or unnecessary usage will significantly impact an oncologist’s income. He or she therefore must carefully weigh each therapeutic decision as to cost and quality, appropriateness and effectiveness of care. The wrong choice will create havoc.

Patients are entitled to high-quality, appropriate care. However, it is economically impossible to deliver every possible type of treatment to every patient. In addition to all the technical, scientific and psychological reasons, it behooves us all to plan our care patterns rather than await retrospective review, and perhaps, payment denial.

Note: Dr. Dollinger is a consultant to Bristol-Myers Squibb. The authorship of this paper is unrelated to that position, and he received no compensation for this manuscript.