Coping With Critical Drug Shortages

An Ethical Approach for Allocating Scarce Resources in Hospitals

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The number of critical medication shortages in the United States has reached an unprecedented level, requiring decisions about allocating limited drug supplies. Ad hoc decisions are susceptible to arbitrary judgments, revealing preformed biases for or against groups of people. Health care institutions lack standardized protocols for rationing scarce drugs. We describe the principles on which an ethically justifiable policy of medication allocation during critical shortages was created at our hospital. Based on supportable scientific evidence and with all clinically similar patients treated as similarly deserving of consideration, drugs were distributed according to a hierarchy of clinical need and predicted efficacy. We explain the ethical rationale for the procedures we adopted, how the policy was implemented at a large academic medical center, and more than 1 year of experience with a number of different medications. Our experience has demonstrated the feasibility and utility of formulating a rational and ethically sound policy for scarce resource allocation in an academic teaching hospital that could be used in a variety of health care settings. The method has proven to be reliable, workable, and acceptable to clinicians, staff, and patients.

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Scarcities of drugs have become a fact of life for physicians, hospitals, and pharmacies in the United States. These shortages present a variety of medical and administrative challenges to practitioners and can jeopardize the safe and effective delivery of clinical care. Unpredictable shortages of common and rarely used medications stem from a variety of causes, including insufficient supply, contamination of raw materials, manufacturing problems, and financial decisions to discontinue production of specific medications. The shortages have been especially dramatic for chemotherapeutic agents. Unexpected shortages have affected generic and brand-name drugs, leading to similar results: the rapid failure of the supply chain, generating significant deficiencies in prescription medications. A bill has been introduced in Congress to attempt to address some of these issues, but its fate is unclear (Preserving Access to Life-Saving Medications Act, S 296, 112th Cong, 1st Sess [2011]).

See also Invited Commentary

One of the earliest critical drug shortages occurred in 1997 and 1998 with intravenous IgG. Doctors and hospitals responded to the crisis in a number of ways. Several institutions restricted use of intravenous IgG to evidence-based indications, which diminished but did not eliminate the scarcity of this agent. Furthermore, once the shortage ended, use returned to its prior level, presumably owing to prescribing patterns reverting to original practice.

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Fortunately, many medications in a given class can be switched to an equivalent alternative, with minimal consequences for patients. In addition, numerous drug therapies are prescribed for reasons that are supported by equivocal or by no scientific evidence and could be replaced with another drug or perhaps discontinued with no harm to patients. However, for other drugs, especially antineoplastic agents, few, if any, substitutes exist. When the demand outstrips the supply, how should we choose to allocate scarce medications? Few physicians or health care institutions have prepared to perform this task equitably and fairly, while facing the possibility of having to deny access to potentially life-saving treatment to some patients, although a number of plans for pandemic influenza several years ago provided some experience with executing such complex decisions.

How does one choose which patients should receive a scarce drug? What rules or procedures should be followed when making such consequential decisions? In fact, little guidance is available; thus, many hospitals deal with these decisions on an ad hoc basis. This process has the potential for major abuses, intentional or otherwise, in which some patients are judged to be more deserving than others on the basis of who they are rather than their medical condition. For instance, should VIPs and those who are well insured be prioritized over the poor, the uninsured, and those who belong to already medically marginalized groups, such as undocumented immigrants and members of some ethnic minorities? This situation frequently happens under existing conditions, without scarcity. The situation of scarce medications somewhat resembles that with solid organ transplantation. Rationing of health care is usually discussed as an elective decision to restrict access to certain resources due to a deliberate choice to limit materials or capital and therefore divert one’s assets to other goods. However, allocating scarce drugs is unequivocal rationing, by which we mean “explicit mechanisms that allow people to go without beneficial [health care] services.” Hence, allocation of medicine also requires an approach that is sensitive to some of the ethical pitfalls associated with rationing medical resources in general. Based on the assessment that drug shortages will continue to be a major challenge in clinical practice, we decided to develop a policy that could ration the available supplies of scarce medications in an ethical manner.

In this report, we describe the application of a comprehensive and ethically defensible policy to oversee allocation of scarce drugs that has the virtue of transparency and conforms to the standards of procedural justice. We also present our experience using this policy for more than 1 year, during which a number of critical drug shortages were managed successfully.

**POLICY DEVELOPMENT**

In brief, we adhered to the general guidelines of the “accountability for reasonableness” process as originally described by Daniels and Sabin and the method discussed by Rosoff. Since it was initially proposed in the 1990s, this approach has achieved a wide level of acceptance, but not without some criticism. We based our policy development on this method for the following 2 reasons: it is well-grounded philosophically on a foundation of substantive principles of justice, especially those initially elaborated by Rawls, and it is amenable to implementation at a practical, institutional level.

In this account, the following 4 primary ethical benchmarks must be achieved for a health care limit-setting policy to be considered just: transparency or publicity (the development, rules, and implementation of the policy should be open to all for review), relevance (the policy and the reasons supporting it must be judged clinically relevant to the population of patients and health care providers affected by its application, and those reasons should be rationally acceptable by others), appeals (method for people to appeal a decision that they feel has been wrong must be built in), and enforcement (the institution that “owns” the policy must guarantee its implementation such that the rules will be followed by all). Because of concerns that this procedure might not ensure or maximize the chances of an equitable outcome that could be dispassionately viewed as impartial, we added a fifth standard: fairness (clinically similar patients will be treated similarly; no “special” people, physicians or patients, will receive exceptional consideration). We believe that including this component will add further confidence in the essential blindness of the system to personal distinctions of this sort and enhance its legitimacy in the eyes of patients and health care providers. The policy was written by our hospital’s ethics committee, which is composed of members of the staff from a wide variety of disciplines and representatives of our community.

To apply these principles into a practical policy, we created a committee composed of members of the hospital ethics and pharmacy and therapeutics committees, the pharmacy leadership, the chief medical and nursing officers, and risk management/hospital counsel. We started by generating an outline that incorporated the benchmarks described in the previous paragraph to guide the development of a policy (eAppendix 1; http://www.archinternmed.com). This process resulted in a policy that was approved by the ethics committee and the executive committee of the medical staff (eAppendix 2). The existence of this new policy and its details were announced to the entire staff via a variety of electronic venues. An information sheet in English and Spanish was distributed to patients who could be affected by a shortage. In addition, a process was put in place to hear appeals in a timely manner from patients (or physicians) who would not have a conflict with the allocation committee.

One of the locally unique aspects of this policy is that we have a compounding pharmacy that enables us to formulate many drugs from precursor ingredients. This permits us to mitigate some shortages (those drugs available as generics) but raises the problem of potentially needing to use drugs before they have passed the standard ste-
rility-testing period. We have addressed this concern by agreeing to release drugs after a shorter quarantine, but only if patients willingly give informed consent to receive the medication under these circumstances. We do not know whether commercial compounding pharmacies could fulfill this function for those institutions lacking their own facility.

We also have a uniform policy of not using medications from “gray market” vendors because we cannot ensure a proper chain of custody or the integrity of the medication, although using these medications could give the appearance of lessening the gravity of the shortage. Finally, we decided to adopt a practice that would halt any investigational uses of scarce drugs so as to conserve the supply, unless the study application was for a standard treatment (such as the control arm of a clinical trial). To date, we have had more than 1 year of experience using this policy with a number of different types of drugs in short supply.

EXPERIENCE WITH CRITICAL SHORTAGES

Although each shortage is distinctive in some respects, we have been able to maintain a uniform approach by strictly adhering to the policy. Once the central pharmacy becomes aware of a shortage (via a wide variety of information sources), an immediate inventory of our existing and potentially available stocks is made and a memorandum is sent to the allocation committee. If scarcity of a product is projected, the committee usually meets within 48 hours, and physicians who are affected by the shortage directly are invited to attend to offer their clinical expertise and advice or to create a prioritization scheme.

Recent drug shortages have crossed all therapeutic categories. Several common themes have emerged. Agents that are manufactured by a single entity have the most impact when supply disruptions occur. However, even when multiple companies produce medications, shortages can still occur (eg, when primary ingredients are lacking). We currently take a weekly inventory of more than 20 unique oncology agents and a daily inventory of 70 to 100 nononcology agents for shortages. Common themes to successful management of drug shortages include comprehensive communication across all affected providers and early identification of emerging supply issues. Having an established procedure to guide our allocation decisions has led to a standardization of distribution choices even in moments of apparent crisis. We will give detailed descriptions of our experience with 2 drugs, bleomycin sulfate and methotrexate sodium, both chemotherapeutic agents. We have chosen these drugs because they represent prototypical shortages, and the way in which our policy was applied to each reveals different aspects of prioritization allocation decisions. In addition, anticancer drugs constitute a significant percentage of the total shortage problem and rarely have equivalent substitutes available.

Situation of absolute scarcity have required us to make difficult decisions, perhaps best demonstrated by the shortage of bleomycin, a chemotherapeutic agent that is used in the frontline treatment of Hodgkin disease and germ cell tumors. Conservation measures included having all eligible patients arrive at the clinic on the same day to minimize wastage from single-use vials. We also maintained a small enough new supply to treat all existing patients and anticipated new patients from our immediate referral area (at least for a few months). The committee decided not to start therapy for any patients using this drug unless we could ensure a complete course of treatment. However, our institution has customarily taken regional referrals from a very large geographic area; if this practice continued, and these patients were considered to be as eligible as local patients, then we would have less drug and, shortly thereafter, none. We elected to restrict new patient referrals to those from our proximate region, where most of our patients traditionally are located. We also pledged our assistance to more distant institutions and physicians to help them locate some supply of this drug for their patients’ use.

With other absolutely scarce resources, such as solid organs, influenza vaccines, and intensive care unit beds during a pandemic, surveys of the public have yielded mixed endorsements of various distribution approaches. Therefore, our method may require revision in the future. However, when evidence suggests differential efficacy between 2 potential recipients of a drug, the next patient in line may not be the most needy candidate. Furthermore, this allocation scheme has been criticized as favoring the well-informed and economically privileged. If 2 clinically equivalent patients apply for the drug when a sufficient amount exists for only one, a coin will be tossed to choose between them (as of this writing, this method has not been used).

Another shortage that demonstrates somewhat different prioritization is methotrexate, a drug commonly used in a variety of disease conditions ranging from childhood acute lymphoblastic leukemia to rheumatoid arthritis. The current scarcity affects only parenteral forms of the drug; oral preparations remain available. In addition to the regular members of the allocation committee, representatives of the adult and pediatric oncology departments were present. We decided to restrict the remaining supplies of preservative-free methotrexate for intrathecal use in patients with acute lymphoblastic leukemia and switch therapy for arthritis patients from subcutaneous to oral administration. Absolute priority would be given to patients with childhood acute lymphoblastic leukemia and osteosarcoma, a rare bone tumor for which methotrexate is prescribed; this drug is used in curative regimens in both diseases. If a sufficient supply remained after these current and anticipated new patients have a stock reserved, then a priority list of palliative uses was also approved, in descending order of published efficacy. The maximum doses for the latter were also restricted to those in the literature and rounded to the nearest whole gram to minimize wastage. A 2-month reserve was projected. In addition, we agreed to take new patients referred to the hospital if (and only if)
they had 1 of the 2 conditions for which this drug played a curative role; no patients seeking palliative use would be accepted. Finally, the compounding pharmacy was instructed to purchase methotrexate powder to prepare our own supply should commercial sources continue to be unavailable in the future; this approach was stressed because we could not be sure of our projections for actual need and use.

CONCLUSIONS

In this article, we report that implementing a functioning policy to allocate drugs that are in short supply in a large academic medical center is feasible and practical; we also demonstrate that an ethically justifiable rationing approach can be acceptable to cope with the challenges posed by ongoing critical drug shortages. We believe that our experience could prove helpful to similar institutions, community hospitals, and other practice settings. The main virtues of this approach are transparency, its fairness for patients and health care providers, and its ability to be rapidly put into practice. We have had no disagreement with the rules from patients, physicians, or hospital leadership. The process of developing the policy was inclusive of all of the stakeholders, was open and public to the staff and patients, and incorporated a mechanism by which disagreements with its application can be heard and adjudicated.

Clearly, the initial response to any shortage is an attempt to maximize efficiencies of distribution and to minimize wastage; in some cases, this effort has served as a sufficient stop-gap measure to tide us over until the scarcity is relieved. Further conservation of supplies results from permitting drugs to be used only for clinical indications in which the evidence of efficacy is strong. For drugs with acceptable substitutions of a reasonable therapeutic equivalent, the problems have been resolved also (eg, the replacement of tobramycin for gentamicin sulfate when the latter was unavailable, except for premature infants in whom the evidence of efficacy of the former drug was strong). However, although these measures are effective, they do not correct the problem in all cases. We have increasingly used our compounding pharmacy to prepare drugs when feasible (exclusively generically available medications). Although we realize that most hospitals do not have easy access to similar institutional facilities, creating regional collaborations between hospitals that have them and those that do not should be considered to share the costs and benefits. Consideration could also be given to using commercial compounding pharmacies to achieve the same result, if practicable.

Hence, although our experience has been quite positive, several unresolved questions and challenges remain. For instance, we do not specifically address how to make the “tragic choice” originally described by Calabresi and Bobbitt between 2 equally viable options to bestow a benefit that can only be given to one. We came very close to having to make this choice during the cytarabine shortage, but the relative scarcity was relieved just before this became necessary. The approaching exhaustion of the supply of liposomal doxorubicin hydrochloride makes this kind of choice likely to be necessary, although the “tragedy” of the choice is somewhat lessened by the clinical situations of the affected patients (with already relapsed or progressive disease). A variety of approaches to solve this morally challenging problem have been tried, most notably in the allocation of scarce solid organs, but the truth of the matter is that we do not know and cannot predict the circumstances or the outcome of a situation in which seriously ill patients will have to do without beneficial drugs when they have been accustomed to receiving them.

Unfortunately, no one correct answer to this dilemma exists. Although “first come, first served” may sound intrinsically fair, problems remain with this approach, especially that it favors well-informed patients and those with greater resources. We have decided that when 2 patients are truly clinically equal and no other distinguishing characteristic can be used to differentiate one who may receive more overall benefit than the other (eg, some might argue that when choosing between a teenager and an elderly adult, our moral intuition would favor the child), we will simply flip a coin, assuming that we have exhausted other approaches first. However, this method also may have its downside. In addition, we have not satisfactorily addressed whether we have greater obligations to some patients than others based on their prior relationship with the institution (do existing patients have a higher claim on resources than new ones?) or their distance from the hospital (local, regional, national, etc); it might be said that we “solved” this problem with the approach to the bleomycin shortage, but only because we believed we could help distant hospitals locate some drug for their own use without depleting our stock. Of course, some of the latter dilemmas could be addressed by forming regional consortia of hospitals to pool their scarce resources and use similar rationing schemes, but this solution is unlikely to occur anytime soon.

Finally, some have argued that the youth of patients should play a determinative role in forced rationing decisions. Except for the case of the gentamicin shortage, where we reserved existing stocks for use in premature infants for clinical efficacy and safety reasons, this conundrum has not been resolved satisfactorily. In addition, the relative paucity of class A evidence in children (compared with adults) supporting the efficacy of many drugs commonly used in the pediatric population would seem to discriminate against this group of patients ex ante. To compensate for this fact, we have accordingly lowered our criteria for pediatrics to accommodate this fact. However, the appropriateness of this response to the situation remains unclear. Certainly our moral intuition supports favoring the young over the old, but actual data supporting this notion are scant. Several surveys from different countries (including the United States) have been performed, with decidedly mixed results. For each region to conduct its own study to determine the opinions of the local population on this important mat-
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