standards of care, and sales of a number of both reference and educational books and videotapes. The ASHP describes itself as having its primary emphasis on efficacy and safety, since proper use of drugs in and of itself leads to lower health care costs.[27]

Medical errors are costly and often avoidable. The ASHP emphasizes the importance of training in the safe use of medication, and its standards, books and educational materials provide such support. Such quality control and safety programs have lead to relatively low medication error rates in dispensing, versus prescription and drug administration. According to the ASHP, 39% of medication errors are due to mistakes in prescribing and 59% due to mistakes during administration of the drug to the patient, while only 11% occurred in the dispensing process. These results demonstrate the need for expanding the role of pharmacists into the areas of prescribing and administration support, where their expertise could help reduce errors and their associated human and economic costs.

The ASHP surveyed MCO based pharmacists in 1998 to try to understand the current use of pharmacoeconomics in MCO formulary policy formulation. The results showed a perceived quality gap in pharmacoeconomic data used by drug companies to market their products. While 58% of those pharmacists surveyed said drug companies use pharmacoeconomic data to sell to MCOs, only 33% said that the information was of high quality. Furthermore, 94% said they would like to see more scientifically rigorous pharmacoeconomic studies from drug makers, and 71% felt their MCO was in a position to put pressure on manufacturers to conduct more rigorous studies. Ninety percent felt that the FDA should apply the same rigor in assessing a manufacturer's pharmacoeconomic claims as it does in assessing clinical claims, and 96% felt the FDA should apply the FTC's "competent and reliable" evidence standard in assessing pharmacoeconomic claims.[28]

Currently about 45% of pharmacists surveyed said their MCO uses the pharmacoeconomic data provided by manufacturers, in making formulary decisions. While 76% of pharmacists said they were well equipped to critically analyze pharmacoeconomic data supplied by manufacturers, only 38% felt that

the physician members of their MCO P&T committee were similarly well-equipped. Fifty percent of those surveyed said that at least one pharmacist in their MCO was well trained to conduct pharmacoeconomic studies, and 51% said their MCOs routinely used their own pharmacoeconomic analyses when making formulary decisions. The results of this survey suggested that in 1998, there was much work to be done in improving the quality of data supplied by manufacturers for pharmacoeconomic analysis, as well as the capabilities of MCO-based and other P&T committees to both critically analyze and perform their own analyses. Pharmacists need to play an important role on such committees for their work to be effective.[29]

AMCP

The Academy of Managed Care Pharmacy (AMCP) is a more recently established pharmacist organization that promotes the use of managed health care concepts by the profession. The organization publishes a journal, offers continuing medical education (CME) for pharmacists, and performs research. Without knowledge and training in managed care concepts such as pharmacoeconomics, pharmacists are limited to the traditional role of dispensing of drugs from either hospital-based or retail pharmacies. However, with adequate training, pharmacists can work side by side with physicians, and hospital and health plan executives, in such roles as managing the medication of the chronically ill through the practice of clinical pharmacy, planning and implementing patient safety programs such as drug utilization review, promoting effective patient education, developing hospital, MCO, and PBM formularies and designing health insurance benefits programs.[30]

The AMCP has also recently become concerned about the quality of pharmacoeconomics analysis going into formulary development by the P&T committees at MCOs and hospitals in the US. Both the inputs and methodology vary greatly among such organizations, and poorly performed analyses can lead to unsound formulary development. In 1999, the AMCP together with the ASHP, NCQA, AMA, and the Department of Veterans Affairs, joined a coalition of 50 organizations in issuing the "Principles of a Sound Drug Formulary". These are the guiding principles from this document, published in 2000:

- "Formulary system decisions are based on scientific and economic considerations that achieve appropriate, safe, and cost effective drug therapy

- The formulary system encompasses drug selection, drug utilization review, and other tools to foster best practices in prescribing, dispensing, administration, and monitoring outcomes

- The P&T Committee or equivalent body, comprised of actively practicing physicians, pharmacists, and other health care professionals, is the mechanism for administering the formulary system, which includes developing and maintaining the formulary and establishing and implementing policies on the use of drug products
- Physicians and other health care professionals provide oversight of the formulary system
- The formulary system must have its own policies, or adhere to other organizational policies, that address conflicts of interest and disclosure by P&T committee members
- The formulary system should include educational programs for payers, practitioners, and patients concerning their roles and responsibilities
- The formulary system should include a well-defined process for the physician or other prescriber to use a non-formulary drug when medically indicated"

With regard to economic considerations, the Principles specifically state that formulary decisions should be based on "cost factors only after the safety, efficacy, and therapeutic need have been established". It goes on to state that evaluating drug cost should be based on their impact on total health care cost. Finally it mentions that financial incentives should only be used to promote cost management as a part of the delivery of quality medical care, and should not interfere with the delivery of medically necessary care. The Coalition has defined an important role for pharmacoeconomic analysis, but only to the extent that it is used as a part of delivering high quality health care, and never to defend the delivery of second rate care. It also promotes open disclosure of potential conflicts of interest among P&T committee members, since many

participate in clinical trials and continuing medical education sponsored by the same manufacturers. These activities are normal, but how the committee ensures that manufacturer support does not influence formulary decisions is key to the credibility of the process.

The AMCP has gone one step further and issued a Format for Formulary Submissions, beginning with Version 1.0 in 2000 followed by Version 2.0 in 2002. This serves as a guide for P&T committees to request information from pharmaceutical manufacturers to be used in preparation of a drug monograph. It describes the sections of a complete formulary submission dossier as containing the following sections:

1."Disease and Product Information
2.Supporting Clinical and Economic Information
3.Cost-Effectiveness and Budget Impact Model Report
4.Product Value and Overall Cost
5.Supporting Information: Reprints, Bibliography, Checklist, Electronic Media, and Appendices"

It goes on to describe the recommended steps for this dossier submission, whose key points include:

1.As manufacturers should keep managed care organizations aware of the status of their pipelines, approximately 6 months before anticipated new product launch, the pharmacy staff will issue a request for information to the manufacturer, with above-specified content.
2.The manufacturer and pharmacy staff will hold a pre-submission meeting to discuss the submission of the requested data, establish a deadline, and resolve any issues around data secrecy, economic model assumptions, etc.
3.The manufacturer should provide the report in both paper and electronic forms to the pharmacy staff at least 2 months prior to the product review
4.The pharmacy staff reviews and requests any needed clarification of the data before preparing a product monograph for P&T committee review
5.Clinical pharmacists prepare the monograph, including all data, and arguments both pro and con inclusion of the product in the formulary

6. Upon reaching a recommendation, the P&T committee will inform the manufacturer of its decision, the rationale for a denial or restriction, and the standard appeals process.

It is unknown just how many P&T committees use the AMCP guidelines, dossier request format, and schedule, but to date, more than 300 pharmacists have been trained in its use. The AMCP hopes that these guidelines and training will move the formulary process away from discussions of single product acquisition price and rebates, and on to the effect of the formulary on the health and well-being of the population. Transparencies in all these procedures can also help erase suspicion about the inappropriate use of financial incentives in the multibillion dollar pharmaceutical and managed care industries. Clearly this AMCP initiative is also doing much to raise the influence of pharmacists in hospitals and MCOs.[31]

Pharmacoeconomics in Use

Introduction

MCOs, hospitals and physician groups all use P&T committees to determine and manage drug formularies. Kaiser Permanente and the Veterans Health Administration are two particularly innovative integrated healthcare delivery systems that have focused on the opportunity to actively manage drug selection within their systems, and employing pharmacoeconomic analysis. Each has promoted the role of pharmacist from merely dispensing drugs to patients, to a more equal partner in the analysis, selection, and proper administration of drugs to the benefit of both physician and patient. In addition, pharmacists in both organizations are involved in innovative programs to more effectively use drugs.

Kaiser Permanente

Kaiser Permanente (KP) is a large, group practice HMO, based in Oakland California. The non-profit health plan has approximately 8.4 million members,

mostly in California. The medical group, serving KP's members exclusively, has more than 11,000 physicians of all specialties. The HMO is fully integrated, meaning it operates its own hospitals, outpatient clinics, pharmacies, laboratories, and all other ancillary services. KP owns 29 hospitals and 423 outpatient clinics exclusively for the use of its members. Members (or their employers) pay an annual premium, plus modest co-payments at the time of service, for all their healthcare needs for the year, including prescription drugs. The medical group, hospitals, pharmacy, etc. must perform all their activities within this pre-determined budget of total premium revenue. This financial arrangement aligns the incentives of the hospital, physician, and member, to keep the patient healthy and out of the hospital. [32]

As discussed above, pharmaceutical products are a significant and growing portion of health care spending in the US, and KP is no exception. KP spends approximately $2.5 billion per year on prescription drugs. But KP has unique advantages compared to the normally fragmented system of health care financing and delivery in the US. As a large purchaser, KP can negotiate directly with manufacturers. As a closed system of health plan, doctors, hospitals, and pharmacists, KP has the ability to more proactively use the results of pharmacoeconomic analysis to manage the cost-effectiveness of the drugs dispensed to members. KP can expose all of its physicians to information on an ongoing basis about which drugs are preferred and why, and also given feedback on their use of preferred versus non-preferred drugs. They can also control access to KP physicians by drug company sales reps. Pharmacists play an integral role in pharmacoeconomic analysis, selection of cost-effective drugs for the formulary, and development of methods to assure formulary compliance.

KP has a number of organizations supporting cost-effective use of drugs. Two internal research groups are Drug Information Services (DIS) and Pharmacy Outcomes Research Group (PORG). PORG has a staff of 5, including 3 pharmacists, who undertake prospective and retrospective studies in the area of cost-effectiveness, variation if drug utilization, program evaluation of pharmacy clinics, and study of both clinical outcomes and associated use of health care resources. PORG is essentially an in-house pharmacy think tank.

DIS has a staff of 37, including 20 pharmacists, and is a part of the Pharmacy Strategy and Operations Group in KP's California Division. Nine of the pharmacists are specialists in specific therapeutic areas, such as cardiovascular, anesthesiology/pain, etc. Since the pharmacists specialize, they develop working relationships with specialist physicians in the same areas. DIS has responsibility for administering the formulary process. In addition, they also prepare a forecast of drugs likely to be approved next year, for what indications, and at what cost to KP. They also provide a number of pharmacy information services to KP members and physicians.

KP has an open formulary which means that while use of formulary drugs is expected and encouraged, doctors are still free to prescribe any drug, under an exception rule. As a principle, all drugs submitted for the KP formulary by physicians are considered for inclusion. The P&T committee meets 4 times per year. In the end, a consensus is achieved, and the whole committee gets behind the decision of whether or not to include a specific drug. The process is dynamic, in that any time new information becomes available, a decision can be reconsidered at the next meeting. In the interim, if new drugs are approved by the FDA they can be used immediately by KP physicians under the exception rule. Similarly, if significant side-effects are found in the interim between meetings drugs could be removed from the formulary immediately.

The formulary process begins by preparation of a monograph by DIS. They gather all information available about a product, from peer-reviewed articles, to advertising pamphlets. They request an AMCP format dossier from the manufacturer, including any pharmacoeconomic models on a CD-ROM, so they can be manipulated, including adjusting cost assumptions to match KP's actual costs. Apparently large companies have implemented the AMCP format, while many smaller companies have not. DIS will consider the economic effects of both the effectiveness and safety (e.g. the cost of expected side-effects) when modeling the economic impact of a drug. They will use the manufacturer's model, if available, and model how the drug changes the use of all associated resources.

KP's Pharmacy Division operates the pharmacies and purchases pharmaceutical products in line with P&T committee policies. Within the Pharmacy Division, the Drug Use Department contains two groups that work with the P&T committees specifically to promote more cost-effective drug use, the Drug Utilization Group (DRUG) and Clinical Management of Pharmaceuticals (CMoP). DRUG works with doctors on an ongoing basis to promote cost-effective drug use habits today, while CMoP takes a historical look at patients on off-formulary drugs for long periods of time and works with the doctor to try to understand the reasons for the off-formulary prescription.

KP's pharmacy has undertaken a number of formulary strategies to reduce the cost of drugs. For example, in the areas of antidepressants known as selective serotonin reuptake inhibitors (SSRIs), there are many products on the market, but they all have basically the same effect according to the scientific literature. Fluoxetine (Prozac) has now gone off patent and is available in generic form for a lower price then the brand name SSRIs. In turn, KP's pharmacy purchasing group has negotiated a favorable price with a generic fluoxetine manufacturer in exchange for promoting the product among their physicians. The purchasing group feels they need to be able to "deliver" between a 50-90% "market share" within KP of a single product in order to gain a favorable negotiating position with manufacturers.

The pharmacy department uses a number of methods to promote formulary products among KP physicians in order to gain necessary market share for favorable negotiations. Pharmacy offers lectures and educational literature, has a telephone consultation service where doctors can ask questions about all drug use in their patients, and has designed tools just for KP physicians. For example, pocket sized cards for doctors list the choices of drugs in a category, such as SSRIs, and note the much lower price per month to KP of prescribing fluoxetine, $44/month, versus fluvoxamine (Luvox) at $120/month or paroxetine (Paxil) at $377/month. They want the doctor to be able to see the differences in price, weigh it in with the benefits, and make up their own minds.

To track results of these efforts, DRUG and CMoP provide weekly reports of new SSRI "starts" (i.e. new patients on SSRIs) to each region, facility, and

individual provider. This allows evaluation of formulary compliance at all levels, and the reasons behind non-compliance to be examined. The results of these efforts for SSRIs is that nearly 70% of new prescription starts are generic fluoxetine, accounting for only 16% of total antidepressant costs, whereas the other 30% of new starts being filled by brand name products account for the other 84% of costs. Overall, 70% of KP's prescriptions are filled by generics, which account for only 15% of total drug costs, whereas 30% are filled with brand name that account for 85% of total drug costs. Overall, in categories where generics are available, 98% of drugs dispensed are generic.

Within KP, pharmacoeconomic analysis provides additional perspectives when considering new drugs that are only marginally different than their predecessors, but sold at substantially higher prices. For example, traditional NSAIDS have come off patent, and companies have developed a new generation of NSAIDs known as COX-2 inhibitors. These products are sold primarily as being safer than traditional NSAIDS, due to reduced GI bleeding, and now account for about 1/2 the US NSAID market. The cost of the new drugs far exceeds that of the traditional NSAIDS. Using the results of a peer-reviewed study published by Stanford University researchers[33], pharmacists and their physician rheumatologist colleagues developed a GI bleed risk scorecard, that easily fits in a physician's pocket. The card has an easy to use flow chart that determines which patients really need the additional GI protection from the COX-2 inhibitors. Based on the assessed risk, it recommends categories of drugs, and lists the name and price of each drug available. This allows the doctor to easily assess the patients true need for a COX-2 inhibitor at $30-120 per month, versus a traditional NSAID at $2-5 per month.[34] Recently published results showed that due to these efforts, use of COX-2 inhibitors in lower-risk patients was reduced 66% in KP Northern California patients. Total COX-2 inhibitor prescriptions were only 4% among KP members, versus 45% for patients outside KP. [35]

VHA

The Veterans Health Administration (VHA) is an integrated healthcare system serving the needs of US veterans. The VHA has a budget of more than

$22 billion, employs 180,000 healthcare professionals, and operates 163 hospitals, 800 clinics, 135 nursing homes, and a variety of other facilities for its beneficiaries. As the federal government is the largest purchaser of drugs in the US, the VHA is actively involved in efforts to promote cost-effective drug use.[36]

The VHA National Drug Formulary lists drugs that must be available at all VHA medical centers, and lists about 80% of drugs dispensed by the VHA. At the national level, the VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel consists of physicians and pharmacists that maintain the formulary and VHA pharmacy policies. This national formulary, along with all drug monographs, VHA drug pricing, and a variety of other information about VHA drug policy is available on-line at www.vapbm.org. In addition, each of the 21 regions has its own P&T committee and formulary, based primarily on the national formulary. Each regional committee can add drugs to its formulary with permission of the national formulary committee. Finally, there are also P&T committees at each VHA medical center that review local drug policy and use.

A brief look at some of the VHA National PBM Drug Monographs available on the Internet shows that acquisition price of the new drug is listed in comparison to existing drugs, and other costs that may change as a result of introduction are described in the conclusions and recommendations. Pharmacoeconomic benefit is analyzed when considering drugs for the national formulary, and compared with all other potential outcomes. In the San Francisco region, the P&T committee has also begun to analyze older, expensive drugs, such as proton pump inhibitors and gabapentin, to look at whether they are used effectively and determine guidelines for more cost-effective treatment of patients with cheaper drugs when possible, similar to efforts at KP. The VHA also provides its own tools to promote physician use of the formulary and cost-effective prescribing, such as physician pocket guides.

VHA pharmacies serve both in- and outpatient populations, with about 90% of prescriptions filled for outpatients. The pharmacies have introduced automation, and for example, the San Francisco VHA Medical center fills

approximately 2,500 prescriptions per day, 1,500 of which are mailed to patients. The pharmacy department employs 55 persons, half of whom are pharmacists, and the other half technicians. The efficiency achieved through automation has allowed the pharmacists to concentrate more on the work of clinical pharmacy, spending time consulting with patients and physicians about drug choice, dose adjustment, and patient compliance.[37]

A recent example of a project spearheaded by VHA clinical pharmacists expanding their role and influence in the VHA was in the area of drug misuse and potential benefit of clinical pharmacy intervention. The VHA estimates that misuse of drugs costs the US healthcare system more than $70 billion per year in avoidable medical costs. This study evaluated the recommendations and interventions of clinical pharmacists on patient outcomes, healthcare cost, patient harm avoidance, and physician acceptance of the recommendations, in out- inpatient, and skilled nursing facility settings. Examples of typical interventions were in cases where upon pharmacist review of a physician prescription, the pharmacist recommended a dosage change to optimize therapy, or because of potential drug interactions, recommended changing the drug to minimize patient toxicity.

Overall, 92% of 600 such interventions recorded during the study period were accepted by the prescribing physician, leading to improved clinical outcomes in over 30% of cases, and no change in outcome in 40%. The interventions saved $1,000, $325, and $745, in inpatient, outpatient, and skilled nursing facility settings, respectively, for an average savings of $700 per clinical pharmacist intervention. Even when adding in the cost of the clinical pharmacist, the study showed overall reduced costs of errors of 20%. The computer system used to track the interventions and outcomes is now in place nationwide in the VHA.[38]

Summary

Pharmacoeconomics refers to both specific economic analyses, and the viewpoint of including costs when considering the purchase of new medical products and services, in addition to effectiveness and safety. However, each

constituent of the healthcare world uses what is loosely referred to as pharmacoeconomics differently, depending on what their goals are. The result is often a confusing mixture of anecdotes and analyses, that may be of little value to many stakeholders. P&T committees at hospitals and MCOs must choose new pharmaceutical products for their patients using data on effectiveness, safety, and increasingly, pharmacoeconomics. The drug monograph is a dossier containing data that the P&T committee uses to help make formulary decisions regarding new drugs. A number of organizations have a stake in the growth of pharmacoeconomics. The FDA does not require pharmacoeconomic studies for new drug approval, but does regulate the use of outcomes data critical to quality analyses. PhRMA, as a representative of large drug manufacturers, broadly promotes the use of pharmacoeconomics in part to justify the high price of new pharmaceutical products. The ASHP is the oldest professional organization, representing primarily hospital-based pharmacists. A recent study of their members reported that while 58% of pharmacists said that pharmaceutical companies use pharmacoeconomic data to sell to their MCOs, 94% said they would like to see more scientifically rigorous studies from makers. The AMCP promotes managed care concepts, including pharmacoeconomics, among its pharmacist members, many of whom sit on P&T committees. The AMCP recently published a suggested format for more complete and rigorous dossiers to be submitted by manufacturers to such committees, including more rigorous pharmacoeconomic models. Within this environment, two integrated healthcare delivery organizations, KP and the VHA, are actively promoting efficient formulary policies, including the use of pharmacoeconomic analyses. Increased availability of both good and bad pharmacoeconomic analyses requires pharmacists trained in the art to help providers, PBMs and MCOs use such analyses to the maximum benefit of the patient population, and not just to any one specific stakeholder.

Section 3: Implications for Japan

Japan is facing a future of increasing healthcare costs, due primarily to its aging society. In order to maintain its low proportion of GDP spent on healthcare, Japan will have to introduce pharmacoeconomic analysis as one new pillar of new product evaluation from the viewpoint of efficient healthcare resources utilization.

A comparison of drug utilization under the Japanese and U.S. health care systems reveals use in Japan to be characterized by a national formulary, the determination by central government of fixed prices and national standardization of insurance reimbursement, the still incomplete separation of medical practice and drug dispensation (bungyo), and an immature generic drug market.

In the U.S., virtually no use is currently made of pharmacoeconomics in government regulation, unlike in Australia and Canada. However, there is strong interest in pharmacoeconomics among medical professionals and facilities, including government–run institutions such as the VHA, due to the high level of interest in managed care and the efficiency of medical care provided by medical institutions.

Bearing in mind the differences between the markets in the two countries, we need to consider the key points for successfully introducing pharmacoeconomics in Japan. Let us consider first the potential for use of pharmacoeconomics in the inclusion of drugs in the insurance formulary and determination of officially fixed prices. In the U.S., the FDA does not use pharmacoeconomics in its approval of new drugs, and there is less outpatient drug reimbursement under public insurance such as Medicare, thus there is not much to learn in this situation.

However, considering the impact of private insurers and managed care in particular on the cost of health expenditures in the U.S., the use of pharmacoeconomics in determining the inclusion of drugs in Japan's national

formulary could help to control health expenditures in Japan. As it is difficult to conceive of only some new drugs approved by the government becoming recommended for such a national formulary, pharmacoeconomics' role would most likely be as a guide for determining prices at the national level.

For insurers, as payers, to use pharmacoeconomics requires that each insurer should have its own formulary containing its own recommended drugs. This would mean the intervention of insurers in the prescription of drugs by physicians, which would give Japanese insurers greater powers than at present, as with managed care in the U.S.

In the healthcare service market (including drugs), the market mechanism is not considered to function well, due especially to the asymmetry of information between non-physicians and physicians. Those involved in the supply and demand for healthcare services in the U.S., however, use pharmacoeconomics as a source of data complementing market mechanisms in order to engage in more efficient decision-making.

In Japan, too, the optimum types and uses of drugs need to be selected by medical institutions, as the patients' proxies, using appropriate information incorporating data on cost performance. In this case, the process of bungyo must be completed on the provider side such that there are no remaining incentives for physicians to dispense one drug over another, or any drug at all, to their outpatients. The new prospective payment system will also need to be spread to all hospitals, such that drugs used for inpatient care become viewed as costs, not sources of income. With these changes, hospital P&T committees will have a reason to discuss pharmacoeconomics when choosing new drugs. This will create a larger role for pharmacists on these committees. The pharmacy profession will have to introduce new educational programs for its members and promote new standards for data analysis and evaluation.

Insurance benefits in Japan are paid on a fee-for-service basis, giving individual medical institutions little incentive to reduce medical expenses. Controlling health expenditures overall therefore requires that economic evaluations be made of drugs at the level of payers (insurers) and the central

government. However, the increasing payment of flat-rate insurance benefits (e.g. with the recent introduction of the Diagnosis Procedure Combination (DPC) system) will increase the importance of pharmacoeconomic studies in medical institutions in Japan.

Finally, when the reimbursement changes above take place such that saving money in healthcare becomes important to their customers, manufacturers will have to provide more pharmacoeconomic data to sell their products ahead of the competition, and to justify the high cost of new products. This change will emphasize the need for the pharmacist profession to become a leader in pharmacoeconomics, and guide their institutions away from making decisions based on poor or inadequate analyses, to solid evidence-based ones.

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市中肺炎治療における抗菌薬の使用法に関する薬剤経済学的評価

Ⅰ．目的

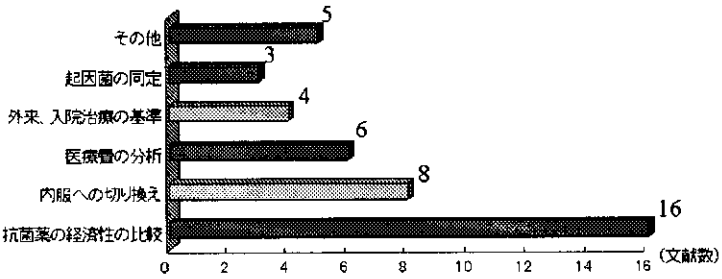
日本の医療制度の中で経済性の良い薬物療法を実施していくためには、日本の医療の実態下において薬剤経済学的分析を行う必要がある。今回、我々は医療費削減に対して効果的なアプローチについて検討するため、市中肺炎の入院治療を例にとって、薬剤経済学的分析を行うこととした。

Ⅱ．背景

2－1．市中肺炎治療に関する薬剤経済学的研究の現状分析

研究を開始するに当たり、市中肺炎治療の薬剤経済学的研究の現状を調査するため、医療経済学的研究論文のデータベースである“HEED（Health Economic Evaluation Database）2001年5月版”を用いて、Community-Acquired Pneumonia（市中肺炎）を検索語としarticle titleを検索した。HEEDは英国製薬工業協会(Association of the British Pharmaceutical Industry : ABPI）のシンクタンクであるThe Office Health Economics（OHE）が作成し、提供しているデータベースである。

検索の結果、約1万2000文献中42論文が抽出された。得られた論文を分類すると、「市中肺炎治療に対する複数種の抗菌薬の治療結果と経済性を比較した研究」が最も多く42論文中16件、次いで「抗菌薬の注射投与から内服への切り換えによる治療結果や経済性に関する研究」8件、「国家規模や医療機関単位での市中肺炎治療に要する医療費に関する分析」6件、「市中肺炎患者の外来/入院治療の判別基準の適用による医療費の変動に関する研究」4件、「起因菌の同定に基づく適切な抗菌薬選択がもたらす経済効果に関する研究」3件、「その他」5件となっていた(Fig.1)。



(全42文献)
検索式(article title) : Community-Acquired Pneumonia
(HEED 2001年5月版)

Fig.1 HEEDの検索で得られた市中肺炎に関する論文のテーマ別分類

これらのうちで今回我々が

注目したのは、薬剤師が関与しやすい「注射投与から内服への切り換えによる治療結果や経済性に関する研究」である

注射薬と内服薬の使い分けの基本は経口摂取が可能かどうかにある。外来治療では症状は軽く経口摂取も可能であることから、ほとんどの場合、内服薬が選択される。一方、入院治療においては注射薬が選択されることが多いが、経済性を考えると、同等の効果がある内服薬が存在し、経口摂取が可能であれば、入院治療においても内服薬が選択されることが望ましいと言えよう。

市中肺炎治療に関する各種の診療ガイドラインでは、「外来治療か入院治療かの適用に関する基準」や「抗菌薬の注射投与から内服への切り換え基準」が設定されている。前者に関しては日本呼吸器学会[1]、日本感染症/日本化学療法学会[2]、米国胸部学会[3]、米国感染症学会[4]のガイドライン、後者に関しては日本呼吸器学会[1]、米国胸部学会[3]、米国感染症学会[4]のガイドラインに記述がある（Table 1）。しかし、これらの基準の設定根拠となった研究報告には、大規模臨床試験で評価されたものはほとんど無く、また各診療ガイドラインにおいて両方の基準を併せて用いたときの治療結果や経済性の検討は行われていなかった。

そこで、我々は外来/入院治療の適用基準と内服への切り換え基準を有し、カナダでの大規模臨床試験により有用性が検証されているMarrieらが開発したクリティカルパス[5]（以下、Marrieのパス）に着目した。

Table 1 各診療ガイドラインにおける基準の設定と根拠

	注射から内服への切り換え基準	設定根拠	外来/入院の適用基準	設定根拠
日本呼吸器学会	△	×	○	×
日本感染症学会/日本化学療法学会	×	×	○	×
米国胸部学会	○	○	○	○
米国感染症学会	△	×	○	○

＊ ○：基準もしくは設定根拠が具体的に記述されている
△：基準もしくは設定根拠が記述されているが具体的ではない
×：全く記述されていない

Ⅱ－２．　Marrieのクリティカルパス

Marrie のパス[5]は、カナダの 19 施設延べ 1743 症例を対象にパスを導入した病院と導入しなかった病院で比較を行い、パスの導入による入院日数の短縮、医療資源の消費の削減などの有用性が検証されているものである。

このパスは、①市中肺炎患者に対する外来/入院治療の適用の基準（以下、外来/入院の適用基準)、②抗菌薬の注射投与から内服への切換え基準（以下、内服への切り換え基準)、③退院基準の３つから構成されている（Fig.2)。このパスの薬剤経済学的な有用性を検証した研究[5]では、治療結果や患者の QOL（Quality of Life）には有意差が認められなかったにもかかわらず、パス導入施設では軽症患者の入院率の低下、入院日数や抗菌性注射薬の投与日数の短縮などの効果が得られ、統計学的に有意となっていた。

以下に、Marrie のパスの３つの基準について解説する。

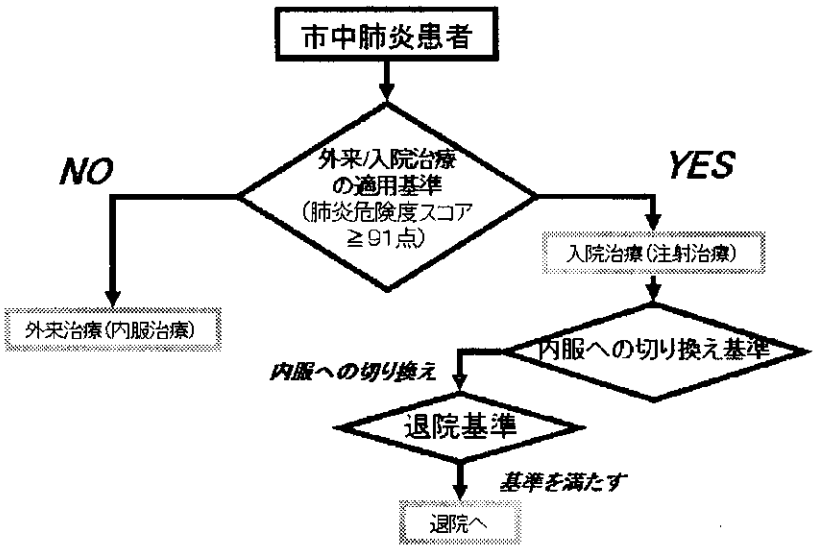


Fig.2 クリティカルパスの概略（Marrie ら,2000）

Ⅱ－２－１．市中肺炎患者に対する外来/入院治療の適用の基準

Marrie のパスでは市中肺炎患者の外来/入院の適用基準として、Fine らの肺炎危険度スコアリング[6]を用いている（Fig.3）。このスコアリングでは、患者の年齢、合併症、理学所見および検査所見の計 20 項目に与えられたポイントを加算し、その合計点から 30 日以内の死亡率に対する危険度に応じて、肺炎患者を５段階（危険度Ⅰ～Ⅴ）に分類する。パスでは、この肺炎危険度スコアが 90 点以下であった患者（危険度Ⅰ～Ⅲ）では外来治療とし抗菌薬は内服投与とする。一方、91 点以上の患者（危険度Ⅳ、Ⅴ）では入院治療とし抗菌