〔資　　料〕

Impact of Introduction of an Authorized Generic Drug Supply System on the Pharmaceutical Market Analyzed Using Statin Prescription Data

医薬品市場に対するスタチン類のオーソライズドジェネリック導入の影響

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Summary: Medical costs are steadily increasing due to increased health concerns in the aging population and advances in medical technology. The share of generic drugs in Japan is still low compared with that in other countries. Annual changes in prescription amounts of statin generics upon introduction of an authorized generic (AG) system were analyzed using national medical database open data from National Database of Health Insurance Claims and Specified Health Checkups of Japan. Several patent-expired drugs containing statins are available, and the prescription of generic drugs, including AGs, is increasing. Sale of AGs before the expiration of generic drugs accelerated the transition from branded drugs to generic drugs over a short period. However, the total usage rate of generic drugs for which AGs were not launched did not differ from that of drugs with AGs. Although AGs approved by the manufacturer of the branded drug are more reliable than conventional generic drugs, they do not always have a high market share. As the introduction of the AG system may have an impact on the pharmaceutical market, it is necessary to monitor trend changes using generic drugs with the AG system over the years.

Key words: generic drugs, authorized generics, NDB Open Data, statins

要旨：人口の高齢化や医療技術の進歩等に伴い，医療費は増加し続けている．日本のジェネリック医薬品のシェアは，諸外国と比較して未だに低水準である．レセプト情報･特定健診等情報データベースのオープンデータを用いて，オーソライズドジェネリック（AG）制度の導入に伴うスタチンの後発医薬品の処方量の年次推移を分析した．特許期間が終了した複数のスタチン薬が利用可能であり，AG を含むジェネリック医薬品の処方が増加している．一般的なジェネリック医薬品よりも先行して AG が発売されると，先発医薬品からジェネリック医薬品への移行を短期間に促進した．しかし，AG が発売されていないジェネリック医薬品においても，AG が発売されている医薬品のジェネリック医薬品との総使用率での差は認められなかった．先発医薬品メーカーに承認された AG は，一般的なジェネリック医薬品よりも信頼性はあるが，必ずしも市場で高いシェアではない．AG 制度の導入は，医薬品市場に影響を与える可能性があるため，AG 制度が導入されたジェネリック医薬品の使用動向を長期間調査する必要がある．

キーワード：ジェネリック医薬品，オーソライズドジェネリック，NDB オープンデータ，スタチン類

Introduction

National medical costs continue to increase due to the aging population and advances in medical technology. Many countries are promoting policies to reduce medical costs by using inexpensive generic drugs [1-6]. Japan is also frequently amending laws to reduce national medical costs by promoting prescription of generic drugs instead of expired patented drugs. The share of generic drugs in Japan increased to 78.3% in 2020 [7], but this share had

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already exceeded 80% in 2012 in the United States[8]. In the United States, a system has been established in which a pharmaceutical company that manufactures branded drugs evaluates the equivalence of a generic drug with a parent drug based on an application and transfers their patent with guarantee as an authorized generic (AG) drug[9,10].

AGs are classified into three types during the manufacturing process. If a related subsidiary manufactures a drug (AG-1) using the same raw materials, manufacturing method, factory, and efficacy/effect, excluding indications subject to reassessment, it is considered a generic drug with the same pharmaceutical characteristics as the branded drug, and a bioequivalence test is not required. It is possible to apply for its certification as an AG drug from a company other than an affiliated company to manufacture AG-2 using the same raw materials and manufacturing method as those for the branded drug, but at different factories. AG-3, the third category of AGs, is specified to be manufactured using the same manufacturing method but different raw materials in different factories. AG-2 and AG-3 require approved bioequivalence tests. A patent license (approval) from a pharmaceutical company for branded drugs must be obtained by the manufacturer for all AGs. AGs can be released before the patent for a branded drug expires. AG certification provides high added value to guarantee the quality of pharmaceutical products compared to that of conventional generics[11,12].

In 2009, the Ministry of Health, Labor and Welfare (MHLW) began operating National Database of Health Insurance Claims and Specified Health Checkups of Japan (NDB). This database can be used to analyze detailed medical information associated with individual information. To use NDB information, a paid usage application to the MHLW and clear information protection are required. In contrast, NDB Open Data provides statistical data that clearly show the current state of medical care in Japan and the results of specific medical examinations such that this valuable NDB full data is accessible to the public in an easy-to-understand manner. NDB Open Data consists of basic spreadsheets that can be read by conventional applications and includes the top 30 prescribing drugs and all other generic drugs for the first published fiscal year 2014 (FY2014) only; it also includes the top 100 for the following years[13,14].

Table 1　Launched date of statins

Drug	Formulation	Launched date
Rosuvastatin	Branded	2005.4
	Authorized	2017.9
	Generic	2017.12
Atorvastatin	Branded	2000.5
	Authorized	–
	Generic	2011.11
Pitavastatin	Branded	2003.9
	Authorized	2018.1
	Generic	2013.12
Pravastatin	Branded	1989.10
	Authorized	–
	Generic	2003.7
Simvastatin	Branded	1991.12
	Authorized	–
	Generic	2004.7
Fluvastatin	Branded	2003.6
	Authorized	–
	Generic	2009.11

Several patent-expired drugs containing statins are available and the prescription of generic drugs, including AGs, is increasing. In this study, we investigated trends in the use of AGs and other generic drugs containing statins using NDB Open Data and assessed the market impact of AG introduction on generic drug supply systems.

Launched date of branded and authorized generic and other generic statins analyzed is listed in Table 1. By 2011, generic atorvastatin, pravastatin, simvastatin, and fluvastatin were launched, but their AGs were not. Rosuvastatin AG was launched in September 2017 and preceded the conventional generic drug launch in December 2017. Meanwhile, generic pitavastatin was launched in 2013, and its AG was launched in 2018.

Methods

Consumption data (tablets/fiscal year) were extracted for the six branded statins: rosuvastatin, atorvastatin, pitavastatin, pravastatin, simvastatin,

fluvastatin, and their corresponding generic drugs, including AGs from the 2015–2019 annual NDB Open Data [13]. The rosuvastatin and pitavastatin AGs were categorized as AG-1. Statin consumption data were extracted and compared by gender, age, and prescribing categories, such as outpatients issued in-hospital and out-of-hospital prescriptions and inpatients.

Results

Fig. 1 shows the amount and ratio of the branded and generic drugs containing each statin used in each fiscal year. With the launch of generic drugs, branded statins drugs have been replaced with generic statin drugs over the years. The share rate of generic drugs gradually increased after the launch, reaching 66.0% to 81.7%.

The share rates for atorvastatin and pravastatin generics, for which AGs have not been released, were high at 81.7% and 79.2%, respectively, whereas that for fluvastatin was 66.0%. In 2019, the share rate of rosuvastatin was 23.1% for the branded drug, 51.0% for the AG, and 25.9% for conventional generics. The overall share rate of rosuvastatin generics was 76.9%, which was similar to the overall average for 2020. Although pitavastatin AGs were launched in 2018 at a share rate of 3.4%, the share rate of generic pitavastatin drugs (64.5% in 2018) increased to 65.6% in 2019.

Discussion

The policy of using generic drugs is being promoted to suppress the increasing burden of medical expenses. As a result of the government's aggressive

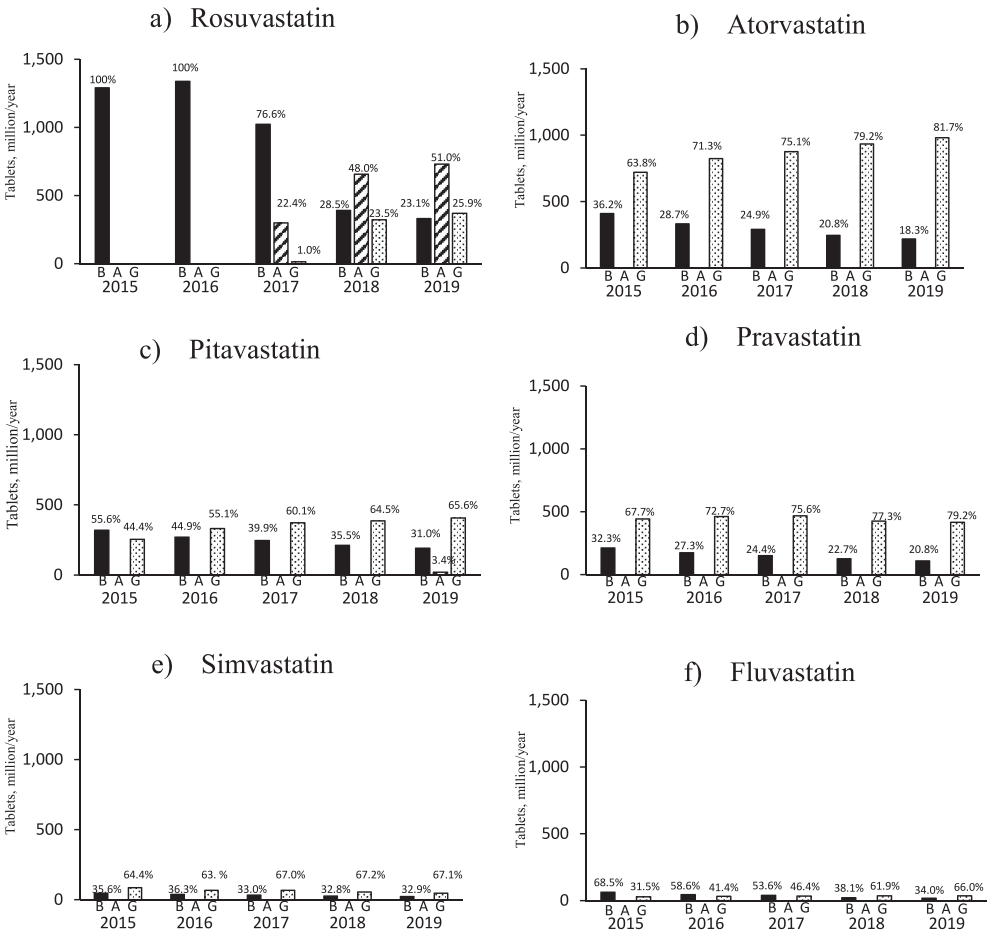

Fig.1 Consumption and share rate of statins in the fiscal year
B, branded drug; A, authorized generic drug; G, generic drug
The percentage in the figure denotes the consumption rate.

promotion of generic drug use, the share of generic drug sales in Japan reached 78.3% by 2020[7]. The recently introduced AG system allows generic drug manufacturers to obtain generic drug quality certification from patented-drug manufacturers and transfer market patents before the end of the patent period[4]. The AG system, which was launched with exemption of the bioequivalence test, is considered highly reliable by healthcare providers and patients. Some AGs are also marketed following the approval of bioequivalence test results after the patent period ends for the branded drug.

Several patent-expired drugs containing statins, first-line drugs for dyslipidemia, are available, and the prescription of generic drugs, including AGs, is increasing. In this study, the impact of AG introduction on the annual usage of branded and generic statin drugs was analyzed using annual NDB Open Data from the MHLW.

If AGs were launched before the patent for the branded drug expired, the official price of the generic drugs was set to be low. However, with the reform of the official pharmaceutical pricing system in 2018, the price of conventional generic drugs was set to be the same as that at the time the AG price changed in 2018[15]. The price difference between rosuvastatin AG and its conventional generic drugs has disappeared owing to the revision of the pharmaceutical pricing system. Therefore, it is possible to consider that the superiority of AGs has improved and their quantity used has increased. However, pitavastatin AG was launched in 2017, and the influence of the launch of AGs was small because the usual generic drug was launched in 2013.

According to the NDB Open Data, the share rate of generic drugs is gradually increasing, but rosuvastatin, in which AGs were launched prior to generic drugs, has promoted the transition to generic drugs, and the total usage volume of rosuvastatin has also increased. Rosuvastatin AG was exempt from bioequivalence testing and inherited the manufacturing patent of the branded drug, indicating that there are few concerns for patients and doctors regarding the safety and efficacy of the drug at the same price as conventional generics. Pharmacists explain that rosuvastatin AG has the same efficacy and safety with different packaging.

Based on the same national price of AGs and conventional generic drugs, it is inferred that AG-1, which has the same functional aspect as the branded drug, can easily be accepted by users. The timing of introduction of AGs is considered one of the important factors in this regard. Drug price margins, such as delivery prices, should also be considered when assessing their superiority. Manufacturers of generic drugs may develop new formulations not sold as AG drugs, such as orally disintegrating tablets.

The limitation of this study is that the NDB Open Data are provided as a simple tabulation result and do not reflect the adoption standards of hospitals and pharmacies. If multiple low-content drugs are used instead of high-content drugs, there is a possibility that a large number of low-content drugs are counted. It is necessary to carry out a detailed analysis considering the adopted standards.

Considering the tight medical financial situation, after the patent for the branded product expires, the medical system will shift to using generic drugs, including AGs, while complying with the relief systems from adverse drug reactions set by the MHLW[16]. It is also necessary to analyze the marketability of AGs for drugs other than statins in detail.

Conflicts of interest

The authors have no conflicts of interest to disclose concerning this article.

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