

京都大学	博士 ( 医学 )	氏名	Gao Jingwei
論文題目	<p>Comparison of adherence, persistence, and clinical outcome of generic and brand-name statin users: A retrospective cohort study using the Japanese claims database  (先発スタチン使用者と後発スタチン使用者における服薬アドヒアランス、継続率および臨床的アウトカムの比較：レセプトデータベースを用いた過去起点コホート研究)</p>		
(論文内容の要旨)	<p>Statins are recommended for primary and secondary prevention of cardiovascular diseases. However, patients do not always adhere to their prescribed treatments in real-world situations. Non-adherence to statin treatment results in an increased risk of cardiovascular events and all-cause mortality. There is a lack of evidence regarding adherence, persistence, and their influence on clinical outcomes associated with generic drug use in the Japanese population. This study compared adherence, persistence, and clinical outcomes of patients who initiated brand-name and generic statins in the Japanese population.</p> <p>This study identified a cohort of patients <math>\geq 18</math> years old who initiated brand-name or generic statins between 2014 and 2016 in a Japanese claims database. Primary adherence was measured as the proportion of days covered (PDC) within 1 year. Persistence was assessed using the proportion of non-persistent users. Any major adverse cardiac and cerebrovascular event (MACCE) was assessed as a clinical outcome. Propensity score matching was performed to adjust for confounding factors. For the adherence outcome, differences in continuous variables were tested with the Mann-Whitney U test, while differences in the distribution of categorical variables were tested with the chi-square test. Hazard ratios (HRs) and 95% confidential intervals (CIs) of non-persistence and MACCE in the two groups were compared with a conditional Cox proportional hazards model.</p> <p>Among 47,770 patients who met inclusion criteria in the study, 32,130 (67.3%) initiated generic statins. The median age of the patients was 53 (interquartile range: 46–59) years and 60.2% were male. A higher proportion of patients with PDC <math>\geq 80\%</math> [60.2% vs. 57.1%; odds ratio, 1.14; 95% confidence interval (CI), 1.09–1.19; <math>p &lt; 0.001</math>] and a higher PDC value (median, 90.2% vs. 87.9%; difference, 2.3%; <math>p &lt; 0.001</math>) were observed in the generic group. Similarly, fewer patients discontinued statins in the generic group [24.2% vs. 27.7%; hazard ratio (HR), 0.91; 95% CI, 0.87–0.95; <math>p &lt; 0.001</math>]. Differences in MACCE occurrence were not significant between the groups (4.3% vs. 4.2%; HR, 1.04; 95% CI, 0.93–1.17; <math>p = 0.99</math>). The primary results are supported by most subgroup analyses and sensitivity analyses, with only the subgroup analyses of simvastatin users, pitavastatin users, and secondary prevention patients demonstrating discrepancies, which are likely due to the smaller sample size, shorter follow-up and or the characteristics of the subgroup.</p> <p>This study suggested higher adherence and persistence in patients who initiated generic statin treatment, but differences in clinical outcome were not significant. The non-significant result in clinical outcomes suggested the equivalent effectiveness between generic and brand-name statins. It is possible that the better adherence and persistence in generic drug recipients may be due to the lower copayment fees.</p>		

This study contributed the real-world evidence of medication adherence and clinical effectiveness of statins in Japanese population. The results suggested that generic medication did not impair treatment benefits and may improve patient adherence, emphasizing the importance of the current generic promotion policies in Japan.

(論文審査の結果の要旨)

本研究では、後発スタチン使用者と先発スタチン使用者における服薬アドヒアランス、治療継続率及び臨床的アウトカムの比較を目的とした。

レセプトデータベースを用いた過去起点コホート研究を実施した。2014-16年に後発スタチンまたは先発スタチンを開始した18歳以上の患者を特定し、2群に分けた。主要評価項目はアドヒアランス(Proportion of days covered [PDC])及び治療継続率とし、副次評価項目は臨床的アウトカムである主要心脳血管イベント(MACCE)とした。群間のベースライン特性を調整するため、傾向スコアマッチングを行った。

適格患者は後発スタチン群で32,130人、先発スタチン群で15,640人であった。先発スタチン群に比べ、後発スタチン群の方がPDCの中央値(90.2% vs 87.9%)が高く、スタチンを中止した患者割合も低かった(24.2% vs 27.7%)。MACCEの発生率は群間で同程度であったが(4.3% vs 4.2%)、MACCE定義の妥当性が検証されておらず、その発生率を過大評価した可能性がある。

結論として、後発スタチン使用者は先発スタチン使用者に比べ、アドヒアランスと治療継続率が高い可能性が示唆された。

以上の研究は、日本人を対象としたスタチンの服薬アドヒアランスと臨床効果に関する実態の解明に貢献し、後発医薬品の貢献度の理解に寄与するところが多い。

したがって、本論文は博士(医学)の学位論文として価値あるものと認める。

なお、本学位授与申請者は、令和4年6月1日実施の論文内容とそれに関連した試問を受け、合格と認められたものである。