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〔一 般 論 文〕

我が国に於いて行われた臨床試験によるジェネリック医薬品と先発医薬品の臨床的同等性評価のレビュー研究Ⅰ：試験デザインの評価

Review of Clinical Equivalence Evaluation between Innovator and Generic Products in Japanese Clinical Studies I: Evaluation of Study Design

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Summary：Eight Japanese clinical studies were conducted to evaluate the clinical equivalence between an innovator product and one of its generic products, and the articles were published from 1983 to 2006. We reviewed the study designs and statistical issues of these articles.
Six out of eight studies observed changes of laboratory test values in the same individuals before and after switching from an innovator product to a generic product. Only two studies out of eight were conducted with 0.8 or higher power of analysis, successfully showing clinical equivalence between these drugs. Whereas other studies were conducted with fewer subjects than the number required to detect a 20% difference with 0.05 of α and 0.2 of β.
Four studies on pravastatin formulations showed an equivalent level of laboratory data and their variance, with an insufficient number of subjects to detect a statistical difference. Two of them did not show a significant difference, whereas the other two showed significance differences. The former was a comparison of the differences in laboratory data before and after switching of the drug, and the latter was a comparison of change in the ratio of laboratory data before and after the switch. The latter was either with a higher α risk due to the fewer subjects sampled from a higher variable data or with a higher power of analysis, both suggests that the result shown in the latter may be not significant from a clinical viewpoint.
In this review, we concluded that most Japanese clinical studies evaluating the clinical equivalence between the innovator and the generic products published from 1983 to 2006 could not be acceptable because of their poor quality as clinical studies without reliable data.

Key words：generic medicines, clinical equivalence, study design, power of analysis, number of subjects

要旨：我が国において1983年から2006年に公表され，先発医薬品とそのジェネリック医薬品の一つとの臨床的な同等性を評価している論文8報について，試験デザインや統計解析方法の問題点を検討した．8試験のうち6試験は，先発医薬品からジェネリック医薬品に切り替える前後で同一被験者内で臨床検査値を比較する試験として計画されていた．しかしながら，2試験のみが，0.8以上の検出力で試験が実施され，結果は先発医薬品とジェネリック医薬品が臨床的に同等であることを妥当に示していた．一方，他の研究では，0.8以上の検出力を得るために必要な被験者数より少ない被験者数で行われていた．プラバスタチンを対象とした4試験において共通して観察された臨床検査値の値およびその変動が同程度であり，統計的な差を検出するには不十分な症例数で実施されていたが，2試験は有意差が認められず，

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