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ORIGINAL ARTICLE

Efficacy and effectiveness of biologic therapy in inflammatory bowel disease. EFIFECT study☆

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KEYWORDS
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Abstract
Introduction: Randomised controlled trials provide the best scientific evidence for the efficacy of biological drugs in inflammatory bowel disease (IBD). However, findings obtained from these trials might not be reproducible in clinical practice. This study aimed to estimate the percentage of patients with IBD treated with biologics who would have been eligible for randomised controlled trials, and to compare the theoretical efficacy of biological drugs with their effectiveness in clinical practice.
Methods: We performed a retrospective multicentre study in 375 patients with IBD treated with anti-TNF agents and followed-up for 1 year. The eligibility criteria for the trial were taken from the ACCENT, SONIC, ACT, CLASSIC and CHARM trials. Eligible patients were included in a second analysis to compare results in clinical practice versus those hypothetically obtained if the patient had been included in a trial.

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Results: Only 45.6% of 375 patients would have been eligible for pivotal trials. One-year clinical benefit (remission or response) was similar for eligible and non-eligible cohorts (68.4% vs. 68.6%, $p = 0.608$). The clinical benefit was greater for current clinical practice than for a hypothetical trial situation (68.4% vs. 44.4%, $p < 0.001$) in eligible patients.
Conclusion: More than half of patients with IBD treated with biologic drugs would not be represented in pivotal trials. The effectiveness of anti-TNF drugs in clinical practice exceeds their theoretical efficacy.

PALABRAS CLAVE
Eficacia;
Efectividad;
Enfermedad inflamatoria intestinal;
Infliximab;
Adalimumab

Eficacia y efectividad de la terapia biológica en la Enfermedad Inflamatoria Intestinal. Estudio EFIFECT

Resumen
Introducción: Los ensayos clínicos aleatorizados proporcionan la mejor evidencia científica de la eficacia de los fármacos biológicos en la enfermedad inflamatoria intestinal (EII). Sin embargo, los resultados pueden no ser reproducibles en la práctica clínica. Los objetivos de este estudio son analizar el porcentaje de pacientes con EII tratados con fármacos biológicos que habrían podido ser elegidos para un ensayo clínico aleatorizado y comparar la eficacia teórica de los fármacos biológicos con su efectividad en la práctica clínica.
Métodos: Realizamos un estudio retrospectivo multicéntrico en 375 pacientes con EII tratados con anti-TNF con un seguimiento de un año. Los criterios de elegibilidad para la condición de ensayo clínico fueron extraídos de los estudios pivotales ACCENT, SONIC, ACT, CLASSIC y CHARM. Los pacientes elegibles fueron incluidos en un segundo análisis para comparar los resultados en la práctica clínica con los obtenidos tras realizar una estimación teórica si el paciente hubiese sido incluido en un estudio pivotal.
Resultados: Solo el 45,6% de los 375 pacientes cumplían los criterios de selección para un estudio pivotal. El beneficio clínico al año fue similar entre los pacientes elegibles y no elegibles (68,4% vs 68,6%). El beneficio clínico en los pacientes elegibles fue mayor en la práctica clínica que en la condición hipotética de un ensayo clínico (68,4% vs 44,4%, p < 0,001).
Conclusión: Más de la mitad de los pacientes con EII tratados con fármacos biológicos no estarían representados en los ensayos pivotales. La efectividad de los fármacos anti-TNF en la práctica clínica es superior a su eficacia teórica.

Introduction

Crohn disease (CD) and ulcerative colitis (UC) are chronic autoimmune inflammatory diseases of the gastrointestinal (GI) tract.[1,2] Conventional treatment includes the use of corticosteroids and immunosuppressants. The incorporation in the last decade of anti-tumour necrosis alpha (anti-TNF) antibodies, with their good safety profile, has transformed the treatment and prognosis of these patients.[3] Their efficacy is supported in several randomised and placebo-controlled clinical trials,[4–6] which has led to the approval of these drugs by regulatory agencies.

It is generally agreed that randomised clinical trials (RCT) are the best scientific approach to study the effect of a drug or therapeutic strategy. RCTs use strict selection criteria and a defined study protocol to maximise their internal validity.[7] Furthermore, most of the variables that could affect or interfere in the outcome are removed in order to evaluate the effect attributable to the study drug and remove most potential bias. In this way, RCTs evaluate the efficacy of a drug in a selected population and under controlled conditions. However, patient selection can limit the external validity or representativeness of the outcomes in the entire patient population eligible for treatment, and the findings must be carefully extrapolated to clinical practice (CP).

In contrast, observational studies evaluate the efficacy of a drug in real CP conditions, and variables and biases that affect the final outcome may appear during follow-up. The efficacy rates of observational studies in inflammatory bowel disease (IBD) using biologics are superior to the efficacy demonstrated in RCTs. For example, the sustained response rates at 1 year in primary responders with infliximab and adalimumab were 39% and 43%, respectively, in the ACCENT 1[4] and CHARM[5] studies. These results were lower than those obtained in observational studies, which reported rates of over 60% for both anti-TNF.[8,9]

This paper (EFIFECT study) is a theoretical exercise aimed at evaluating the degree of representativeness of patients with IBD treated with anti-TNF in CP and