Abstract:

The purpose of this study was to explore whether patients with Inflammatory Arthritis (IA) (Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS)) would remain in remission following a reduction in biologic dosing frequency and to calculate the cost savings associated with dose reduction. This prospective non-blinded single-centre, observational, non-randomised study commenced in 2010. Patients with Inflammatory Arthritis being treated with a biologic agent were screened for disease activity. A cohort of those in remission according to standardized disease activity indices (DAS28 <2.6, BASDAI <4) for at least six months prior to study entry was offered a reduction in biologic dosing frequency - etanercept 50mg once per fortnight instead of weekly, adalimumab 40mg once per month instead of fortnightly. Patients were assessed for disease activity at 3, 6, 12, 18 and 24 months following reduction in dosing frequency. Cost saving was calculated as the difference in cost between the actual amount of biologic agent used compared with the licensed dosage. The annual spend worldwide on Tumour Necrosis Factor (TNF) inhibitors in RA has been estimated at 18 billion euro. In Ireland, the cost of treating one patient per year at the licensed dosage with the most commonly used agents etanercept or adalimumab is approximately 13,500 euro. The state bears this cost except for those on the Drug Payments Scheme where the cost is shared. The annual spend in Ireland on adalimumab is 130 million euro annually. The purpose of this study was to explore whether patients with Inflammatory Arthritis (IA) (Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS)) would remain in remission following a reduction in biologic dosing frequency - etanercept 50mg once per fortnight instead of weekly or adalimumab 40mg once per month instead of fortnightly.

After obtaining consent, those willing to participate were assessed for disease activity at 3, 6, 12, 18 and 24 months following the reduction in dosing frequency. During the two year period of observation patients with a single flare of disease activity were permitted to remain on the reduced dosing frequency. The flare was treated with one intramuscular injection of Methylprednisolone 120mg. If there was a further flare the frequency of biologic administration reverted to the licensed dosage. Demographic data including gender, age, disease duration, duration of biologic agent, disease type, biologic administered, concomitant methotrexate and concomitant NSAID use were collected. Disease activity and health assessment questionnaire (HAQ) was calculated for patients with seropositive rheumatoid arthritis, seronegative rheumatoid arthritis and psoriatic arthritis. BASDAI and BASFI (Bath Ankylosing Spondylitis Functional Index) were calculated in patients with Ankylosing Spondylitis.

Cost saving was calculated as the difference in cost between the actual amount of biologic agent used compared with the cost if the licensed dosage had been used for two years. Statistical analysis was performed using SPSSv20 for windows. Descriptive statistics were used for demographic data. Paired sample T test was used to compare DAS28, HAQ, BASDAI and BASFI scores at 0, 3, 6, 12, 18 and 24 months. The primary outcome was the percentage of patients who remained in remission at two years following a reduction in biologic dosing frequency.

Results

Seventy nine patients were recruited. All patients had inflammatory arthritis and had been in remission for a minimum of 6 months prior to recruitment. Demographic data is shown in Table 1. Mean age was 49.5 years. Mean duration of inflammatory arthritis was 7 years. (Range 1-40). Fifty seven per cent (n=45) had a diagnosis of rheumatoid arthritis, of whom 78% were seropositive and 22% seronegative. Thirteen percent had psoriatic arthritis (n=10) and 30% ankylosing spondylitis (n=24). 57% (n=45) were taking etanercept and 43% (n=34) adalimumab. The percentage of patients in remission at 24 months was 56% (n=44). This resulted in an actual saving to the state of approximately 600,000 euro over two years. This study demonstrates the reduction in biologic dosing frequency is feasible in Inflammatory Arthritis. There was a considerable cost saving at two years.

Discussion

This study provides further evidence that biologic dose reduction is feasible in Rheumatoid arthritis, Psoriatic arthritis and Ankylosing Spondylitis. A number of studies, both prospective and observational, have in recent years shown significant proportions of patients remaining in remission between 1 and 2 years after dose reduction. The studies have generally used the two most commonly prescribed sub cutaneous biologic agents, Etanercept and Adalimumab. They include relatively small numbers of patients but consistently show a pattern of remission.
maintenance. The rate of remission maintenance varies with the type of inflammatory arthritis, and in general appears lower in rheumatoid arthritis. In Ankylosing Spondylitis approximately 70 to 80 percent appear to remain in remission, with figures of 60 to 70% in Psoriatic Arthritis and 30 to 40% in Rheumatoid Arthritis. In our study the percentage overall of those with Inflammatory Arthritis maintaining remission fell from 83% at 3 months to 56% at 2 years. Only one of the patients in our study, where a single dose of MethylPrednisolone 120mg settled the flare. This was a ‘real world’ decision as it would have seemed excessive to effectively double patients’ biologic dose back to the licensed dose on account of what was frequently a brief flare. While this study included Etanercept and Adalimumab, dose reduction may be possible with other anti-TNF agents and other biologic agents with different targets and mechanisms of action such as Tocilizumab, Abatacept and Rituximab. While the advent of biosimilars should reduce biologic cost by 20-30 percent, the cost of dose reduction offers the potential for savings of at least a similar magnitude. The cost implications of successful dose reduction are considerable. Major cost savings have already been shown in dose reduction studies. The dose frequency reduction in our study resulted in an actual saving in a small cohort of 600,000 euro at 2 years. The estimated annual cost of subcutaneous biologic agents for Inflammatory Arthritis in the Republic of Ireland is approximately 130 million euro. At an average cost of 13,500 euro per patient per annum this suggests there are c.10,000 patients with IA on these agents. It is known that in excess of 50% of patients with moderate to severe inflammatory arthritis do not achieve remission or Low Disease Activity on standard doses. If it was possible for example to successfully dose reduce 25% of those with Inflammatory Arthritis on biologic agents the savings could amount to tens of millions of euro at one year.

This study suggests reduction in biologic dosing frequency is feasible in inflammatory arthritis. It resulted in complete remission in 20% of patients who had previously failed to reach remission with standard licensed doses. A reduction in biologic dosing frequency should be considered in patients with Inflammatory Arthritis in remission or with low disease activity in Rheumatoid Arthritis.

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References