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Adherence to biologic therapy – Does it vary with ethnicity?

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ABSTRACT

BackgroundPoor adherence to therapy remains a significant barrier to improving clinical outcomes in rheumatic diseases and carries a major financial burden. It has been linked to medication related patient beliefs, which were reported to differ between ethnic groups. Little is known about these variations in biologic therapies cohorts. The purpose of this study was to identify potential determinants of adherence to biologic drugs including an assessment of the influence of beliefs about medicines and compare determinants of adherence between patients of Caucasian versus other ethnicities (OE). Relationship of adherence to disease outcome was further explored.

MethodsA prospective survey was undertaken of patients with inflammatory arthritis prescribed self-administered subcutaneous biologic therapies at our centre. Data were collected using a) self reported adherence b) five item compliance questionnaire for Rheumatology (CQR5) and c) Beliefs about Medications questionnaire (BMQ) specific-five items each for necessity and concern scales. The replies were assessed against the disease activity score measured on the day of recruitment to the survey.

Results80 patients contributed to the survey. 90% were prescribed TNF inhibitors. 40 patients were of Caucasian origin and 40 belonged to OE-predominantly of South Asian descent (85%). Disease activity score (DAS) was significantly higher in OE patients with 3.7 (standard deviation (SD) 1.3) compared to Caucasian patients with a DAS of 2.9 (1.6) ($p = 0.031$). Negative beliefs (i.e. higher concern scale scores) about therapy were significantly more prevalent (24/40) (60%) in the OE group compared to the Caucasian cohort (14/40 (35%) ($p = 0.043$). 17/40 (42.5%) of OE patients were poorly adherent to biologic therapy compared to 12/40 (30%) of Caucasian participants ($p = 0.308$). Most respondents (68/80, 85%) agreed that their biologic therapies were necessary for their health. Amongst 12/80 (15%) who disagreed, only two were in the non-adherent group.

ConclusionTo our knowledge, this is the first study to demonstrate ethnic differences in disease activity score and related negative beliefs regarding subcutaneous biologic therapies in people with rheumatic diseases.

1. Introduction

Over the past decade the outcomes of autoimmune inflammatory disorders have altered dramatically thanks to the use of biologic agents. These therapies have led to a sea change in the management of inflammatory arthritis with unprecedented improvement in the signs, symptoms and radiographic damage associated with RA, resulting in improvement in functionality and quality of life [1]. However, these goals are only achievable if patients are adherent to their biologic therapy. Considering these agents are more expensive and generally employed to treat more severe disease, in a financially strapped health care environment, the economic impact of lack of adherence to biologics is arguably more profound.

Adherence to medication is generally defined as the extent to which patients take their medicine as prescribed by their health care professional [2]. Good clinical outcomes are unlikely if patients fail to have their therapy as advised. In addition to carrying increased morbidity and potential mortality burden, there are economic concerns for any health care system. However, it is well established that adherence to therapy in chronic conditions is disappointingly low particularly after the first six months of therapy [3]. Research in patients prescribed disease modifying anti-rheumatic drugs (DMARDs) shows a similar

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picture with estimates ranging from 30% to 80%, depending on the definition of adherence and methodology of measurement used [4]. Poor adherence (PAD) to DMARDs is an increasingly recognised barrier to achieving good clinical outcomes in rheumatic diseases and carries major monetary burden [5].

There can be several causes why such patients may show PAD including health care, socioeconomic, disease, drug or patient related factors at interplay [6]. Evidence suggests that medication related beliefs predict adherence more strongly than socio-demographic or clinical factors [7]. Such beliefs related to PAD are reported to be more prevalent in some ethnic groups [8]. For instance, South Asian RA patients are reported to hold more negative beliefs about DMARDs than White British RA patients [9]. Similarly, they are more likely to use alternative medicine [10,11]. There are similar data from Hispanic populations as well [12]. However, little is known about these variations in biologic therapies cohorts.

Several studies have examined adherence to biologics in RA, with adherence rates reported as low as 32% to near 70% [13–15]. However, most utilised US prescription claims datasets for their analyses which are prone to methodological flaws. Claims database are mainly used for billing purposes. Hence a period of no claim does not confirm PAD, rather a possible interruption perhaps following an infection or at doctor's discretion. Another issue is that these studies do not examine the relationship between PAD and treatment response [16–19].

A more recent study however did investigate the relationship between self-reported adherence to subcutaneous TNF antagonists and response to treatment in a cohort of patients with RA. Patients commencing SC TNF inhibitors were recruited for this study from the prospective arm of the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS). 27% were reported to be non-adherent to their biologic therapy with significant association with poorer disease outcome measured by disease activity score-28 (DAS28). This study however did not explore the causes of non-adherence or any ethnic differences in the study population [20].

We undertook a cross-sectional survey of our patients prescribed self-administered subcutaneous biologic therapies where DAS28 was regularly recorded for their disease assessment. Our centre caters to the needs of 315,000 inhabitants. 40% of the population is composed of ethnic minorities predominantly of Indian subcontinent and Afro-Caribbean descent. Hence it provided us an opportunity to evaluate results in this context.

The purpose of this study was three fold:

a) to identify whether PAD exists in an ethnically diverse patient case-mix prescribed subcutaneous biologic DMARDs at a large urban rheumatology centre
b) to explore the relationship of adherence to biologics and disease outcome measured by validated disease activity score
c) to study the influence of beliefs about medicines as a potential determinant of adherence to biologic agents with a focus on comparison between patients of White and other ethnic origins.

2. Methods

A prospective survey of adult patients presenting consecutively to routine outpatient biologic clinic with rheumatic diseases [RA and peripheral spondyloarthropathy (pSpA)] was undertaken. All RA patients who underwent routine DAS28 assessment were included. Only those pSpA patients who had rheumatoid distribution of joint involvement and where DAS28 was historically used to measure disease activity were recruited. DAS28 had been documented when the patients attended for a routine follow up appointment. Consecutive patients with above criteria were approached by WM to discuss the survey and obtain informed consent prior to their appointment with their respective clinician. As WM did not work in the Rheumatology department, it helped reduce interview bias. Only patients prescribed self-administered subcutaneous biologic therapies for over a year were included in the survey. The cutoff was chosen to ensure the prospective participants had sufficient exposure to the drug and had settled on a stable dose. As biologic therapy can only be commenced in persistently high disease activity in the UK, it helped to exclude primary drug failures and those continuing therapy for disease concerns. Study period was pre-specified as two months.

2.1. Data collection

Data was collected using the following (Table 1):

a) Self reported adherence employing a single question:

When you were last due to take your biologic injection for your arthritis, did you take it:

On the day agreed with your doctor/nurse?
A day before or after the agreed day?
Within a week of the agreed day?
More than a week before or after the agreed day?
Not at all?

This has been previously used in the study by Bluett et al. [20]. Patients were considered adherent if they took their injection on the day prespecified with their health care provider.

b) Previously validated five item compliance questionnaire for Rheumatology (CQR5): In addition to above single self-reported question, adherence was also assessed with CQR5. The 5-item CQR (CQR5) has been previously validated for conventional DMARD therapy prescription in RA patient cohort [21]. CQR5 is a condensed questionnaire that is quicker and easier to administer however maintaining a good level of reliability and validity. Each 5 item in CQR presents a statement, which is related to adherence rated on a 4-point Likert scale ranging from 1 (do not agree at all) to 4 (agree very much). By using CQR5 Adherence Calculator, an estimation of whether the patient is a “high adherer” or a “low adherer” was calculated and the results were presented in dichotomous scale.

Employing two adherence questionnaires allowed more confidence in the results as the single item questionnaire has not been fully validated and CQR5 has never been utilised in biologic cohorts.

c) Beliefs about Medications questionnaire (BMQ) specific- The BMQ specific consists of two five-item scales assessing patients' beliefs about the necessity of prescribed medication (in this case their SC biologic therapy) for controlling their disease and their concerns about potential side effects of taking it [14]. Participants indicate their degree of agreement with each statement on a five-point Likert scale, ranging from 1 = strongly disagree to 5 = strongly agree. Scores obtained for individual items within both scales are added. Thus, total scores for the Necessity and Concerns

Scales range from 5 to 25. Higher scores indicate stronger beliefs. A necessity–concerns differential is calculated as the difference between the necessity and the concerns scales, with a possible range of −20 to