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LETTER

Antifibrotic Drug Adherence, the Patient, the Clinical Service and the Delivery Courier

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Abstract

Aims/Background Antifibrotic medication aims to slow disease progression for those with pulmonary fibrosis and is expensive with a known side effect profile. We have reviewed antifibrotic adherence in a real-world patient cohort.

Methods We selected a random sample of 30 patients prescribed nintedanib for idiopathic pulmonary fibrosis, conducted telephone interviews collecting demographic data and evaluated adherence using the Medication Adherence Report Scale (MARS-5) and the Adherence Starts with Knowledge (ASK-20) survey.

Results 21 (70%) of patients were male and 9 (30%) were female, the median age was 73.8 years. 13 (43%) had no qualifications, 6 (20%) had GCSE/O levels or equivalent, 6 (20%) had AS/A levels or equivalent and 5 (17%) had a higher degree. The median MARS-5 score was 23.5 (range 16–25) suggesting an extremely high level of adherence among this patient group.

Conclusion This study offers insights into medication adherence in a patient group that has not been extensively reviewed before. In this single centre study, there is good adherence to antifibrotic medication. This is likely related to the extensive clinical support provided, which is responsive, accessible, and individualised. Participants specifically mentioned this support when questioned.

Key words: idiopathic pulmonary fibrosis; nintedanib; adherence; pulmonary fibrosis; antifibrotic medication

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Introduction

Pirfenidone and Nintedanib are antifibrotic medications, aimed to slow disease progression, and are approved by National Institute for Health and Care Excellence (NICE, 2013; NICE, 2015) for Idiopathic pulmonary fibrosis (IPF). Nintedanib has been approved by NICE for the use in progressive pulmonary fibrosis Interstitial Lung Disease (PF-ILD) (NICE, 2021) where progression is demonstrated irrespective of the aetiology. This is a positive step forward for those with pulmonary fibrosis other than IPF, allowing access to nintedanib, increasing the number of patients receiving this drug but also the burden on the clinical support services.

Antifibrotic drugs are expensive (Monthly Index of Medical Specialties (MIMS), 2025). The published list price of pirfenidone is similar to nintedanib in the UK,

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i.e., £71.70/day (1 USD = 0.804 GBP, exchange rate as of 2023) when pirfenidone is administered at the full dose of 2403 mg/day and nintedanib at 300 mg/day (Rinciog et al, 2017).

Taking medication at the advised dosing regime is the optimum for pharmacological efficacy. The World Health Organisation (WHO) has reported that adherence amongst patients with chronic diseases averages only 50% in developed countries (Burkhart and Sabate, 2003). Poor medication adherence is known to contribute to morbidity, mortality, and health costs (Brown and Bussell, 2011). Medication intolerance, a therapy-related factor, can be a significant contributor to low patient medication adherence (Burkhart and Sabate, 2003), both Pirfenidone and Nintedanib are associated with side effects and intolerance in some patients (Ley et al, 2011).

Antifibrotic adherence has not been extensively reviewed and published and is not part of standard clinical practice despite the negative impact of nonadherence.

WHO defines adherence as 'the extent to which a person's behaviour (including medication-taking) coincides with the agreed recommendations from the health care provider' (Brown and Bussell, 2011). Measuring adherence can be performed with subjective approaches, e.g., self-reporting questionnaire (SRQ), pharmacy script counts, pill counts, or objective measures, e.g., directly observed therapy, drug level monitoring, and electronic dispersing device (Lam and Fresco, 2015). Objective measures are expensive and often not practical in-service evaluation.

The study has shown subjective measures correlate with objective measures. SRQs and healthcare professional assessments are the most utilised tools for assessing adherence in the clinical setting. There is an inherent risk of patients overestimating adherence in SRQs, however, this is offset by the ease of administration and low costs (Monnette et al, 2018).

The Medication Adherence Report Scale (MARS-5) is an SRQ shown to have good reliability and validity across different medical long-term conditions. It utilises a self-reported adherence scale which assesses both intentional and nonintentional nonadherence and is designed to minimise social desirability bias and presents a setting where non adherence is considered normal (Chan et al, 2020).

The ASK-20 is a SRQ with 20 domains around adherence that aim to identify potential actionable barriers. It has been validated across multiple chronic diseases including lung diseases (Hahn et al, 2008).

Patient interviews incorporating pill count and experience of the drug delivery service is a further measure of adherence and can then be corroborated with pharmacy script counts (Fredericksen et al, 2014).

We aimed to review medication adherence within the clinical setting to enable understanding of the needs and behaviours of those with fibrotic lung disease as well as barriers to treatment allowing adherence improvement and patient outcome.

Methods

A random sample of 30 patients was prescribed Nintedanib for IPF from the ILD clinic at a specialist ILD centre in the UK. The patients were selected by a

random allocation from the excel database of patients prescribed nintedanib. 30 patients were selected as a sample size to achieve the point of saturation in the homogenous population in this qualitative study.

They participated in a telephone service evaluation which consisted of four parts:

(1) Patient demographics (Age, gender, marital status, education level, mode of medication administration, number of regular medications, pharmacy delivery arrangements).

(2) Medication Adherence Report Scale (MARS-5).

(3) Adherence Starts with Knowledge (ASK-20) adherence barrier survey (only completed for those who scored less than 20 on MARS-5 suggesting poor adherence).

(4) Patient experiences of the medication delivery service by courier.

For the MARS-5 adherence questionnaire, the interviewer read out the question and recorded the response *ad verbatim*. The MARS-5 covers five domains; forgetfulness, dose adjustments, routine, frequency and omittance. Patients grade each domain from always to rarely and scored out of five. Total scores are calculated. Scores less than 20 were considered poor adherence.

Patients who scored less than 20 proceeded to the 'Ask-20 barriers to adherence questionnaire' again the interviewer read out the question and recorded the response *ad verbatim*.

Finally, an over-the-phone pill count of the remaining medication in their possession and the date of last pharmacy delivery was completed. At this centre antifibrotic medication prescriptions are reviewed by the pharmacy and 6-month prescriptions are issued to an external company, Polar Speed, who then deliver at 4–8 week intervals. Delivery of medication is handled externally and therefore validation of pill counts is not feasible in this service evaluation.

Each telephone interview took around 20 minutes to complete and was conducted between January 2023 and February 2023.

Results

21 (70%) of patients were male and 9 (30%) were female, the median age was 73.8 years.

Regarding the highest educational level achieved; 13 (43%) had no qualifications, 6 (20%) had GCSE/O levels or equivalent, 6 (20%) had AS/A levels or equivalent and 5 (17%) had a higher degree.

73.3% of patients were on more than 5 medications including antifibrotic medication, the majority 27 (90%) of patients organised their own medication.

The median MARS-5 score was 23.5 (range 16–25) suggesting an extremely high level of adherence among this patient group. Only 2 patients scored less than 20 on MARS-5.

Comments from the survey relating to the reasons for nonadherence were primarily side effect related.

• ‘sometimes holds medication due to diarrhoea’
• ‘occasional diarrhoea causes them to miss a dose’
• ‘holds when has diarrhoea temporarily held whilst having gall bladder removed’
• ‘due to S.E of diarrhoea’

Other reasons for non-adherence were due to lack of understanding of medication and situational.

• ‘didn’t understand how to medication and need a big meal before taking it—was confused about how to take the medication’
• ‘currently frail and wife has been admitted to the community hospital who had been managing medication’
• ‘has mild dementia and her husband got diagnosis of cancer so forgot to take medication due to stress and memory’

As only 2 patients scored less than 20 on MARS-5, there were only results for 2 patients for the ASK-20 adherence barrier survey. They attributed their lack of adherence to forgetfulness and taking less than the recommended dose because they did not feel it was working and/or it made them feel bad.

Home delivery was not an issue for most 20 (67%), but 10 (33%) reported issues including.

• ‘currently has no tablets—has been chasing Polar Speed, frustrated has to wait in for deliveries when life limiting disease’
• ‘Frustrated that has to stay in all day to wait for a prescription. Has oxygen two so two days a month has to wait around when has life limiting condition.’

Conclusion

This study offers insights into medication adherence in a patient group that has not been extensively reviewed before.

In this single centre study, there is good adherence to antifibrotic medication. This is likely related to the extensive clinical support provided, which is responsive, accessible, and individualised. Participants specifically mentioned this support when questioned.

Delivery of medication by courier remains an issue and impacts on quality of life, and remains questionable as to whether this is the best option for this group of patients.

Further work is required to better understand the needs and behaviours of those with fibrotic lung disease and barriers to treatment to further promote adherence and improve patient outcomes.

Key Points

- Pulmonary fibrosis is a progressive life limiting disease, antifibrotic medication aims to slow disease progression but is expensive and has side effects that some patients cannot tolerate.
- Poor adherence to medication results in reduced clinical efficacy, this study aims to review adherence in this randomly selected group of 'real world patients', adherence has not been extensively studied in this group of patients before.
- Adherence was found to be good, potentially reflecting the clinical support required and received by this patient group.
- There are outstanding issues regarding drug delivery that require further input and review.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Author Contributions

JN, EK, SVF and NW designed the research study. JN, EK, NW and WWS performed the research. JN, EK, NW and WWS analyzed the data. EK wrote the first draft. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

No ethics approvals were required as this was a service review. The patients gave verbal consent prior to the starting the questionnaire, and they were made anonymous for data processing purposes. The study was carried out in compliance with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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