Maintenance programmes following pulmonary rehabilitation in idiopathic pulmonary fibrosis: exercise, drugs and rock n' roll

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The evidence for pulmonary rehabilitation (PR) as a non-pharmacological management strategy for people with idiopathic pulmonary fibrosis (IPF) is consistent and continues to accrue. Meta-analysis has demonstrated that it effectively improves exercise capacity, dyspnoea and health-related quality of life,[1] and preliminary data suggest that improved physical performance following PR is associated with improved survival.[2] However, these benefits are short-lived, lasting no more than 6 months.[1] Despite this, no study has investigated strategies to maintain the benefits of PR in IPF, although two have been undertaken in interstitial lung disease (ILD) and demonstrated maintenance of benefit at 6 and 12 months post-PR.[3][4]

The development of pharmacotherapy was a watershed moment in the management of IPF and is now part of standard treatment for select individuals. In particular, nintedanib slows the decline in measures of disease severity[5] and it is hypothesised that there may be a cumulative benefit on exercise capacity by combining nintedanib and exercise. However, due to the relatively recent availability of this therapy, there are limited data, with retrospective analyses reporting conflicting results on the short-term effect of antifibrotic therapies plus PR on exercise capacity.[6][7]

In this edition of Thorax, Kataoka et al report the results of a multicentre randomised controlled trial undertaken in Japan that compared the effect of PR plus a maintenance programme to usual care (no intervention) on 6 min walk test distance (6MWD) at 52 weeks in 88 participants with IPF prescribed nintedanib with select modified MRC and 6MWD criteria.[8] The PR programme, conducted in line with international guidelines,[9] involved twice weekly supervised exercise and education sessions and twice weekly unsupervised home exercise sessions for 12 weeks. The 40-week maintenance programme was a combination of unsupervised home exercise and a supervised PR session undertaken at least monthly.

A large proportion, 84%, of participants in both groups completed the trial. There was no significant between-group difference in the primary outcome, 6MWD or other secondary outcomes (forced vital capacity, dyspnoea, health-related quality of life,

psychological symptoms, physical activity) at 52 weeks. However, there was a significant between-group difference in cycle endurance time at 52 weeks favouring the intervention group, although the trial was slightly underpowered to detect a difference in this outcome.

The authors should be congratulated for undertaking this important research which is the first to investigate the effect of PR plus a maintenance programme on participants with IPF who were prescribed nintedanib. Additional strengths include recruitment from 19 sites and a sample size with sufficient power to detect a change in the primary outcome (6MWD), although no significant change was demonstrated. This trial would be challenging to conduct in some parts of the world due to ethical considerations, as PR is part of standard treatment. However, it clearly demonstrates the importance of including PR in standard treatment as there was no significant difference in 6MWD or cycle endurance time in the control group (nintedanib) at 12 weeks, in contrast to the intervention group (nintedanib plus PR). In addition, there was a significant within-group difference in the intervention, but not the control group and a significant between-group difference favouring the intervention group in cycle endurance time at 26 weeks, although the study was not adequately powered to detect this difference. In ILD, the benefits of PR are known to wane 6 months after programme completion. This research suggests it is possible to significantly improve endurance capacity at this timepoint using a combination of PR plus a maintenance programme. Future research should corroborate these data.

It is important to consider why the intervention was not superior to usual care at 52 weeks, in particular the expected effect of the intervention, primary outcome as well as PR and maintenance interventions, as this may influence future research in this area.

The study was powered to detect whether the intervention was superior to usual care. Given the trajectory of IPF, it is plausible that the intervention may not in fact result in improvement in the primary outcome, but rather maintain or slow the decline in this outcome. Therefore, future trials should be designed and powered to test these hypotheses.

Cycle endurance time was a secondary outcome measure but may have been more suitable as the primary outcome given that endurance capacity has been shown to be more sensitive to change following PR than exercise capacity.[10] The trial was slightly underpowered to detect a difference in cycle endurance time, and although there was no significant difference in this outcome in the intervention group at 52 weeks, there was a significant between-group difference at this time point. When designing future trials, researchers in collaboration with patient representatives should consider what is the most appropriate outcome measure for this type of intervention, for example, endurance capacity, quality of life or given the possible signal associated with PR, survival.[2]

The PR intervention was delivered in line with international guidelines on PR.[9] Although there was a significant improvement in 6MWD following PR in the intervention group, the results were not clinically significant as the mean improvement (18 m) was below the minimal important difference (30 m).[10] This may have negatively impacted the effect of the maintenance programme.

There is a framework to guide the development and testing of complex interventions including interaction of the intervention with context, underpinning programme theory, stakeholder involvement and intervention refinement.[11] Although the maintenance programme was similar to interventions that demonstrated significant long-term improvements in ILD3 the authors did not describe whether the programme was adapted for IPF. For example, qualitative research involving people with IPF cited a preference for longer PR programmes, exercise equipment at home, maintenance exercise classes delivered by a support group and social support.[12] The maintenance programme did not appear to be underpinned by a behavioural change theory to encourage long-term adherence to health-enhancing behaviours nor was it clear whether stakeholders, for example, patient representatives and PR professionals were involved in the codesign of intervention in order to enhance acceptability and adherence. Lastly the authors did not describe whether the intervention was tested and/or refined through feasibility or pilot testing. These are factors which should be considered in future research.

In conclusion, this study demonstrates the importance of including PR as part of the standard management strategy of people with IPF prescribed nintedanib, and suggests that a maintenance programme may improve endurance capacity. These are important contributions to the literature on PR for people with IPF. Future research of PR maintenance programmes should incorporate intervention codesign, be underpinned by behaviour change theory and consider the most relevant primary outcome as well as the likely effect of the intervention on this outcome.

Ethics statements

Patient consent for publication

Not applicable.

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