Matthew Smith PhD Report

I have now been awarded a PhD from the University of Cambridge, and I am extremely grateful for the generous support of the TWJ Foundation that helped me to reach this point. The grant provided enabled me to write my thesis immediately following data collection and analysis, and before returning to full time clinical activity. I am certain this improved the quality of my writing and allowed a more in-depth analysis. I have summarised the PhD below, and would be happy to provide any further details if requested.

Research summary

Eustachian tube dysfunction (ETD) is a commonly diagnosed disorder of Eustachian tube (ET) opening and closure, which may be associated with severe symptoms and middle ear disease. The development of balloon Eustachian tuboplasty (BET), a potential new treatment for obstructive ETD (OETD), has led to a resurgence of interest in the disorder. BET involves cannulation and dilation of the ET with a high-pressure balloon, and has the potential to have a huge clinical impact if found to be effective. However, two major hurdles had prevented progress with the technique: 1) The mechanism for the intervention was unknown; 2) There was a poor understanding of how ETD should be defined, diagnosed and measured. Definitions for obstructive and patulous forms of ETD were primarily based on non-specific symptoms or examination findings, rather than measurement of the underlying function of the ET. As a consequence, patients diagnosed with ETD represented a heterogeneous group at high risk of misdiagnosis, and BET studies adopted numerous and often inappropriate outcome measures.

To explore the mechanism of BET, novel methods were employed to measure both elastic and non-reversible (plastic) deformation of the ET in human cadavers. It was found for the first time that structural changes occur during BET, that these are limited to the first inflation, and that they vary in magnitude with balloon size. Most permanent deformation of the ET appeared to occur at pressures far below those currently recommended for clinical use, and was greatest at the narrowest point, believed to be the site of obstruction in OETD. Histological and mechanical studies demonstrated that the deformation was likely to be due to crushing of mucosa, cartilage and muscle, with cracks generated in the apex of the ET cartilage. Having demonstrated that BET has a mechanical effect on the ET, next methods of selecting candidates for treatment and then measuring the clinical effect were explored.

Many tests of ET function had been proposed, both for diagnostic use or as outcome measures, but they had mostly remained poorly understood and experimental, not entering clinical use. A systematic approach was adopted to characterise, develop and optimise existing and novel tests of ET function, both symptom-based patient-reported outcome measures (PROMs), and tests that measure ET opening.

Fourteen tests of ET opening and two PROMs were then assessed for diagnostic accuracy as indicators of obstructive or patulous ETD. Given the lack of an established gold standard to diagnose ETD, two methods were adopted to establish reference standards: expert panel consensus and latent class analysis. It was found that ETD-related symptoms were non-specific, with PROMS unable to discriminate patulous or obstructive ETD from other otological conditions. Tests of ET opening correlated with one another, but not with symptoms or the clinical diagnosis of the expert panel. Latent class analysis confirmed that PROMs had no diagnostic value, and that clinical assessment appeared of less diagnostic value than tests of ET opening.

On the basis of these findings, I concluded that current methods of diagnosing ETD appear inadequate. I suggested that revised ETD definitions, and a proposed standardised diagnostic pathway and outcome set, all based primarily on the underlying ET function, should be adopted for clinical and research use. These will allow us to select patients and measure efficacy in future comparator trials designed to determine whether BET is of benefit. If found to be clinically effective, the new knowledge regarding the mechanism of BET will then allow further improvement of the device and technique.

Personal development

More than I could have predicted, the time out of training to complete the PhD has taught me how to be a researcher. Even more than broadening my understanding of study methodology and statistical analyses, I found some of the most valuable lessons related to the practicalities of funding and delivering medical research in a university or an NHS Trust. The PhD has also developed my ability to publish and disseminate research outcomes. Aside from the thesis, I have 12 papers from the PhD, eight of which have already been published. I have also presented the work internationally, and won three prizes for these talks.

I leave my PhD enthused to continue a career as an ENT trainee and then consultant actively involved with research. As a start, there are many studies relating to ETD that we now hope to proceed with, and existing and new collaborations are providing exciting opportunities. During my PhD I also helped to start INTEGRATE, the National ENT Trainee Research Network, and now taking over as Chair I hope to be able to pass on to other trainees some of the skills and enthusiasm I developed for research during my PhD.

Matthew Smith