ISRCTN16013232 https://doi.org/10.1186/ISRCTN16013232

Can the mandibular advancement devices used for sleep apnoea reduce night time reflux?

Submission date
05/09/2022

Recruitment status
No longer recruiting

Registration date
13/10/2022

Overall study status
Ongoing

Last Edited
20/05/2025

Condition category
Digestive System

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
This project tries to help with two serious problems that patients often suffer from at the same time: Obstructive Sleep Apnoea (OSA) where parts of the airway collapse during sleep and gastro-oesophageal reflux disease (GORD) where stomach acids backtracks into the mouth causing pain, chronic cough, sore throat and tooth erosion. OSA affects 24.5% of the population and 45% of these suffer from GORD. It is thought that blocking the airway increases pressure in the stomach, forcing acid into the mouth until the patient breathes again. Our PPI group have informed us that if you can manage the sleep apnoea, you can also reduce the stomach acid reflux. CPAP, the gold standard treatment for OSA has been shown to reduce night-time reflux but this has never been tested for Mandibular Advancement Devices, a not-as-effective therapy that is better tolerated by patients. MADs. As nobody has investigated this before, we need to assess practical things, like if a patient can wear reflux checking devices and sleep devices at the same time. We will see if there will be any problems experienced in the patient journey of the trial and sort through any problems that may come up when multiple teams need to work together.

Who can participate?
Patients with both OSA and reflux.

What does the study involve?
Participants will receive CPAP therapy or a MAD. We will check their reflux levels and sleep breathing at nighttime while they are wearing ther devices and compare them with their reflux levels at start of the trial. When we are confident that the trial design is good and patients are happy participating in it, we will apply for funding for a bigger trial to check if the MAD can reduce reflux, improve patient's quality of life and if this will represent a cost saving to the NHS.

What are the possible benefits and risks of participating?
There is no direct, immediate benefit to you from taking part in this research study. However, you will receive your assessment and treatments over a shorter time period, be offered both types of treatment and have increased information about your sleep device and whether it also helps your reflux. You will also have helped the dental and medical profession gain a better understanding of how sleep treatments impact on gastric reflux.

We do not know how easy it will be for patients to manage the gastric reflux pH testing, the sleep study and wear their device to treat their sleep condition at the same time. It has been done before but the comfort of this for patients has not been reported on. We think it will be slightly harder for those in the CPAP group as the facemask and pH probe may put pressure on the skin at night-time. However, everything will be done to make it as comfortable as possible. There are no lasting side effects and everything we use is standard of care and safe.

Where is the study run from?
Guy's and St Thomas' NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
April 2022 to May 2026

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Dr Saoirse O'Toole, saoirse.otoole@kcl.ac.uk
Dr Gabriella Wojewodka, gabriella.wojewodka@kcl.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Dr Saoirse O'Toole

ORCID ID
https://orcid.org/0000-0002-2144-1847

Contact details
Centre for Clinical, Oral and Translational Sciences
Floor 17, Tower Wing, Guy's Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT
+44 20 7188 7188
saoirse.otoole@kcl.ac.uk

Type(s)
Scientific

Contact name
Dr Gabriella Wojewodka

Contact details
King's College London
Oral Clinical Research Unit

Faculty of Dentistry, Oral & Craniofacial Sciences (FoDOCS)
Floor 26 Tower Wing, Guys Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT
-
gabriella.wojewodka@kcl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
304665

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 53478, NIHR202744, IRAS 304665

Study information

Scientific Title
Can mandibular advancement device treatment for obstructive sleep apnoea reduce nocturnal gastro-oesophageal reflux: a feasibility study

Acronym
MAD Reflux

Study objectives
There is a growing body of evidence that Continuous Positive Airway Pressure (CPAP) therapy, the gold standard therapy for obstructive sleep apnoea, can reduce levels of gastro-oesophageal disease by maintaining a patent airway, thus reducing intrathoracic pressure differentials. This study tests the hypothesis that mandibular advancement devices, which also maintain a patent airway, may also have a similar impact on intrathoracic pressure differentials and may improve reflux. In addition, the greater compliance observed with mandibular advancement devices may mean that reflux is suppressed for a greater proportion of the night.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 25/08/2022, East Midlands - Nottingham 2 Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 20 71048016; nottingham2.rec@hra.nhs.uk), ref: 22/EM/0157

Study design

Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Obstructive sleep apnoea and nocturnal gastro-oesophageal reflux

Interventions
Visit 1 (Screening Visit)
Medical history will be updated, and a full intraoral soft tissue and hard tissue examination will be completed. Participants will complete a reflux symptom index (RSI) questionnaire, Epworth Sleepiness Scale (ESS) questionnaire, Leicester Cough Questionnaire and a quality of life questionnaire (EQ-5D-5L).

Patients will initially attend our gastroenterology department in the afternoon of Visit 1 to have a 24-hour impedance catheter placed for reflux monitoring.

Patients will then undergo reflux monitoring using Sandhill Scientific multichannel impedance pH catheters (ZANBG44) which are inserted trans-nasally after applying local anaesthesia (xylocaine).

For the home sleep study, participants will be provided with a type 2 sleep study device, the WatchPAT 200 (WP200; Itamar Medical Ltd., Caesarea, Israel), and given comprehensive instructions on how to perform a home sleep study.

After their overnight sleep study with reflux monitoring, they will return the following day to the gastroenterology department for removal of the impedance catheter and return of the WatchPAT. The gastroenterology data will be captured by ZepHrTM recording device and data will be analysed using the BioVIEW Analysis software (5.7.1.0). The polysomnography data will be analysed by a qualified sleep technician.

Participants who meet the inclusion/exclusion criteria will be randomly allocated in a 1:1 ratio to either the CPAP (10) or the MAD (10).

Visit 2 (Intervention)
Following inclusion and randomisation, the intervention for participants will consist of either a mandibular advancement device (n=10, Somnomed Avant) with the dental sleep medicine department or continuous positive airway therapy (n=10) with the sleep medicine department.

- Mandibular Advancement Device Group
Intraoral digital impressions and a digital protrusive record will be taken using 3M true definition intraoral scanner (3M ESPE, UK). A mandibular advancement device (SomnoMed Avant, Somnomed UK) with a compliance chip for objective compliance monitoring will be constructed and fitted 3 weeks later. Following checks for fit, retention and comfort, the appliance will be titrated using subjective patient improvements in sleep and quality of life to gauge successful titration.

- CPAP Therapy Group
A CPAP mask will be fitted and patients will be issued with an autoset CPAP device (APAP, S8/S9, ResMed Ltd, Sydney, Australia) for home use. The patients will be instructed upon use.

The patients in both groups will be given a period of three weeks to become accustomed to sleeping with the device.

Visit 3 (Repeat pH impedance testing and questionnaires)
Participants will repeat the RSI questionnaire, ESS questionnaire, Leicester Cough Questionnaire and QoL questionnaire. The pH impedance testing and Watch-PAT testing will be repeated as described above. Compliance levels for the MAD and CPAP therapy on the same night will be obtained.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
mandibular advancement device

Primary outcome(s)
Current primary outcome measure as of 13/06/2023:

1. Percentage of approached patients who were screened for the trial measured using the percentage of patients eligible of those screened at Day 2 of the screening visit.
2. Percentage of eligible patients who were randomised measured using the percentage of screened patients who met the eligibility criteria versus those who were randomised at the randomisation timepoint.
3. Percentage of patients who completed the trial measured using number of patients who were randomised versus those who completed the trial at Day 2 of the final visit.

Previous primary outcome measure:

1. Patient screening to recruitment ratio
2. Patient willingness to be randomised and retention in the study
3. Acceptability of the trial and interventions in terms of the burden placed on patients such as, two impedance monitoring tests, following the same diet on the day of the test and ability to wear the Watch-PAT device and the CPAP or a MAD at the same time.

Key secondary outcome(s))
Current secondary outcome measures as of 13/06/2023:

1. Patient acceptability of the trial measured using qualitative interviews throughout the trial.
2. Hours that device is worn during sleep measured using the average number of hours worn per night as detected from the output from the therapeutic device throughout the trial period.
3. To assess the most sensitive quality of life questionnaire prior to the full trial by recording EQ-5D-5L, ICE-CAP A, and SWEMWBS at baseline and post intervention.

4. Rating of both therapies measured using a Visual Analog Scale (VAS) at Day 2 of final assessment visit (trial completion).
5. Number of potential participants identified by the care team with and without screening of referral letters measured using number of participants identified on clinics before the prescreening clinic and after the pre-screening.
6. Change in Reflux Symptom Index (RSI) using changes detected in the RSI validated questionnaire at baseline and post intervention.
7. Change in Epworth Sleepiness Scale (ESS) using changes detected in the ESS validated questionnaire at baseline and post intervention.
8. Change in cough using changes detected in the validated Leicester Cough Questionnaire at baseline and post intervention.
9. To identify and measure indicative costs and outcomes and select suitable economic outcomes measured by documenting health resource use including intervention costs, appointment times and attending health care practitioners throughout the trial.
10. To determine the acceptability of the intervention and economic data collection methods measured using qualitative questions at the qualitative interview (various timepoints).

_____

Previous secondary outcome measures:

1. To determine an estimate of effect size of the clinical effectiveness of MADs and CPAP therapy at reducing nocturnal gastro-oesophageal reflux will be assessed. This will be done both while the device is in situ to determine the effect of the device and over the entire sleep duration to assess if the numbers of hours the therapy is used influences the overall clinical effectiveness.

Completion date
31/05/2026

Eligibility

Key inclusion criteria
1. Adult patients aged 18 years old and over
2. Confirmed OSA with Apnoea-Hypopnoea Index (AHI) score between 10 and 30
3. Confirmed gastro-oesophageal reflux disease with greater than 6 percent of acid exposure time < pH 4 over 24 hours
4. Patient will not have previously had CPAP or MAD therapy
5. Sufficient healthy teeth to support a mandibular advancement device (10 teeth in each jaw, no periodontal pockets > 5, no frank cavitation or loose crowns/bridges)
6. Willing and able to provide informed consent to the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Pregnancy or breast feeding
2. Unable or unwilling to stop GORD medication 2 days prior to assessment or unable to undergo manometry and pH impedence testing
3. Known liver disease or oesophageal/gastric varices
4. Previous surgery or intervention for reflux such as fundoplication
5. Any previous treatment for oesophageal neoplasia.
6. Unable/unwilling to tolerate either a CPAP mask or a mandibular advancement device
7. Medical history likely to impact on attendance or 24-hour impedance testing
8. Participation in other research within previous 30 days

Date of first enrolment
20/02/2023

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guy’s Hospital
Oral Clinical Research Unit, FoDOCS
London
United Kingdom
SE1 9RT

Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publicly available repository (King's Open Research Data System (KORDS) (https://kcl.figshare.com/browse), full anonymised dataset will be available for 5 years as of when the results have been published). Access to the data can be provided by contacting the study's Chief Investigator.

IPD sharing plan summary
Stored in publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		24/08/2023	25/08/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version 2	16/08/2022	13/10/2022	No	Yes
Participant information sheet	version 2.0	08/03/2022	26/04/2023	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 3.0	22/09/2022	13/06/2023	No	No