ISRCTN33764131 https://doi.org/10.1186/ISRCTN33764131

Two ways to give a calming medicine to children with heart disease before submitting them to anesthesia for cardiac surgery or catheterization. Which works better for them?

Submission date
05/04/2026

Recruitment status
No longer recruiting

Registration date
09/04/2026

Overall study status
Completed

Last Edited
09/04/2026

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
The study aims to assess the safety and effectiveness of two different routes of administration of midazolam as premedication for children with congenital heart disease allocated to receive general anesthesia in the theatre or cath lab.

Who can participate?
Children aged 6 months to 8 years with heart disease allocated to receive general anesthesia

What does the study involve?
Participants are randomly allocated to receive midazolam as premedication either by mouth or under the tongue. Midazolam concentration is measured in blood samples 30 min after intake, along with blood pressure, heart rate, oxygen saturation, sedation, separation from parents, and mask acceptance.

What are the possible benefits and risks of participating?
The benefits of premedication before anesthesia are to reduce preoperative anxiety and fear and to improve anesthesia induction. Children with congenital heart problems usually undergo interventions in the operating theater or cath lab more than one time so they might be more difficult to handle due to their prior experience. They even sometimes refuse to swallow the premed and that has led us to compare an alternative route of administration, the sublingual, that requires less cooperation from the child. Even though premedication of pediatric patients with midazolam is a standard procedure in our hospital, we are aware and alert in case of possible risks such as respiratory depression, oversedation or cardiovascular effects, especially in the vulnerable pediatric cardiac population.

Where is the study run from?
Onassis Hospital (Greece)

When is the study starting and how long is it expected to run for?
July 2021 to October 2022

Who is funding the study?
Alexander S. Onassis Public Benefit Foundation (Greece)

Who is the main contact?
Theofili Kousi, t.kousi@onasseio.gr

Contact information

Type(s)
Principal investigator, Scientific, Public

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Study information

Scientific Title
Oral versus sublingual midazolam premedication in pediatric cardiac population: pharmacokinetic, hemodynamic, and behavioral outcomes

Study objectives
Dose- and age-adjusted pharmacokinetic models; age- and weight-adjusted hemodynamic models; Fisher exact tests for behavioral outcomes.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/03/2021, Ethics Committee Onassis Cardiac Surgery Center (Onasseio Nosokomeio 356 Leoforos Syngrou, Athens, 17674, Greece; +30 (0)2109493374; a.gkouvelou@onasseio.gr), ref: Β.03. Π.Ε.Ε 709 (ΙΩ Γ 010) / 25.02.2021

Primary study design

Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Uncontrolled

Assignment
Parallel

Purpose
Basic science, Treatment

Study type(s)

Health condition(s) or problem(s) studied
Pediatric cardiac surgery or cardiological intervention in the cath lab with general anaesthesia, requiring premedication

Interventions
Children receiving preoperative midazolam as premedication before cardiac surgery or cath lab intervention. Patients were classified according to administration route: oral (Σ) or sublingual (Y). The dataset contained 68 children in total (33 oral and 35 sublingual). Date of birth was used to estimate age in years with 2021 as the study year; age was calculated relative to 01/07/2021 for analytic consistency.

Oral treatment group (Σ):
Generic drug name: midazolam
Dosage: 0.5 mg/kg
Method: oral route, by mouth
Frequency of administration: once
Total duration and follow-up: 30 minutes

sublingual treatment group (Y)
Generic drug name: midazolam
Dosage: 0.3 mg/kg
Method: sublingual, under the tongue
Frequency of administration: once
Total duration and follow-up: 30 minutes

Randomisation process: computer-generated random numbers

Intervention Type
Drug

Phase
Phase III/IV

Drug/device/biological/vaccine name(s)
Midazolam

Primary outcome(s)
1. Pharmacokinetics measured using plasma midazolam and 1-hydroxymidazolam concentrations at 30 min after drug administration

2. Safety measured using blood pressure, heart rate, and SpO_2 (BP values were recorded either as systolic/diastolic/MAP or as systolic/diastolic only; when MAP was not explicitly recorded, MAP was calculated as DBP + (SBP−DBP)/3) at baseline, 15 minutes, and 30 minutes after drug administration

3. Sedation measured using sedation score coded as follows: A = anxious, B = restless, Γ = calm and awake, Δ = sedated but easily woken, and E = deeply sedated. Positive outcomes for these two variables were predefined as Γ or Δ at 15 and 30 minutes after drug administration

4. Separation from parents measured using score coded as A = easy, B = mild resistance, and Γ = strong resistance; positive outcomes for these variables were predefined as A at 30 minutes after drug administration

5. Mask acceptance measured using score coded as A = easy, B = mild resistance, and Γ = strong resistance; positive outcomes for these variables were predefined as A at 30 minutes after drug administration

Key secondary outcome(s)

Completion date
03/10/2022

Eligibility

Key inclusion criteria
1. Pediatric congenital population
2. Programmed intervention in operation theater or cath lab
3. General anaesthesia required

Healthy volunteers allowed
No

Age group
Child

Lower age limit
6 Months

Upper age limit
8 Years

Sex
All

Total final enrolment
65

Key exclusion criteria
1. Age below 6 months
2. Weight below 5 kg
3. Weight above 40 kg

Date of first enrolment
14/07/2021

Date of final enrolment
02/10/2022

Locations

Countries of recruitment
Greece

Sponsor information

Organisation
Onassis Hospital

ROR
https://ror.org/02a7ga636

Funder(s)

Funder type

Funder Name
Alexander S. Onassis Public Benefit Foundation

Alternative Name(s)
Onassis Foundation, Alexander S. Onassis Foundation, Fondation Onassis, Public Benefit Foundation, A. Onassis, Public Benefit Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Liechtenstein

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available