



Effect of Music on the Reduction of the Sedative Dose During Coronary Angioplasty: A Control-case Comparison Clinical Study

MusicSeda

STUDY PROTOCOL

Version n°1.0 dated of 10/10/2018

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SIGNATURE PAGE OF THE PROTOCOL

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TABLE OF CONTENTS

SIGNATURE PAGE OF THE PROTOCOL	2
1. PROTOCOL SYNOPSIS	4
2. SCIENTIFIC JUSTIFICATION	6
2.1. CURRENT STATE OF KNOWLEDGE	6
2.2. RESEARCH HYPOTHESES	6
3. OBJECTIVES	7
3.1. PRIMARY OBJECTIVE	7
3.2. SECONDARY OBJECTIVES	7
4. STUDY DESIGN	7
5. ELIGIBILITY CRITERIA	8
5.1. INCLUSION CRITERIA	8
5.2. NON-INCLUSION CRITERIA	8
5.3. PATIENT RECRUITMENT	8
6. NATURE OF ROUTINE CARE ASSESSED IN THE RESEARCH	8
7. EVALUATION CRITERIA	9
7.1. PRIMARY ENDPOINT	9
7.2. SECONDARY ENDPOINTS	9
8. GESTION OF SERIOUS ADVERSE EVENTS	10
9. STATISTICAL ASPECTS	10
9.1. SAMPLE SIZE CALCULATION	10
9.2. STATISTICAL METHODS	10
10. SOURCE DATA AND DOCUMENTS ACCESS RIGHTS	10
11. ETHICAL AND REGULATORY CONSIDERATIONS	11
12. REFERENCES	11

1. PROTOCOL SYNOPSIS

ADMINISTRATOR	American Hospital of Paris
RESEARCH RESPONSIBLE	Gilles Boccara Department of Anaesthesia and Intensive Care American Hospital of Paris
TITLE	Effect of Music on the Sedative Use During Coronary Angioplasty
VERSION	1.0
JUSTIFICATION / CONTEXT	Music therapy has been validated in the management of chronic pain and anxiety disorders. A program of music therapy will be proposed by the American Hospital of Paris. The objective of this study is to evaluate the effect of the music on the sedative use during coronary angioplasty.
OBJECTIVES	<p><u>Principal objective</u> To evaluate the effect of music therapy on the use of sedative medication during the intervention.</p> <p><u>Secondary objectives</u> To evaluate the effect of music therapy on anxiety and pain scores. To evaluate the effect of music therapy on physiological parameters. To evaluation patient's satisfaction.</p>
STUDY DESIGN	Non-blinded, non-randomized controlled pilot study with no follow-up visit. It is composed of two group of patients: control group without music intervention and music group. The study will measure and compare sedative medication used during the coronary angioplasty procedure.
INCLUSION CRITERIA	<ul style="list-style-type: none"> - Patients aged ≥ 18 years - Patient needs a coronary angiography and/or angioplasty - Patient gives verbal consent to participation in the study
EXCLUSION CRITERIA	<ul style="list-style-type: none"> - Patient aged less than 18 years at time of enrolment - Patient who do not agree music for cultural and/or personal reasons - Patient with serious psychiatric disorders - Patient with not paired deafness or paired one with devices that are incompatible with wearing a headset.
MUSIC SESSION	Music therapy will be administered through a hardware and software provided to the investigative team by the Music-Care Company. The music intervention will be administered via a smartphone- (and computer-) based application called Music Care.
EVALUATION CRITERIA	<p><u>Primary evaluation criterion</u> Use of sedative medications (consumptions in intravenous midazolam and/or propofol required to reach sedation score 1 from 4 and/or BIS range of 80-90) during the procedure.</p> <p><u>Secondary evaluation criteria</u></p> <ol style="list-style-type: none"> 1) Pain and anxiety scores using the Numeric Rating Scale (NRS), the Visual Analog Scale (VAS) and the Amsterdam Preoperative Anxiety and Information Scale (APAIS).



	<p>2) Physiological parameters: BIS, heart rate, systolic, diastolic and mean arterial blood pressure, oxygen saturation.</p> <p>3) Satisfaction of the patient</p>
PLANNED SAMPLE SIZE	100 patients
PLANNED CENTERS	1 centre: American Hospital of Paris
DURATION OF THE RESEARCH	<ul style="list-style-type: none">- Duration of inclusion period: 2 months- Duration of patient participation: procedure duration (around 45 minutes)- Total duration of the study: 2 months
STATISTICAL ANALYSIS	<p>Analysis of the primary endpoint</p> <p>Comparison of consumption of medication (dose) will be performed using Student t-test or Wilcoxon rank sum test (non-parametric form of student t-tests, if distribution is not normal).</p> <p>Analysis of secondary endpoints</p> <p>Secondary endpoints as quantitative variables will be analysed using Student t-test or Wilcoxon rank sum test (non-parametric form of student t-tests, if distribution is not normal). No statistical test was performed on physiological parameters.</p>
EXPECTED RESULTS	<p>To propose a new therapeutic and non-drug approach in patients undergoing coronary angiography.</p> <p>To improve the relationship between medical team and patients.</p> <p>To reduce the treatment consumption.</p>

2. SCIENTIFIC JUSTIFICATION

Anxiety, stress and pain have always been sources of emotional distress for patients undergoing invasive procedures in clinical settings.

Drug approaches such as analgesics and anxiolytics use are used to address these issues. But, with regards to new recommendations from Health Authorities, the use of pharmacological products tends to be reduced. Alternative and non-drug interventions, including music therapy, are then investigated in the next couple of years. These interventions may have the ability to reduce pain and anxiety while increasing relaxation during the procedure.

Coronary angiography is one of these procedures in which patients tend to present stress and anxiety.¹

Music therapy is a recent discipline with a trend of development in hospital services and in specialised ambulatory care centres. Several controlled studies allowed to validate the utilisation of music therapy in chronic or sharp pain, as well as in anxio-depressive disease. In this domain, the work of Stephane Guetin, psychologist and music therapist, helped using Music Care software to elaborate a standardised computerised method allowing its use by caregivers and patients themselves.^{2, 3}

Researches on music therapy effect on invasive medical procedures are few.

The demonstrated effects of music therapy on chronic pain and anxio-depressive disease allow to assume a benefic effect of this technique in the coronary angiography.

Scientific data of music therapy on patients undergoing invasive procedure are positive and suppose its interest in this indication, but additional and more specific studies are needed to evaluate its indication on this specific procedure.

The standardised and validated music therapy technique named as *Music care* seems to be a useful tool in standard cares and clinical research.

2.1. CURRENT STATE OF KNOWLEDGE

Recent clinical and neurophysiological studies made it possible to highlight the positive effect of music therapy in pain treatment⁴. By shifting the attention, music decreases muscular tension and reduces anxiety. In pre and postoperative pains, patients under music decreased their drug consumption up to 30%.

The effects of music therapy are generally related to the fact that the individualized music broadcasting improves interactive components of pain. The impact of music therapy might be due to neurophysiologic effects, specific to pain, and to the music effect on sensory (attenuation of the conduction of afferent fibres), cognitive (memory encoding, diverts attention), affective (stimulates the production of endorphins) and behavioural (psychomotricity, muscular hypertonia) components. The effect of the music therapy is based on the impact of music on the components of the painful experience and the modification of pain perception.

Psychological factors can interfere in the reduction of chronic painful phenomenon: music is chosen by the patient with his personal preferences, it allows to respond to an individual listening request. Listening to the patient after the music session allows him to evacuate their tensions.

A single music therapy session was found to be effective for decreasing anxiety and promoting relaxation, as indicated by decreases in heart rate, blood pressure, BIS and respiratory rate over the intervention period in intubated patients during weaning phase.⁵

2.2. RESEARCH HYPOTHESES

The study is based on the hypothesis of an effect of music therapy during invasive procedures using its action on the 4 components: sensory, affective, behavioural and cognitive.

3. OBJECTIVES

3.1. PRIMARY OBJECTIVE

To evaluate the effect of music therapy on the use of sedative medication during the intervention.

3.2. SECONDARY OBJECTIVES

- To evaluate the effect of music therapy on anxiety and pain scores.
- To evaluate the effect of music therapy on physiological parameters.
- To evaluation patient's satisfaction.

4. STUDY DESIGN

This is a non-blinded, non-randomized controlled pilot study with patients who will be followed during their coronary angiography procedure and with no follow-up.

Patients will be recruited from the coronary angiography patient pool of the American Hospital of Paris and assigned to one of 2 groups in a non-randomized manner. It is expected to enrol around 100 patients, and this is estimated to be obtained in a period of 2 months approximately. Patients will be placed in the control group, without music intervention, or assigned to the music group. Assignment will be done in this manner due to limited availability of the hardware and software to the investigation team. Patients in both groups will be matched based on age, sex, weight, height, American Society of Anesthesiology (ASA) score, and prior medical history, including diabetes, hypertension, chronic kidney disease and stroke. Each patient will receive a standardized sedation, using intravenous sufentanil and midazolam titration to reach Bispectral index (BIS) score below 90 and sedation score ≤ 1 .

- **Entry in the study:** Verbal consent to participation in the study will be obtained from each patient prior to enrollment. Before their inclusion in the study, patients will be verbally given details about the methods and techniques of the music session. They will be given the choice to opt out of the music session if they desired to undergo the procedure without.

- **Inclusion:** the following data will be collected: demographic and baseline characteristics, anxiety before the procedure using the Amsterdam Preoperative Anxiety and Information Scale (APAIS).

- **Music therapy session implementation**

The intervention group will administer "U" sequence between 10 minutes prior to the beginning of the procedure until its end.

- **Evaluation during the procedure: the following data will be collected:**

- consumptions in analgesics, anxiolytics and hypnotics from 10 minutes prior to the procedure until its end
- physiological parameters, such as BIS, heart rate, systolic, diastolic and mean arterial blood pressure, oxygen saturation at different time points between T0 (10 minutes prior to the beginning of the procedure) and T45 (45 minutes after it).

- **Final evaluation at the end of the procedure:** the following data will be collected right after the end of the procedure in the recovery room:

- pain and anxiety scores as measured the Numeric Rating Scale (NRS)
- satisfaction was also collected using a scale from 0 to 5, with a higher score for a high satisfaction.

5. ELIGIBILITY CRITERIA

5.1. INCLUSION CRITERIA

- Patients aged of at least 18 years
- Patients who need a coronary angiopathy and/or angioplasty
- Patients who give his informed consent.

5.2. NON-INCLUSION CRITERIA

- Patients aged less than 18 years
- Patient who do not agree music for cultural and/or personal reasons
- Patients with serious psychiatric disorder
- Patients with not paired deafness or paired one with devices that were incompatible with wearing a headset

5.3. PATIENT RECRUITMENT

Patients will be recruited from the coronary angiography patient pool of the American Hospital of Paris and assigned to one of 2 groups in a nonrandomized manner: Control or music intervention.

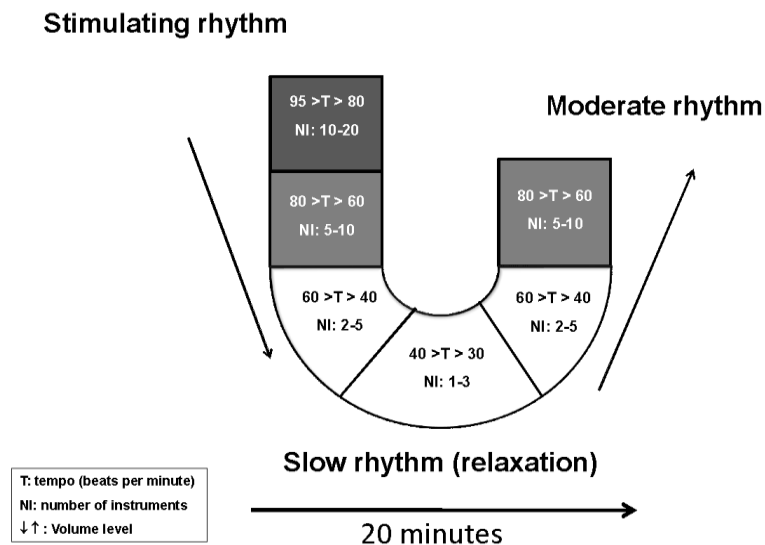
Inclusion and exclusion criteria will be checked by the responsible of the study during the inclusion visit. This study will enrol around 100 patients.

6. NATURE OF ROUTINE CARE ASSESSED IN THE RESEARCH

The Music Care app is a receptive music intervention, allowing the patient to choose the preferred style between different sequences of instrumental music. All musical pieces were recorded in high-quality recording studios with professional musicians.

Music Care utilizes the “U” technique (Figure 1), designed to gradually relax the listener. In the current study, music sequences during patients’ sessions were based on the mount “U”, and instrumental musical works were selected for a varying numbers styles (classical, jazz, world music, etc.) and adapted to the patient's style via patient request. The “U” technique is implemented using a musical sequence of 20 minutes that was divided into 5 different musical pieces at 3 to 4 minutes each. Initially, the objective is to represent the patient's state of tension by stimulating musical rhythm (80-95 beats per minute (bpm)). From there, the remaining 4 sub-pieces are presented in a blended fashion in an attempt for the patient to gradually fall into a relaxed state via a gradual reduction in musical tempo (40-80 bpm), orchestral size, frequencies, and volume (descending arm of the “U”). The music session then reaches a phase of maximum relaxation (downward phase of the “U”) before a phase that gradually returns to baseline dynamics (ascending arm of the “U”).

Figure 1: The “U” sequence



The training to *Music care* software for the doctors in charge of the study will be done by a music therapist from AM-ARC, with a validated diploma and experience in clinical research.

7. EVALUATION CRITERIA

7.1. PRIMARY ENDPOINT

Use of sedative medications.

The studied variable will be the consumptions in intravenous midazolam and/or propofol required to reach sedation score 1 from 4 and/or BIS range of 80-90 during the coronary angioplasty and/or angioplasty.

7.2. SECONDARY ENDPOINTS

- Pain and anxiety scores.

Pain and anxiety scores will be measured using the Numeric Rating Scale (NRS), the Visual Analog Scale (VAS) and the Amsterdam Preoperative Anxiety and Information Scale (APAIS) will be completed right after the end of the procedure in the recovery room.

- Effect on physiological parameters.

The following physiological parameters will be measured: BIS, heart rate, systolic, diastolic and mean arterial blood pressure, oxygen saturation between 10 minutes prior to the beginning of the procedure until 45 minutes after it.

- Satisfaction of the patient

Satisfaction will be measured using a scale from 0 to 5, with a higher score for a high satisfaction.

8. GESTION OF SERIOUS ADVERSE EVENTS

No procedure for serious adverse events is imposed by the research. Nevertheless, declaration of serious adverse events to the regional center of pharmacovigilance is mandatory for all doctor and health professional.

9. STATISTICAL ASPECTS

9.1. SAMPLE SIZE CALCULATION

As this is a pilot study, no formal sample size calculation has been performed. However, the number of participants necessary was estimated at 100 in order to get a sufficient power. Since there was no follow-up, increasing the sample size was not necessary to mitigate for missing data.

9.2. STATISTICAL METHODS

Baseline characteristics

Baseline characteristics will be summarized. Qualitative variables will be described using number of patients, percentage. Quantitative variables will be described as number of patients, mean, standard deviation, confidence interval of the mean, median, Q1, Q3, minimum and maximum.

Analysis of primary endpoint

Comparison of consumption of medication (dose) will be performed using Student t-test or Wilcoxon rank sum test (non-parametric form of student t-tests, if distribution is not normal). The analysis will be performed in intent-to-treat.

Analysis of secondary endpoints

Secondary endpoints as quantitative variables will be analyzed using Student t-test or Wilcoxon rank sum test (non-parametric form of student t-tests, if distribution is not normal). No statistical test was performed on physiological parameters.

All the tests will be realized using BiostaTGV website with $\alpha = 5\%$. A statistical analysis plan will be prepared and will detailed the different analyses.

10. SOURCE DATA AND DOCUMENTS ACCESS RIGHTS

The administrator is in charge to obtain the agreement of all the parties implicated in the research in order to guarantee direct access to source data, reports and documents everywhere the study is conducted in case of quality control and audit.

Source data or document is defined as any original document which allow to demonstrate the existence, or the accuracy of a data collected during the research.

The data will be entered in Excel. They will be managed by the investigator and stored on the computer server of the American Hospital of Paris, which will safeguard them.

11. ETHICAL AND REGULATORY CONSIDERATIONS

Since the techniques and methods used in this research are usually carried out, it can be used as part of research to evaluate routine care as defined by Law No. 2004-806 of 9 August 2004 (Article L1121-1, paragraph 2 and Article R1121-3 of the Public Health Code).

The administrator and the person(s) who directs and supervises the research undertake that this research will be carried out in accordance with Law No. 2004-806 of 9 August 2004, as well as in accordance with Good Clinical Practice (I.C.H. version 4 of 1 May 1996) and the Helsinki Declaration (which can be found in its full version on the website <http://www.wma.net/en/30publications/10policies/b3/>).

The research shall be conducted in accordance with this Protocol. Except in emergency situations requiring specific therapeutic procedures, the person(s) who directs and monitors the research undertakes to comply with the protocol in every respect.

This research received the favorable opinion of the Institutional Reviewer Board of the American Hospital of Paris.

12. REFERENCES

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