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Analgesic effect of music during laser retinal photocoagulation in diabetics: A randomized, placebo-controlled, crossover trial

Efeito analgésico da música durante a fotocoagulação retinal a laser em diabéticos: Um estudo cruzado, randomizado e controlado por placebo

Efecto analgésico de la música durante la fotocoagulación con láser retiniana en diabéticos: Un estudio cruzado, aleatorizado y controlado con placebo

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Abstract

Objective: To prospectively evaluate the analgesic effect of self-selected music for patients with diabetic retinopathy who underwent laser retinal photocoagulation (LRP). Methodology: This is a controlled, randomized, blinded, two-period crossover clinical trial. Twenty patients (40 eyes) with proliferative diabetic retinopathy who underwent LRP was enrolled. Listening to the patient's favorite music before and during the LRP was the non-pharmacological intervention. The control group (CG) was composed of patients who received only standard pharmacological treatment and the experimental group (EG) of those who received the intervention associated with standard pharmacological treatment. Pain was measured using the Numerical Verbal Scale. Differences in pain scores were tested using Aligned Rank Transformed ANOVA, Mann-Whitney U and Wilcoxon tests. The effect size of the differences was assessed using Rank Bisserial and Partial Square Effect Sizes. Results: Participants were

predominantly male (60%), adults (57.4±9.1 years), with comorbidities (65%), with visual impairment ≥ 1 year (65%). Participants who heard music had lower pain scores (EG: 4.80±2.46) compared to those who did not (CG: 6.75±1.59; p=0.013). The application of self-selected music showed a large size of the analgesic effect (η^2=0.189). Conclusion: Listening to the patient's favorite music, associated with standard analgesia, is effective in relieving acute LRP-related pain and should be incorporated into clinical practice for the multimodal treatment of pain in this procedure.
Keywords: Diabetes Mellitus; Photocoagulation; Pain management; Music; Retina.

Resumo
Objetivo: Avaliar prospectivamente o efeito analgésico da música de preferência do paciente com retinopatia diabética que foram submetidos à fotocoagaluação retiniana a laser (FRL). Metodologia: Trata-se de um ensaio clínico controlado, randomizado, cego e crossover de dois períodos. Participaram vinte pacientes (40 olhos) com retinopatia diabética proliferativa que foram submetidos à FRL. A escuta musical de preferência do paciente antes e durante a FRL foi a intervenção não farmacológica testada. O grupo controle (GC) foi composto por pacientes que receberam apenas o tratamento farmacológico padrão e o grupo experimental (GE) por aqueles que receberam a intervenção associada ao tratamento farmacológico padrão. A dor foi mensurada pela Escala Numérica Verbal. As diferenças dos escores de dor foram examinadas por meio dos testes Aligned Rank Transformed ANOVA, Mann-Whitney U e de Wilcoxon. O tamanho do efeito das diferenças foi avaliado usando Tamanhos de Efeito Rank Bisserial e Parcial Square. Resultados: Os participantes eram predominantemente do sexo masculino (60%), adultos (57,4±9,1 anos), com comorbidades (65%), com deficiência visual ≥ 1 ano (65%). Os participantes que ouviram música apresentaram menores escores de dor (GE: 4,80±2,46) comparados aos que não ouviram (GC:6,75±1,59; p=0,013). A aplicação de música de preferência do paciente mostrou um grande tamanho do efeito analgésico (η^2=0,189). Conclusão: Ouvir música de preferência do paciente, associada à analgesia padrão, é eficaz no alívio da dor aguda relacionada à FRL e deve ser incorporada à prática clínica para o tratamento multimodal da dor nesse procedimento.
Palavras-chave: Diabetes Mellitus; Fotocoagulação; Manejo da dor; Música; Retina.

Resumen
Objective: To prospectively evaluate the analgesic effect of self-selected music for patients with diabetic retinopathy who underwent laser retinal photocoagulation (LRP). Methodology: This is a controlled, randomized, blinded, two-period crossover clinical trial. Twenty patients (40 eyes) with proliferative diabetic retinopathy who underwent LRP was enrolled. Listening to the patient's favorite music before and during the LRP was the non-pharmacological intervention. The control group (CG) was composed of patients who received only standard pharmacological treatment and the experimental group (EG) of those who received the intervention associated with standard pharmacological treatment. Pain was measured using the Numerical Verbal Scale. Differences in pain scores were tested using Aligned Rank Transformed ANOVA, Mann-Whitney U and Wilcoxon tests. The effect size of the differences was assessed using Rank Bisserial and Partial Square Effect Sizes. Results: Participants were predominantly male (60%), adults (57,4±9,1 years), with comorbidities (65%), with visual impairment ≥ 1 year (65%). Participants who heard music had lower pain scores (EG: 4,80±2,46) compared to those who did not (CG: 6,75±1,59; p=0,013). The application of self-selected music showed a large size of the analgesic effect (η^2=0.189). Conclusion: Listening to the patient's favorite music, associated with standard analgesia, is effective in relieving acute LRP-related pain and should be incorporated into clinical practice for the multimodal treatment of pain in this procedure.
Palabras clave: Diabetes Mellitus; Photocoagulation; Pain management; Music; Retina.

1. Introduction

Several treatments can cause acute pain, especially the ophthalmologic procedures. Laser retinal photocoagulation (LRP) is considered the first-choice treatment for diabetic retinopathy (Evans, Michelessi, & Virgili, 2014; Song et al., 2018; Wadhwani et al., 2019). However, pain during treatment can lead to reduced therapeutic efficacy due to higher rates of abandonment of treatment, increasing the risks of visual loss (Inan et al., 2016; Quigley et al., 2019; Santo, Auge, & Ferraz, 2016).

In this context, procedural pain is highlighted by its high prevalence and repercussions, being the result of tissue and/or nervous injury resulting from health procedures (Czarnecki et al., 2011). Despite its relevance, procedural pain has been underestimated in the care environment, since it is considered inherent to the procedure without considering its deleterious effects (Cakmak et al., 2017; Lee, 2016; Song et al., 2018).

Randomized clinical trials have investigated the pharmacological management of LRP-related pain (Araújo et al., 2015; Pirelli et al., 2019; Ramezani et al., 2017; Santo et al., 2016). However, there is still little evidence to recommend the best non-pharmacological management practices for pain associated with LRP (Ribeiro, Ribeiro, Pinto, & Ribeiro, 2020). Non-pharmacological methods are important therapeutic resources for pain relief. The effectiveness of manual acupuncture in pain relief during LRP was investigated (Chiu & Wu, 2011). However, there is a knowledge gap regarding the analgesic efficacy of music in the management of LRP-related pain.

Thus, this research aimed to evaluate the analgesic efficacy of music in patients with diabetes submitted to argon LRP. Our hypothesis was that the patient's preferred listening to music associated with standard pharmacological therapy during LRP has greater analgesic efficacy than isolated pharmacological therapy.

2. Methodology

Study design and participants

This was a controlled, randomized, two-period, crossover and blinded trial developed in an ophthalmology service in Aracaju, Sergipe, Brazil. Randomized controlled trial (RCT) is a type of clinical study that test the efficacy of an intervention administered to a group, by comparing it to other group that receive no intervention or a placebo. In the crossover design, half of the participants are randomly assigned to start with the control period and then switch to active treatment; the other half begins with the active treatment and then switches to control (Hulley et al., 2013).

Sample size

The sample was composed of patients with diabetes mellitus (DM), adults (≥18 years), who had indication of bilateral argon LRP for treatment of proliferative diabetic retinopathy. The following patients were excluded: those with eye pain at the time of the intervention; those with altered hearing acuity; those who did not like music or associated it with negative experiences; and those who used analgesic in the last six hours.

The sample was simple randomized, and the sample size calculation was obtained as recommended by Chow et al. (2017) for crossover type studies, with a repetition by the following equation:

$$n = \frac{(Z_\alpha + Z_\beta)^2 \sigma^2}{2\delta^2}$$

Where Z_α and Z_β are the Z scores associated with the level of significance α and testing power 1- β; σ^2 is the variance of pain and δ^2 is the desired effect size (number of standard deviations). Thus, assuming 5% significance, 80% power of test, effect size of 0.45 (mean) and variance of 5.15, the sample size was 20 individuals (40 eyes).

Outcomes, variables, and measures

Pain was considered the primary outcome of the study. The scale used was the Numerical Verbal Scale (NVS), which ranges from 0 (no pain) to 10 (the worst possible pain). The patient reported the value corresponding to the pain score presented. Secondary outcomes were the physiological parameters of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and oxygen saturation (SpO_2) were collected before and after LRP. The variables gender, age, education, skin color, marital status, comorbidities, onset of symptoms (in years), eye in which symptoms started, and musical preference to describe the sample were used to characterize the sample.

Laser retinal photocoagulation

The argon LRP was performed under mydriasis, with administration of ophthalmologic solution tropicamide 1%, administered at the time of the patient's admission to the institution. Immediately at the beginning of the procedure, a drop of anesthetic eye drops of 0.5% proxymetacaine hydrochloride was administered, according to the institutional protocol.

The procedures were performed by two ophthalmologists of the institution, who attend in opposite shifts with standardization of the technique to ensure the safety of the patient, using the same apparatus. Standard bilateral LRP for proliferative diabetic retinopathy was performed on a PUREPOINT Laser System device (Alcon Laboratories, Inc., Fort Worth, TX). Each eye inserted in the study was treated per session, with planned number of shots between 400 and 600, with parameters initially programmed at 150 mW, 200 ms duration and 250 µm with Volk Area Centralis lens. When no greyish-white mark was reached, the potency was increased until the standard required for treatment was reached.

In the first treatment session, the right eye was included, and, after the minimum seven-day washout period, the left eye was included. In order for the analyses to be comparable, the technique to encircle the posterior pole of the retina (around the vascular arches) was standardized. The LRP technique in our test was standardized for bias reduction and was based on previous studies that showed no significant difference in the presence of pain in relation to the power of the laser shots provided (Araújo et al., 2015; Castro et al., 2014; Chiu & Wu, 2011; Ko, Shim, Lee, & Cho, 2009; Ramezani et al., 2017; Richardson & Waterman, 2009).

Allocation

To evaluate the analgesic effect of music in patients during LRP, patients were allocated to two groups: control (CG) and experimental (EG). Since this is a crossover trial, participants were randomized into two allocation sequences: initially in the EG (CE sequence) or in the CG (CE sequence) (Carvalho, Silva, Grande, 2013). The CG was made up of patients who received only the pharmacological treatment with anesthetic eye drops, according to institutional protocol. The experimental group was composed of patients who received the musical intervention, besides the administration of the anesthetic eye drops.

Intervention protocol

The music was used during the procedure, around 10 to 15 minutes long, according to the musical taste of the participant. The headphones were put on just before the session started and the volume was adjusted by the patient himself. Music was transmitted by smartphone, using the Spotify® application for your selection. Previous studies show that the use of music preferably by patients favors better therapeutic effects in reducing the painful phenomenon (Cakmak et al., 2017; Chen, Seth, Rao, & Huang, 2012; Kühlmann et al., 2018; Lee, 2016; Li et al., 2019; Lunde, Vuus, Garza-Vilarreal, & Vase, 2019; Quigley et al., 2019; Song et al., 2018).

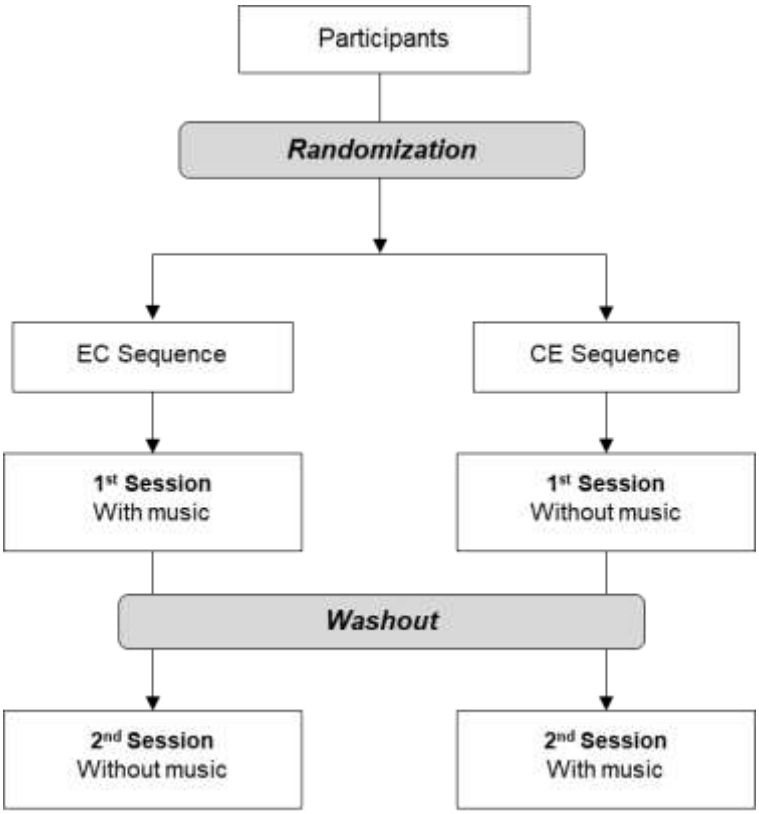
Blinding

Because it was an intervention with music, the patient could not be masked. However, the physician who performed the LRP was not aware of the patient's allocation, as the patient made use of the headset regardless of the allocation sequence. EG participants were instructed to adjust the volume of the device before the start of the session and not to communicate its allocation to the physician and the research assistant who measured the outcome. In addition, the researcher who evaluated the primary outcome was also masked for not having access to information from the randomization process.

Randomization

Randomization occurred when the patient was included in the study during the first session of the procedure (Ramezani et al., 2017) and after a minimum period of seven days (whashout), they were allocated to the opposite group, being controls themselves (Choi, Park, Bellan, & Chung, 2018), as shown in Figure 1.

Figure 1. Randomization of the crossover design.



Source: Authors.

Randomization was done by shuffling sequential numbered, opaque, and sealed envelopes, being sealed by research assistant not involved in the process after opening (Carvalho et al., 2013). Randomization control was performed by recording on the data collection instrument.

Data collection

The data collection was performed by two research assistants (Assistants 1 and 2), duly trained by the researcher for the intervention with music and data collection. The first stage was performed by Assistant 1 at the time of patient admission and consisted of an interview using a sociodemographic and clinical form. Randomization was performed at that time. Next, the participant was approached by Assistant 2, who was unaware of the patient's allocation. At this stage, the participant was guided on the use of the NVS and on the approach that would be taken after the procedure was completed. Pain and physiological parameters were measured before LRP.

At the beginning of the procedure, Assistant 1 placed the headset with or without the musical listening, according to the previous randomization, adjusting the musical volume for the participants of the EG and guiding them not to report on their listening. At that time, Assistant 2 and the doctor were unaware to which group the patient had been allocated. Finally,

Assistant 1 followed the procedure until it was finished, and activating Assistant 2 as soon as the procedure was finished, and the headset was removed. The patient was approached again by Assistant 2, who performed the pain measurement and verification of the physiological parameters immediately after the procedure was performed.

Statistical analysis

The categorical variables were described by absolute and relative frequencies and the continuous ones in the form of mean±standard deviation (SD). The associations between categorical variables were tested using Pearson's Chi-square tests with Monte-Carlo and Fisher's Exact simulations. The Shapiro-Wilk test was used to check the normality of data. Since the distribution was not parametric, the outcomes were analyzed intragroup (before versus after) and intergroup (CG versus EG) using the Aligned Rank Transformed ANOVA (ART-ANOVA) tests (Wobbrock, Findlater, Gergle, & Higgins, 2011), Mann-Whitney U and Wilcoxon.

Rank Biserial and Partial Square Effect Sizes were calculated to evaluate the effect size of observed differences. The Biserial Rank correlation has no established cutoff points, however, the closer to 1 the greater the evidence in favor of the observed difference (Kraemer, 2014) and the further away from 1 the lower the evidence in favor of the observed difference. Partial Square can be interpreted by Cohen (1988): negligible (η^2<0.01), small (0.01<η^2<0.06), medium (0.04<η^2<0.14) and large (η^2≥0.14).

Carryover effect is a statistical measure used to assess the influence of the sequence of allocation of participants in cross-studies to verify whether the initial allocation in the EG may interfere with the outcome of the second session. For this, we use the Aligned Rank Transformed ANOVA test (ART-ANOVA) (Wobbrock et al., 2011).

The level of significance adopted was 5% and the software used was the R Core Team 2020 through the ARTool (Kay & Wobbrock, 2020) and emmeans packages (Lenth, 2019).

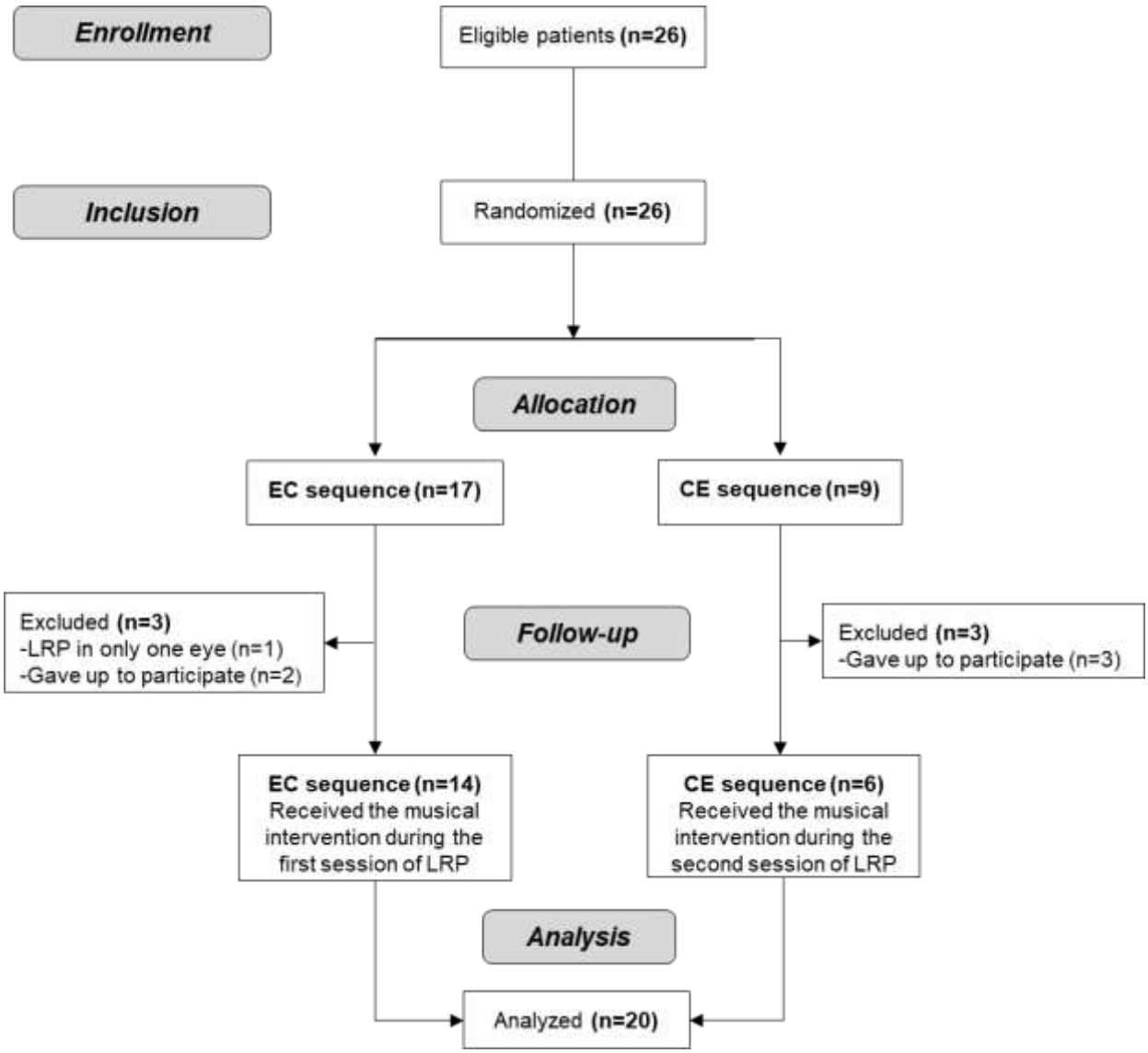
Ethical considerations

The study met the standards recommended by the Consolidated Standards of Reporting Trials (CONSORT 2010) and was registered in the Brazilian Registry of Clinical Trials - ReBEC (RBR-8NQYWT; UTN: U1111-1233-7085). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the study protocol was reviewed and approved by the local ethics and research committee (register: 85976818.4.0000.5546; ordinance: 2.587.211). Written informed consent was obtained from each patient before entering the study.

3. Results

In this study, 26 patients met the eligibility criteria, of which 17 were randomized to start in the EG and later allocated to the CG (EC sequence) and nine patients were initially allocated to the CG (CE sequence). However, six patients were excluded, resulting in a sample of 20 patients and a total of 40 eyes, as represented in the flowchart of Figure 2.

Figure 2. CONSORT flowchart.



Source: Authors.

Characteristics of participants

The Table 1 presents the baseline characteristics of study participants according to the allocation sequence.

Table 1. Baseline characteristics.

Variables	Allocation sequence n (%)		Total	p-value
	EC	CE		
Age, Mean ± SD	57.0 ± 9.5	58.5 ± 8.8	57.4 ± 9.1	0.745[T]
Sex				
Male	7 (50.0)	5 (83.3)	12 (60.0)	0.325[F]
Female	7 (50.0)	1 (16.7)	8 (40.0)	
Level of education				
≥ 8 years	7 (50.0)	1 (16.7)	8 (40.0)	0.325[F]
< 8 years	7 (50.0)	5 (83.3)	12 (60.0)	
Race/color				
Nonwhite	14 (100.0)	6 (100.0)	20 (100.0)	-
Comorbidities				
Yes	8 (57.1)	5 (83.3)	13 (65.0)	0.354[F]
No	6 (42.9)	1 (16.7)	7 (35.0)	
Time of visual impairment				
< 1 year	7 (50.0)	-	7 (35.0)	0.051[F]
≥ 1 year	7 (50.0)	6 (100.0)	13 (65.0)	
First impaired eye				
Right	3 (21.4)	2 (33.3)	5 (25.0)	0.690[Q]
Left	3 (21.4)	2 (33.3)	5 (25.0)	
Both	8 (57.1)	2 (33.3)	10 (50.0)	
Musical genre self-selected				
Regional	6 (42.9)	4 (66.7)	10 (50.0)	0.628 [F]
Others	8 (57.1)	2 (33.3)	10 (50.0)	

[Q] Pearson's Chi-Square with Monte-Carlo simulations.
[F] Fisher's Exact test.
[T]T test for independent samples.
Source: Authors.

The sample was considered homogeneous, and no significant associations were observed between the analyzed variables. It was predominantly composed of men (60%), adults (57.4±9.1 years), with low schooling (60%), with companion (65%), with non-white skin color (100%), who had other comorbidities besides the DM (65%), who had visual impairment for ≥ 1 year (65%). Half of the participants had been submitted to LRP before, the visual symptoms started bilaterally and presented regional musical preference.

Analysis of analgesic efficacy

The Table 2 shows the evaluation of the analgesic effect of music during LRP and reveals that patients who heard music had lower post-procedural pain scores (EG: 4.80±2.46) compared to those who did not hear music (CG: 6.75±1.59; p = 0.013). The song presented a large analgesic effect size (η^2=0.189).

Table 2. Analysis of analgesic effect of music.

Variables *(mean±SD)*	Intragroup analysis (Before vs. After)						Intergroup analysis (CG vs. EG)		
	CG			EG			p-value[MW]		η^2
	Before	After	p-value[W]	Before	After	p-value[W]	Before	After	
Pain intensity	0	6.75±1.59	<0.001	0	4.80±2.46	<0.001	1.000	0.013	0.189
HR	80.75±10.66	82.1±12.84	0.383	80.25±13.17	77.8±11.73	0.286	0.818	0.218	0.010
SBP	137.5±19.7	139.5±14.32	0.618	138.5±14.24	133.5±15.99	0.104	0.731	0.167	0.006
DBP	86.5±13.49	87.5±11.64	0.43	84.5±10.99	84.5±10.99	0.614	0.483	0.392	0.021
SpO_2	98.7±0.92	98.25±2.29	0.236	98.95±0.22	98.75±0.44	0.046	0.287	0.853	0.023

[W]Wilcoxon test.
[MW]Mann-Whitney U test.
η^2 eta-square.
Source: Authors.

Intragroup (before vs. after) and intergroup (before vs. before and after vs. after) analyses were performed. Before LRP, participants in both groups reported no pain (CG vs. EG: 0 vs. 0; p=1.000). On the other hand, a significant difference between pain scores was observed after painful stimulus in both groups (CG: 0 vs. 6.75±1.59; p<0.001; EG: 0 vs. 4.8±2.46; p<0.001). Regarding vital parameters (HR, SBP, DBP and SpO2), there was no statistically significant difference between the groups (Table 2).

Carryover effect analysis

The carryover effect analysis is shown in Table 3.

Table 3. Carryover effect analysis.

Analysis	F	p-value	η^2
Pain			
Group	13.30	0.002	0.423
Session	0.14	0.709	0.008
Carryover effect	1.76	0.201	0.089
HR			
Group	1.20	0.287	0.063
Session	1.16	0.649	0.009
Carryover effect	1.59	0.223	0.081
SBP			
Group	1.54	0.230	0.079
Session	0.04	0.851	0.002
Carryover effect	0.87	0.362	0.046
DBP			
Group	0.24	0.627	0.013
Session	13.17	0.002	0.422
Carryover effect	0.38	0.545	0.021
SpO_2			
Group	3.61	0.074	0.167
Session	4.73	0.043	0.208
Carryover effect	5.40	0.032	0.231

F – statistics of F test for Aligned Rank Transformed ANOVA. η^2 – Partial Eta-square. Source: Authors.

The results corroborate the previous analysis, showing that there is a difference in pain perception between the groups (η^2=0.423; p=0.002). Additionally, no influence of the allocation sequence on the analgesic effect obtained with the musical intervention was evidenced (η^2=0.008; p=0.709). On the other hand, the allocation sequence was associated with a significant difference between the means of DBP and SpO_2 between sessions.

4. Discussion

Although LRP-related pain causes physical and mental discomfort to patients, it is still underestimated since there is a gap in knowledge about the use of non-pharmacological methods for the management of pain during LRP (Ribeiro et al., 2020). To the best of our knowledge, this is the first randomized cross-blind controlled trial, which demonstrates the analgesic effect of the patient's music of choice during LRP in patients with proliferative diabetic retinopathy.

Acute procedural pain is still a neglected phenomenon in health care (Cakmak et al., 2017; Lee, 2016; Song et al., 2018), particularly in ophthalmic procedures (Araújo et al., 2015; Castro et al., 2014; Chen et al., 2012; Chiu & Wu, 2011; Quigley et al., 2019; Ramezani et al., 2017; Santo et al., 2016). These findings corroborate our results, since most of the patients who underwent argon LRP reported pain, despite the anesthetic used, which demonstrates the nociceptive nature of the procedure.

As well as several ECRs that evaluated the pain during LRP in patients with diabetic retinopathy, our study standardized the technique of LRP, since it is unrealistic to provide number of shots with the same value for all patients undergoing LRP. In this sense, a study analyzed whether the power of the shots could influence the presence of severe pain and concluded that there is no significant difference in pain intensity (Santo et al., 2016).

The ophthalmologists performed standardization by providing as much power and quantity of laser as possible, between 400 and 600 shots per session, which assumes that the final laser energy received was as corresponding as possible, in order for the analyses to be comparable, while the area treated in the first session, in the right eye, was the same as on the second day of treatment, in the left eye (Araújo et al., 2015; Castro et al., 2014; Chiu & Wu, 2011; Ko et al., 2009; Ramezani et al., 2017; Richardson, Waterman, 2009).

Procedural pain from LRP can cause deleterious effects and ineffectiveness of therapy. Thus, pharmacological and non-pharmacological measures, which can mitigate the effects of painful experience, should be instituted in health services, aiming at best practices based on scientific evidence and the promotion of patient comfort, well-being and satisfaction.

Faced with the need for adequate pain management, several non-pharmacological resources have been used as adjuvants to pharmacological treatment (Chiu & Wu, 2011; Chlan & Halm, 2013; Dik & Lohmann, 2020; Fonseca, Lopes, & Ramos, 2013; Lee, 2016; Nilsson, 2008). Among them, music is highlighted as a low-cost resource, easy to apply and effective in reducing pain (Cakmak et al., 2017; Chen et al., 2012; Chlan & Halm, 2013; Kankkunen & Vaajoki, 2019; Krishnaswamy & Nair, 2020; Lee, 2016; Li et al., 2019; Song et al., 2018). Despite the advantages cited and the safety of using music, this is the first study that investigates its analgesic effect on LRP using music of the patient's choice.

Music has been used as an adjunct to pharmacological treatment in the relief of acute or chronic pain, such as in cancer care (Krishnaswamy & Nair, 2020), during lithotripsy (Cakmak et al., 2017), during intravitreous injection procedure (Chen et al., 2012), in the care of critically ill patients (Chlan & Halm, 2013), before and during the biopsy procedure (Song et al., 2018) during image guided musculoskeletal injections (Li et al., 2019), during postoperative (Kankkunen et al., 2019) and during LRP (Quigley et al., 2019).

According to our results, the measured physiological parameters (HR, SBP, DBP and SpO_2) did not change significantly in the face of painful stimulus. The study points out that vital signs alone are not valid and reliable indicators for the evaluation of pain, since they can suffer interference from several factors, such as drugs used by the patient and their basic

diseases (Ribeiro et al., 2018). Thus, the significant carryover effect observed in the parameters of DBP and SpO_2 do not invalidate the interpretation of the analgesic effectiveness of music during LRP.

The objective of our study is similar to the one performed by Quigley et al. (2019), which sought to evaluate the analgesic effect of classical music during LRP in patients with DM. However, the results were divergent since the authors did not observe analgesic efficacy of the musical intervention. One of the hypotheses is that the analgesic effect is greater when the music is chosen by the patients themselves (Cakmak et al., 2017; Chen et al., 2012; Kühlmann et al., 2018; Lee, 2016; Li et al., 2019; Lunde et al., 2019; Quigley et al., 2019; Song et al., 2018).

This study had some limitations due to the nature of the intervention and impossibility of masking the participants. However, the professional who applied the LRP and the research assistant who measured the outcome were unaware of the allocation of participants, which reduced the potential biases. On the other hand, the main strengths were the methodological rigor of the blinding and randomization steps, the effect size and carryover effect analyses, as well as the freedom of choice of the musical genre by the patient.

In addition, the crossover designed contributed to the reduction of biases related to pain subjectivity, once cognitive-behavioral, socio-cultural and personality aspects may influence the perception of painful experience (Ramezani et al., 2017). Thus, we believe that this bias can be reduced when the patient is controlling him/herself. In cross studies there is a restriction imposed for the cases of risk of accumulation of effect of the intervention. However, because it is a musical listening, the individual did not suffer this type of risk (Dutra & Reis, 2016).

5. Conclusion

The association between the patient's preferred music listening and standard pharmacological analgesia has a greater analgesic effect than the isolated use of standard analgesia. Therefore, it is suggested that music be incorporated into the analgesia protocols during the LRP procedure to provide patients with adequate pain management, decrease the possible deleterious effects, provide humanized assistance based on scientific evidence using a low cost, effective, safe, and easy to implement resource. Once evidence to support the recommendation of the use of non-pharmacological methods in the management of acute pain during LRP is still incipient, so we suggest the conduct of new clinical trials, multicenter and with larger samples, to strengthen the power of evidence of the analgesic effect of the self-selected music in ophthalmic procedures.

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