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Non-pharmacological analgesia in children and babies beyond the neonatal age

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Abstract

Introduction: Pain is a major problem in clinical management of children. Pharmacological analgesia is the most commonly used analgesic treatment, but in some cases the use of non-pharmacological analgesic treatments (N-PAT) has been proposed.

Purpose: Our aims were to review the effectiveness and safety of N-PAT for pain relief in children, and to point out which are the most effective.

Material and Methods: We retrieved the clinical trials published in the years 2017-2022 in two databases: PubMed and Index Medicus, analyzing them with the PRISMA method. We used the following key-words: distraction, pain, child. Then we refined our search using in the same databases the key-words "pain" and "child", matched with the terms that describe the N-PAT: "Virtual reality", "Robot", "Audiovisual distraction", "Audio Distraction", "Buzzy", "Videogames", "Parents verbal interactions", "Distraction cards", "Magic glove", "Ipad", "Picture book", "Kaleidoscope", "Soap bubbles" and "Hand massage". Exclusion criteria were: reviews, case reports, papers in a language other than English, including patients other than children older than one month of age.

Results: We have screened 126 articles and 66 were excluded from the final pool. The most studied painful stimulation was needle procedures, where the most effective N-PAT was virtual reality, followed by the buzzy system. In the case of other painful procedures, few studies were available; however, in any of these painful stimulations effective analgesia was obtained with the use of virtual reality. Several studies eventually show that the combination of N-PAT with analgesic topic drugs provides more effective analgesia.

Conclusion: Some non-pharmacological treatments appear actually effective. The research in this field should be implemented to get more conclusive data, but our results are in favor of more extended use of N-PAT during potentially painful procedures.

Introduction

Pain is an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage[1].

Children may be exposed to painful interventions for the purpose of diagnosis, or treatment[2]. The painful interventions most commonly performed in children include phlebotomy, injection, and vaccination. During these interventions, it is highly important to use methods that have a pain relieving effect[3]. Pharmacologic and non-pharmacologic analgesic treatments (N-PAT) can be used separately or together to reduce the pain during invasive procedures[4]. Studies of both pharmacologic and N-PAT in procedural pain relief determined that N-PAT were as effective as pharmacologic methods[4,5,6]. N-PAT

can be preferred in relieving procedural pain, because pharmacologic methods can have side effects[7], but also because several studies support the effectiveness of N-PAT in managing the pain associated with invasive procedures in children[8,9,10]. Moreover, the non-pharmacological approach to pain prevention is important in the vision of a humanized treatment of the young patient, who needs to find a welcoming and non-stressing environment, under the condition that interventions used for optimal pain management should be effective, reliable, child-friendly, and hopefully should not extend the procedure time[11].

Several studies have been performed in the neonatal period to evaluate the efficacy of N-PAT[12,13,14], but much less in the postnatal period. For this reason, we felt that an updated review of the state of the art on N-PAT (Table 1) in older children was important.

Study Purpose

The purpose of this article is to provide a critical assessment of the evidence-based literature on N-PAT in pediatric age.

Materials and Methods

We retrieved the clinical trials published in the years 2017-2022 in two databases: PubMed and Index Medicus. In the first phase of our search, we used the following key-words: distraction, pain, child. To make our search more complete, in the second phase we searched papers in the same databases using the key-words "pain" and "child", but matching them with each of the following terms that describe the most used N-PAT: "Virtual reality", "Robot", "Audiovisual distraction", "Audio Distraction", "Buzzy", "Videogames", "Parents verbal interactions", "Distraction cards", "Magic glove", "Ipad", "Picture book", "Kaleidoscope", "Soap bubbles" and "Hand massage".

Inclusion criteria were: dealing with children with postnatal age ranging 1 month-17 years; use of a validated pain scale to assess pain; availability of raw data of pain reported by the children during the painful procedure; articles in English; fully available statistical data. We screened the whole pool of papers using the PRISMA criterion (Table 2).

Results

We found in total 197 articles of which 83 were found during the first search on databases and 114 during the second part; 71 were removed during the second search, because they were duplicates of the first research. Out of these 126 articles, 65 were excluded for reporting data on pain in newborn and adult (n=6), data not on pain (n=27), incomplete statistical data (n=11), non-English written articles (n=3), pilot studies (n=8), too small sample of babies (n=1), inability to retrieve the full text of the paper (n=10). A total of 61 articles were included in this review[75-116] (Table 2).

The included articles described the following non-pharmacological analgesia techniques: Virtual reality (n=27)[15-40], Robot (n=2)[41,42], Audio visual distraction (n=8)[21,43-48], Audio distraction (n=3)[46,47,49], Buzzy (n=17)[16,36,50-64], Videogames (n=3)[43,44,65], Parents verbal interactions (n=2)[43,66], Distraction cards (n=5)[10,16,50,51,67], Magic glove (n=1)[50], IPad (n=5)[33,39,52,68,69], Picture book (n=1)[69], Kaleidoscope (n=3)[32,49,67], Soap bubbles (n=1)[54], Hand massage (n=1)[49] (Table 3). The data on how many times the method used was significant in a given setting can be found in Table 4. Out of the 61 selected studies[15-74], 40 concern needle related procedures[16-19,22,26,27,31,32,36,38,41-43,45,46,50-62,66,67,69,71,117], 8 dental treatment[15,20,24,25,30,35,44,64], 6 medical procedures in children with burns[21,23,47,65,68,72], 4 surgery procedures[29,34,37,49], 1 endoscopic procedures[28] and 2 oncology and rheumatology disease[39,40].

Here we report the results for each painful procedure.

Needle related procedures: The most effective N-PAT were the virtual reality in 12 studies[16,18,19,22,27,31,32,36,38,117], in 2 studies it was the audiovisual distraction[43,45], in 10 the buzzy system[16,36,53-55,57-60,62], in 4 the distraction cards[10,16,51,67], in 1 the picture books[69], in 2 the kaleidoscope[32,67], in 2 the soap bubbles[54,55], in 1 the videogames[43], in 2 the parental verbal interactions[43,66], in 1 the combination of distraction cards with the buzzy system[50], in 1 the audio distraction[46] and in 1 the iPad[68,69]. In no study the robots, magic glove and hand massage were effective.

Dental treatment: The most effective N-PAT was the virtual reality in 4 study[15,24,25,30], in 2 studies it was the buzzy system[63,64] and in no study the robots, audiovisual distraction, videogames, parents verbal interactions, distraction cards, magic glove, iPad, picture book, kaleidoscope, soap bubbles, hand massage and the combination of distraction cards with buzzy system.

Table 1: The 5 most used non-pharmacological analgesia techniques with definition

VIRTUAL REALITY	Simulated experience of real or ureal situations lived through an external device (VR glasses, VR headsets)
BUZZY DEVICE	Handheld device about the size of a computer mouse that buzzes (vibrates) on the skin
AUDIOVISUAL DISTRACTION	Passive distraction like watching television or video with the phone
VIDEOGAMES	Active audio-visual distraction like PlayStation
PARENTAL VERBAL INTERACTION	Mother/father speaking and cuddling the child during procedures.

Table 2: Studies included in the analysis

First Author, year	Population	Setting	Intervention	Other intervention	Primary outcome		p-value
					Intervention	control	
15 Shetty V, 2019	N= 118 (5-8 year old)	Group 1	VR	N/A	SCL: pre 83.45 (12.03) ng/ml intra 68.45 (13.03) ng/ml post 62.55 (13.28) ng/ml WBFPS mean and median: 2.42 (1.47), 2 (0.52)	SCLcontrol: pre 78.35 (14.13) ng/ml, intra 70.72 (13.65) ng/ml, post 62.13 (13.83) ng/ml WBFPS control: 5.6 (1.22), 6 (4,6)	SCL pre-intra: p<0.001 Intra-post: p<0.001 Post-intra: p<0.001 WBFRPS: <0.001
43 Gamze Inan, 2019	N= 180 (6-10)	Group 2	AVD	VG PVI	WBFPS: AVD: 3.02 ± 2.94 VG: 1.42 ± 1.74 PVI: 2.89 ± 3.00	WBFPRS control: 5.11 ± 3.78	VG vs AVD and PVI: p<0.05 VG/AVD/PVI vs control: p<0.01 AVD vs PVI: ns
16 Birgül Erdogan, 2021	N= 142 (7-12)	Group 2	DC	VR B	WBFPS B: 0.9 ± 0.9 VR: 0.9 ± 0.9 DC: 1.4 ± 1.2 VAS B: 2.2 ± 2.0 VR: 2.7 ± 2.8 DC: 3.4 ± 2.4	WBFPS control: 2.5 ± 1.7 VAS control: 5.2 ± 2.8	WBFPS DC vs control: p<0.05 VR vs control: p<0.01 B: vs control: p<0.01 DC vs B, VR vs B e VR: DC: ns VAS: DC vs control: p<0.05 VR vs control: p<0.01 B: vs control: p<0.01 DC vs B, VR vs B e VR: DC: ns
50 Volkan Susam 2018	N= 64 (3-10)	Group 2	B + DC	MG	Integration WBFPS, VAS and NRS: B+DC: 3.66±2.02 MG: 4.74±2.07	N/A	p=0.039
17 Søren Walther-Larsen 2019	N=59 (7-16)	Group 2	VR	N/A	VAS: 27 (8 to 33)	VAS control (standard of care): 15 (5 to 30	p=0.23
45 N.C.A.C. Oliveira, 2017	N= 40 (6-11)	Group 2	AVD: G1 T1: 22 G2 T2: 18	N/A	WBFPS G1 T1: 1.91 +/- 1.68 G2 T2: 2.67 +/- 2.74 VAS G1 T1: 1.50 +/- 1.87 G2 T2: 2.33 +/- 2.54	WBFPS control: G1 T2: 3.64 +/- 3.06 G2 T1: 6.78 +/- 3.15 VAS control: G1 T2: 3.32 +/- 3.42 G2 T1: 6.28 +/- 2.86	AVD vs control: p<0.01
18 Gülçin Özalp Gerçeker 2021	N= 42 (6-17)	Group 2	VR	N/A	WBFPS: 2.4 ± 1.8	WBFPS control: 5.3 ± 1.8	p<0,01
19 Yen-yu Chen 2020	N= 136 (7-12)	Group 2	VR	N/A	WBFPS: 3.35±2.38	WBFPS control: 4.35±2.95	p=0.031
70 Zoe Grabinski, 2022	N= 40	Group 2	Distarction	N/A	WBFPS 1.4; 95% CI, 0.9-1.9	WBFPS 1.3, 95% CI, 0.5-2.1	ns
68 Sherwood Burns-Nader 2017	N= 30 (4-12)	Group 3	IPad	N/A	WBFPS: 2.53 (1.64)	WBFPS control: 3.20 (1.78)	p=0.29

20 Osama M. Felemban, 2021	N=50 (6-12)	Group 1	VR	AVD	FLACC: VR: 2.58 ± 1.99 AVD: 2.18 ± 2.29 WBFPS: VR: 2.40 ± 2.82 AVD: 2.72 ± 2.99	N/A	p=0.497 p=0.707
41 Samina Ali, 2021	N: 81 (6-11)	Group 2	R	N/A	OSBD-R: 0.78 ± 1.32 WBFPRS: 2 (0, 4)	OSBD-R control: 1.49 ± 2.36 WBFPS control: 4 (2,6)	p<0.05 p<0.13
67 Remziye Semerci, 2020	N=90 (6-12)	Group 2	DC K	N/A	VAS: DC: 2.32 ± 2.55 K: 2.72 ± 3.29	VAS control: 6.24 ± 3.93	DC vs control: p<0.001 K vs control: p<0.001 DC vs K: p<0.938
51 Sevil Inal, 2020	N=218 (6-12)	Group 2	DC	B DC + B	WBFPS: B: 1.38 ± 1.3 DC: 2.43 ± 1.3 DC+B: 0.53 ± 0.9	WBFPS control: 4.46 ± 2.9	DC/B/DC+B vs control: p<0.001
21 Henry Xiang, 2021	N: 90	Group 3	VR	AVD	VAS: IVR: 24.9 [95% CI, 12.2-37.6]	VAS control: 47.1 [95% CI, 32.1-62.2]	IVR vs control: p=0.02
44 F. Guinot , 2021	N= 68	Group 1	VG	PVR (AVD)	WBFPS: IVR: 0±0.26	WBFPS: PVR: 0.94±1.41	p=0.013
71 Aylin Arıkan, 2020	N=216 (6-12)	Group 2	ID	PD	WBFPS: ID: 2.60 (1.54) PD: 2.60 (1.54) VAS: ID: 1.50 (0.65) PD: 1.97 (0.81)	WBFPS control: 7.33 (2.41) VAS control: 3.79 (1.08)	WBFPS: control> PD > ID: p < 0.001 VAS: control>PD>ID: p<0.001
22 Fadime Ustuner , 2021	N: 77	Group 2	VR	N/A	WBFPS: 3.82 ± 1.20	WBFPS: 6.96 ± 2.08	p=0.0001
52 Cozzi, 2018	4-12y (n=200)	Group 2	B	T	Faces pain scale-revised (4-7y) Numerical rating scale (8-12y) median (IQR): B: 3 (1-4.8) T: 2 (1-4.8)	N/A	B vs. T: p=0.72
23 Le May, 2020	7-17y (n=20)	Group 3	VR	N/A	Numerical rating scale of pain (0-10) mean±SD: 3.8±3.4	control: 4.8±3.1	p=0.023
10 Risaw, 2017	4-6y (n=210)	Group 2	DC	N/A	FLACC mean±SD: DC: 2.75±0.97	control: 3.24±0.85	p<0.001
53 Redfern, 2018	3-18y (n=50)	Group 2	B	N/A	WBFS mean±SD: B: 3.56±3.2	control: 5.92±3.4	p=0.015
24 Alshatrat, 2021	5-12y (n=54)	Group 1	VR + local anesthesia	N/A	FLACC mean (SD): VR+local anesthesia: 2.588±3.001	control (local anesthesia): 5.571±3.857	p=0.0132
25 Custòdio, 2020	6-9y (n=44)	Group 1	VR +local anesthesia	N/A	Venham Scale mean (SD): AVE+local anesthesia: 0.41 (1.53)	control (local anesthesia): 1.32 (1.92)	p=0.07
69 Kuo, 2018	3-7y (n=276)	Group 2	PB	iPad	OSBD-R mean (SD): PB: 27.4 (5.6) Cartoons in iPad: 28.9 (6.3)	control (routine oral instructions): 38.5 (14.6)	PB vs. control: p<0.001 iPad vs. control: p<0.001 PB vs. iPad: ns

26 Osmanlliu, 2021	7-17y (n=62)	Group 2	VR+standard of care	N/A	Verbal numerical rating scale (0-10) median (IQR): 3 (1-6)	control (standard of care): 3 (1-5.5)	p=0,75
46 van der Heijden, 2019	3-13y (n=191)	Group 2	AD	AVD	AHTPS mean (SD): AD: 2 (2.05) AVD: 2.86 (2.62)	control (standard of care): 3.10 (2.24)	AD vs. control: p=0.006 AVD vs. control: p=0.328
27 Semerci, 2020	7-18y (n=71)	Group 2	VR	N/A	WBFS mean±SD: VR: 2.34±3.27	control: 5.02±3.35	p=0.001
28 Liu, 2020	7-17y (n=53)	Group 4	VR	N/A	WBFS mean±SD: 0.80±1.06	control (standard of care): 2.26±2.38	p=0.018
29 Buyuk, 2021	5-10y (78)	Group 5	VR	N/A	WBFS mean±SD: VR: 1.35±1.09	control: 3.00±1.52	p<0.01
30 Ran, 2021	4-8y (n=120)	Group 1	VR	N/A	WBFS mean±SD: VR: 1.62±1.13	control (Tell-show-do): 3.59±1.19	p<0.001
66 Erdogan, 2019	1-3y (n=60)	Group 2	PVI	N/A	FLACC mean±SD: PVI: 4.76±2.43	control: 7.66±3.75	p=0.000
31 Jeffrey I. Gold,2021	10-21 y (n=107)	Group 2	VR	N/A	Faces pain scale-revised mean (SD): 1.09 (1.82)	2.19 (2.21)	p=0.002
32 Tuba Koc Ozkan, 2019	4-10 y (n=139)	Group2	VR	K	WBFS mean±SD: VR: (1.76+1.4) K: (2.76+1.8)	6.65+2.2	K vs control: p<.000 VRvs control: p<.000 VR vs K: p=0.039
47 Fatemeh Cheraghi, 2021	6-12 y (n=120)	Group 3	AD	AVD	Ocher Pain Scale: mean±SD: AD:3.97 ±12.13 VD: 3.86 ±12.28	4.08±12.42	AVD vs control: p<0.001 AD vs control: p<0.001 AVD vs AD: p=0.004
33 Demet İnangil,2020	3-18 y (n=120)	Group 2	VR	Tablet	WBFS: mean±SD: VR box: 1.3±2.15 Tablet: 4.55±3.44	4.95±3.65	p<0.001
65 Xiu-Hang Zhang, 2020	1-3y (n=120)	Group 3	Medical screen	VG	MBPS: mean (SD): Medical screen: 6.78(0.82) VG: 7.775(0.80)	8.45(0.51)	p<0.001
72 Xiu-Hang Zhang, 2020	1-3y (n=52)	Group 3	Medical screen	N/A	MBPS: mean (SD): Medical screen: 6.77 (1.42)	8.50 (0.51)	p<0.001
54 Seyda Binay, 2018	3-6y (n=96)	Group 2	B	SB	WBFS mean±SD: ECV: 3.12±0.38 BSB: 2.15±0.35	7.37±0.38	B vs SB: p=0,387 B/SB versus control: p<.000
48 J.-S. Song, 2020	3-7y (n=48)	Group 3	AVD	N/A	WBFS mean (SD): 6 (22.43)	0 (15.66)	p<0,001
49 Muhammet Bulut, 2020	7-11 y (n=140)	Group 5	AD	K HM	WBFS mean (SD): AD: 1.68 (1.13) K: 1.08 (0.98) HM: 1.31 (1.10)	2.45 (0.95)	p=0,000
34 Jordan S. Taylor	6-17 y (n=70)	Group 5	VR	N/A	Verbal Pain Scale mean±SD: VR: 0.4 ±1.1	0.03± 0.2	p=0.073
35 A. Garrocho-Rangel	5-8 y	Group 1	VR	N/A	FLACC mean (SD): VEES 1.03 (2.21)	0.64 (1.31)	p=0.7
56 Yilmaz, 2020	8-16y (n=60)	Group 2	B	N/A	FACES mean (SD): B: 1.36 (1.12)	control: 1.33 (1.15)	p=0.829
57 Bourdier, 2021	18m-6y (n=607)	Group 2	B	N/A	Children's Hospital of Eastern Ontario Pain Scale mean (SD): B: 8.5 (2.6)	EMLA patch: 7.2 (2.4)	EMLA patch vs B: p<0.01

58 Bilgen, 2019	7-12y (n=150)	Group 2	B	ShotBlocker	FACES mean (SD): B: 3.64 (3.10) ShotBlocker: 6.24 (3.20)	control: 7.36 (3.09)	B vs control: p<0.01 B vs ShotBlocker: p<0.01
59 Sahiner, 2018	6-12y (n=60)	Group 2	B	ShotBlocker	FACES mean (SD): B: 1.26 (1.36) ShotBlocker: 0.9 (1.20)	control: 3.2 (2.78)	p=0.008
60 Alemdar, 2019	5-10y (n=195)	Group 2	B	SB Aromatherapy	Oucher pain scale mean (SD): B: 3.51 (3.49) SB: 4.53 (3.25) Aromatherapy: 5.46 (2.75)	control: 5.87 (2.87)	B vs control: p<0.05
61 Ueki, 2020	0-6y (n=118)	Group 2	B	N/A	FLACC mean (SD): BD: 6.98 (3.28)	control: 7.63 (2.79)	p=0.25
42 Lee-Krueger, 2021	4-12y (n=137)	Group 2	R	N/A	Faces Pain Scale-Revised mean±SD: MEDi Robot: 2.74 (2.96)	control: 2.76 (2.97)	p=0.98
55 Yilmaz, 2019	5-10y (n=120)	Group 2	B	ShotBlocker SB	Oucher pain scale mean (SD): B: 3.87 (1.79) ShotBlocker: 4.14 (2.12) SB: 4.75 (1.74)	control: 6.72 (2.16)	ShotBlocker vs Control: p<0.05 B vs Control: p<0.05 SB vs Control: p<0.05
62 Sapci, 2021	3-18y (n=90)	Group 2	B	N/A	FACES mean (SD): B: 2.44 (1.85)	control: 5.77 (2.14)	p<0.05
36 Gerceker 2018	7-12 y (n = 121)	Group 2	VR	B	WBFPS mean (SD): VR: 1.5 (0.2) B: 2 (0.2)	control: 5.1 (0.4)	VR vs control: p<0.05 B vs control: p<0.05
63 Alanazi 2018	6-7 y (n = 60)	Group 1	B + Analgesia	Analgesia	WBFPS mean rank (sum of ranks) B + analgesia: 17.50 (1759.00) Analgesia: 3.50 (10.50)	N/A	WBFPS p <0.001
64 Bilisin 2019	n = 60	Group 1	B + Analgesia	Analgesia	WBFPS mean (SD) B + analgesia: 0.867 (1.136) Analgesia: 3.333 (1.917)	N/A	p<0.01
37 Eijlers R.	4-12 y (n=200)	Group 5	VR	N/A	FPS-r: VR: 2.0 [0.0 to 4.0]	2.0 [0.0 to 2.5]	p=0.699
117 Özalp Gerçeker G	5-12 y (136)	Group 2	VR-Rollercoaster	VR-Ocean Rift	WBFS mean ± (SD) (min-max): VR-Rollercoaster=1.2 ± 2.2 (0-10) VR-Ocean Rift= 1.0 ± 1.5 (0-6)	4.1 ± 3.5 (0-10)	p=0.000
38 Aydın Aİ	(n=120)	Group 2	VR	N/A	WBFS mean ± (SD) VR: 1.68 ± 1.51	2.02±1.96	p=0.006
39 Tennant M	7-19 y (n=90)	Group 6	VR	IPad	VAS mean (SD): VR 10.97 (11.23) IPad 12.82 (11.34)	N/A	p=0.475
40 Arman N	6-18 (n=62)	Group 6	VR	TOAT	NRS mean (SD): VR: 0.64 (1.31) TOAT: 1.04 (1.62)	N/A	p=0.000

Legend: R: Robot, VR: virtual reality, AVD: audio-visual distraction, AD: audio distraction, B: Buzzy system, DC: Distraction Cards, K: Kaleidoscopic, T: tablets, VG: videogames, PVI: parents verbal interaction, SB: soap bubbles, MG: Magic Glove, HM: hand massage, WBFPS: wong baker faces pain rating scale, SCL: salivary cortisol levels, VAS visual analogue scale, NRS numeric rating scale, Others (ID: interactive distraction, PD: passive distraction, TOET, medical screen), OSBD-R: Observed Scale of Behavioral Distress-Revised; CFS: Children's Fear Scale MBPS: modified behavioural pain scale, FLACC: Face Legs Activity Cry Consolability, AHTPS: Alder Hey Triage Pain Score, ns: not significant, CI: confidence intervals
Group 1: Dental treatment, Group 2: Needle related procedures, Group 3: Medical procedures in children with burns, Group 4: Endoscopic procedures, Group 5: Surgery procedures, Group 6: Oncology and rheumatology disease therapy

Table 3: Studies screened from PubMed database

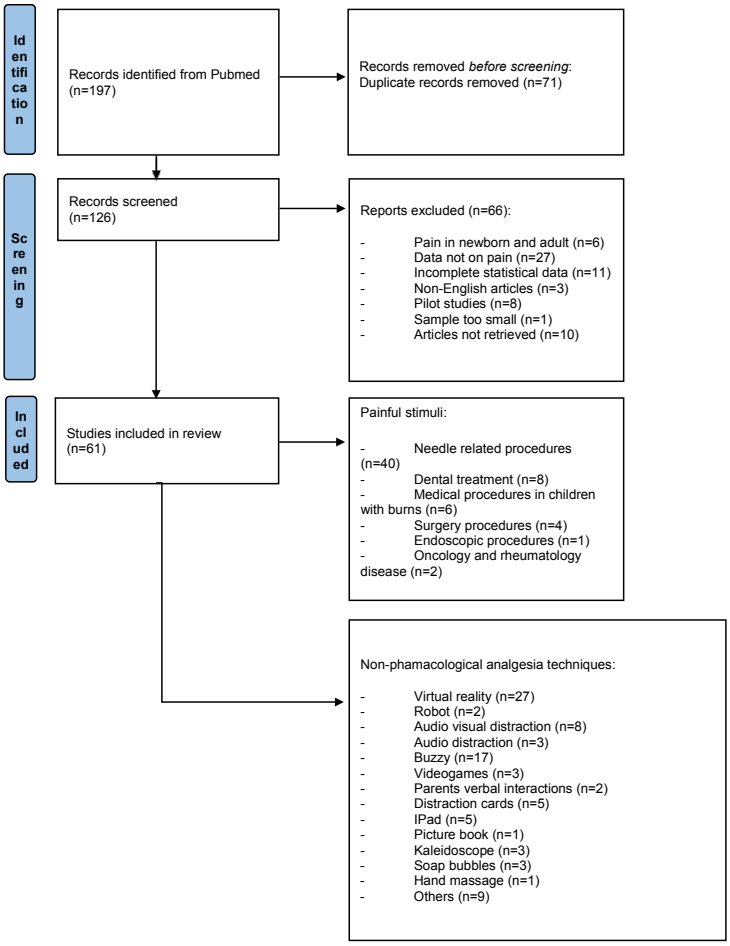

Table 4: Comparisons of non-pharmacological methods vs Standard of care

Technique vs Control	Needle related procedures	Dental treatment	Medical procedures in children with burns	Surgery procedures	Endoscopic procedures	Oncology and rheumatology disease
Virtual reality	S=12 (vs Control) NS=2 (vs Control)	S=4 (vs Control) NS=1 (vs Control)	S=2 (vs Control)	S=2 (vs Control) NS=1 (vs Control)	S=1 (vs Control)	
Robot	NS=2 (vs Control)					
Audio visual distraction	S=2 (vs Control) NS= 2 (vs Control)*		S=2 (vs Control) NS=1 (vs Control)			
Buzzy	S=10 (vs Control) NS=2 (vs Control)	S=2 (vs Control)				
Videogames	S=1 (vs Control)		S=1 (vs Control)			
Parents verbal interactions	S=2 (vs Control)					
Distraction cards	S=4 (vs Control)					
Magic glove						
IPad	S=2 (vs Control)		NS=1 (vs Control)			
Picture book	S=1 (vs Control)					
Kaleidoscope	S=2 (vs Control)			S=1 (vs Control)		
Soap bubbles	S=2 (vs Control) NS=1 (vs Control)					
Hand massage				S=1 (vs Control)		
Audio distraction	S=1 (vs Control)		S=1 (vs Control)	S=1 (vs Control)		
Others	S= 3 (vs Control) NS=1 (vs Control)		S= 2 (vs Control)			

S: Treatment group is significantly better than control; NS: No significant difference

Procedures in children with burns: The most effective N-PAT was the virtual reality[21,23]in 2 studies, in 2 studies the audiovisual distraction[21,47], in 2 studies others techniques (medical screen)[65,67], in 1 study videogames[65], in 1 study audio distraction[47] and in no study the robots, buzzy system, , parents verbal interactions, distraction cards, magic glove, iPad, picture book, kaleidoscope, soap bubbles, hand massage and the combination of distraction cards with buzzy system.

Surgical procedures (circumcision, hormone implant placement): The most effective N-PAT was the virtual reality in 2 studies[29,34], in 1 study it was the audiovisual distraction[49], in 1 study the kaleidoscope[49], in 1 study the hand massage[49] and in no study the robots, buzzy system, videogames, parents verbal interactions, distraction cards, magic glove, iPad, picture book, soap bubbles and the combination of distraction cards with buzzy system.

Endoscopic procedures: The most effective N-PAT was the virtual reality in 1 study[28] and in no study the robots, audiovisual distraction, buzzy system, videogames, parents verbal interactions, distraction cards, magic glove, IPad, picture book, kaleidoscope, soap bubbles, hand massage and the combination of distraction cards with buzzy system.

Procedures correlated to oncology and rheumatology diseases: The most effective N-PAT were the videogames[40] in 1 study and in no study the virtual reality, robots, audiovisual distraction, buzzy system, parents verbal interactions, distractions cards, magic glove, iPad, picture book, kaleidoscope, soap bubbles, hand massage and the combination of distraction cards with buzzy system.

When comparing N-PAT with pharmacological analgesia techniques, one study[57] showed the superiority of the EMLA gel over the use of the buzzy device. Two studies[63,64] showed the superiority of the combined use of buzzy device and analgesia with lidocaine compared to the use of only lidocaine. Two studies[24,25] showed the superiority of the combined use of virtual reality and local analgesia compared to the use of only local analgesics.

As for the effectiveness of NPATs based on the age of children, it seems that virtual reality is more effective in children between the ages of 7 and 12 (average age 10.8 years)[15-40]. While with regard to buzzy devices, the age at which these systems are most effective is between 7 and 10 years (average age 8.9 years)[16,36,50-64,117-121]. Unfortunately, the few published studies regarding the other techniques used do not allow to detect an evident efficacy on a certain age range of the tested children.

Discussion

This review analyzed the clinical trials conducted between 2017 and 2022 and examined which are the most effective non-pharmacological analgesic techniques in the treatment of pediatric pain. The articles analyzed compared specific N-PAT with controls.

Our search showed that virtual reality was the most often used N-PAT, moreover it appears to be the most effective compared vs control in particular in the field of venipuncture. The buzzy device system was the second most used technique. Scarce studies were developed in this period using other N-PAT (Robot, Audio visual distraction, Video Games, Parents verbal interactions, Distraction cards, Magic glove, IPad, Picture book, Kaleidoscope, Soap bubbles, Hand massage).

The use of N-PAT is important to avoid pain in children[2]. Stress and pain are factors that can alter a child's homeostasis, causing fear, increased blood pressure and tachycardia[122]. They can also cause the child's lack of compliance with the pediatrician and nurse, as well as make him lose confidence in them during future visits. The relationship with the healthcare environment must avoid being traumatic[123].

Unfortunately, children and their families still feel uncomfortable when going to a medical visit: for an ancient equation between visit and pain, saying "no pain no gain" seems always true, and analgesia during procedural pain is still scarcely used, though today we have valid tools to avoid pain as this review has shown. Pain management in pediatrics is still defined as "suboptimal"[124], and this has become a "major public health problem"[125].

Procedural pain is less painful than surgical or physically traumatic pain, but it cannot be ignored: we know that repeated stress and suffering even has a negative epigenetic effect on the expression of corticosteroid receptor genes or for the brain growth factor; repeated pain causes growth retardation of the cerebral cortex[126]. This is especially true for hospitalized patients who receive numerous painful events; the physical and psychological risks associated with pain are not absent even when pain is experienced after the first month of life[12,14].

In conclusion, despite the need for further studies, this review shows the effectiveness of several N-PAT. There is enough evidence to recommend the use of these methods, particularly in the context of skin punctures. Further studies must be conducted comparing the various N-PAT and their use in combination with drug analgesia.

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