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Review

Microneedling: Where do we stand now? A systematic review of the literature

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Skin rejuvenation

Summary *Background:* Patients who suffer from scars or wrinkles have several therapeutic options to improve the appearance of their skin. The available treatment modalities that provide desirable results are often overtly invasive and entail a risk of undesirable adverse effects. Microneedling has recently emerged as a non-ablative alternative for treating patients who are concerned with the aesthetic changes that result from injury, disease or ageing.
Objective: This review aims to evaluate the current evidence in the literature on microneedling.
Methods: A systematic literature review was performed by searching the electronic databases PubMed and Google Scholar. The reviewed articles were analysed and compared on study design, treatment protocol, outcome parameters, efficacy measurement and results to evaluate the strength of the current evidence.
Results: Microneedling was investigated in experimental settings for its effects on atrophic acne scars, skin rejuvenation, hypertrophic scars, keloids, striae distensae, androgenetic alopecia, melasma and acne vulgaris. Several clinical trials used randomisation and single-blindation to strengthen the validity of the study outcome. Microneedling showed noteworthy results when used on its own and when combined with topical products or radiofrequency. When compared with other treatments, it showed similar results but was preferred due to minimal side effects and shorter downtime.
Conclusion: This systematic review positions microneedling as a safe and effective therapeutic option for the treatment of scars and wrinkles. The current literature does show some methodological shortcomings, and further research is required to truly establish microneedling as an evidence-based therapeutic option for treating scars, wrinkles and other skin conditions.

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Contents

Introduction

Although topical therapy and invasive surgery have their specific indications in skin treatment, methods that stimulate the body's own regenerative mechanisms have currently gained popularity. Ablative modalities such as lasers, peelings and dermabrasion are based on partial removal of the epidermis to trigger the growth of new skin to replace scarred or aged tissue.[1] Experience has shown that injuring the deeper layers of the skin entails a risk of prolonged healing times, fibrosis of the papillary dermis, excessive scarring, increased photosensitivity and irregular pigmentation.[2–4] These problems prompted the development of non-ablative methods that owe their efficacy to triggering dermal neocollagenesis while preserving the stratum corneum and the epidermal barrier function. The use of energy (e.g. non-ablative lasers, fractional lasers, and intense pulsed light) for this purpose still entails some thermal injury and necrosis,[5] while the use of small needles for percutaneous collagen induction reaches the papillary and reticular dermis in a purely mechanical way. Each individual micro lesion is perceived by the skin as injury, but because the epidermal barrier is minimally disrupted, scarless wound healing will occur. This wound stage is characterised by the presence of transforming growth factor-β3 (TGF-β3), which can be traced immunohistologically and highlights the activity of non-inflammatory wound healing.[6]

Microneedling has by now found its way into clinical practice. The roller device is a drum-shaped tool with a cylindrical head that is rolled back and forth to induce thousands of tiny pores in the papillary dermis (Figures 1 and 2). In addition, there is an electronic pen-shaped device that has adjustable settings to control speed and depth of needle penetration (Figure 3). The unique, non-invasive penetration of the skin that is caused by microneedling can also serve as a way to deliver treatments like topical products or radiofrequency, without causing unnecessary damage to nearby structures. Products such as platelet rich plasma (PRP) and human stem cell conditioned medium (hESC-EPC) are used to enhance the mechanism of percutaneous collagen induction by delivering extra growth factors, while others are combined with microneedling to enhance their penetration and effects [e.g. Minoxidil, depigmenting serum and tranexamic acid (TA)]. The delivery of radiofrequency through a fractional microneedling

Figure 1 Rolling device.

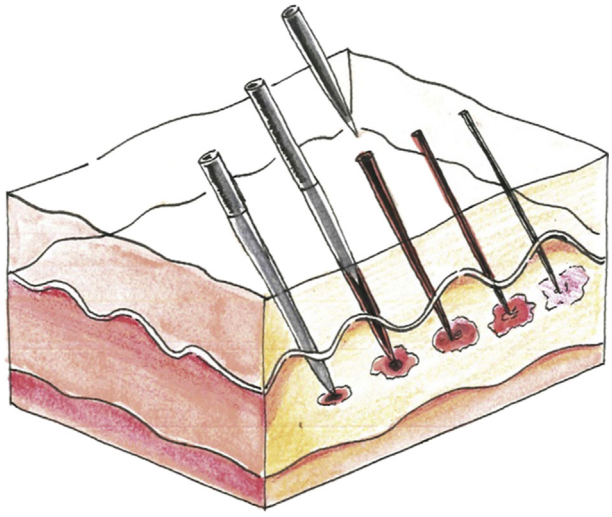

Figure 2 Dermal micro-injury induced by microneedling.

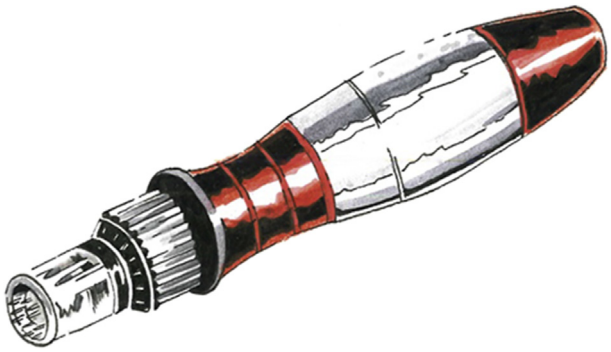

Figure 3 Electrical pen.

radiofrequency (FMRF) device causes thermal injury for therapeutic purposes directly to the dermis by generating a current between paired insulated microneedles. This overcomes the problem of poor penetration depth of bipolar radiofrequency and avoids the thermal damage that occurs with higher levels of energy, which are necessary for penetration.[7]

The trigger to form new skin can have a therapeutic benefit when injury, disease or ageing cause aesthetic changes in the skin. The advantage of avoiding the risks of pigmentation changes or scarring when compared to laser resurfacing and peelings makes it a valuable therapeutic alternative. Because microneedling is a simple treatment with a low complication rate, it was easily applied in experimental settings, and several applications have yet been explored. However, no evidence-based guidelines are presently available. This paper examines the current level of evidence by reviewing randomised controlled trials, controlled clinical trials and prospective clinical trials that assess the effects of microneedling on its own and combined with topical products or radiofrequency. All reports were critically evaluated for methodological strengths and weaknesses, and their data were summarised to estimate the existing evidence and to discuss which lack of evidence needs to be addressed in future studies.

Methods

A systematic review was performed following the PRISMA guidelines. A search for peer-reviewed published articles was performed on the electronic databases PubMed and Google Scholar, followed by a screening of the bibliographies of the included reports. Search terms included *Microneedling*, Percutaneous Collagen Induction, Dermaroller, Dermal Needling, Dermal Rolling, Micro Needle and *Skin Needling*. All terms were obtained from medical literature that describes microneedling and were combined with the Boolean operator 'OR' into one major search filter (Table 1). No limitations or language restrictions were set.

The last search was conducted on the 12th of August 2016. The retrieved articles were assessed for eligibility by screening study characteristics and outcome parameters. Randomised controlled trials, controlled clinical trials and clinical trials were included. Treatment protocols were accepted when they included microneedling alone, microneedling with topical products as well as FMRF. Studies that used microneedling in combination with other treatments that did not specify the additional benefit of microneedling in comparison with a control group were not included. Microneedling had to be a clearly determined variable in the research. An exception was made for FMRF because of its explicit technical contribution to the mechanism of radiofrequency delivery. Studies were allowed to use active and inactive controls. Outcome measures were screened for the presence of patient- and observer-based assessment and the mentioning of adverse effects.

Methodological data were extracted from the reports on a selection of study characteristics and were summarised in Table 2. The heterogeneity was reduced by grouping the reports on indication and design. Outcome data were extracted on clinical improvement reported by patient and observer, and numerical and histological outcomes. The statistically significant differences compared to control were simplified to a double plus or double minus. The statistically significant differences compared to baseline (outcomes in prospective clinical trials) were simplified to a single plus or minus. Adverse effects were simplified to a symbol when a statistical analysis was carried out.

Outcome parameters based on the judgement of patients and observers inevitably carry a subjective component. There are several well-known methodological constructions available to prevent bias from affecting the validity of findings. All included RCTs and CCTs were screened for their use of randomisation, blinding, and full outcome reporting. Attrition bias was evaluated by screening the exclusion

Table 1 Search results.

	Google Scholar	PubMed
Search term	((((microneedling) OR percutaneous collagen induction) OR skin needling) OR dermaroller) OR dermal needling	All in title: microneedling OR 'dermal needling' OR 'percutaneous collagen induction' OR 'skin needling' OR dermaroller
Results	139	156

Table 2 Methods.

	Participants	Dropouts	Intervention	Comparison	Efficacy measurement			No. of treatments	Follow-up
					Cat	Num	Histo		
Acne vulgaris									
CT									
Kim et al.	25	0	FMRF	baseline	x	x		3	12
Lee et al.	20	0	FMRF	baseline	x	x		1	8
Androgenetic alopecia									
RCT									
Dhurat et al.	100	6	MN + minoxidil	MN	x	x		12	12
CT									
Dhurat et al.	4	0	MN + minoxidil	baseline	x			12	72
Atrophic acne scars									
RCT									
Alam et al.	20	5	MN	negative control	x			3	24
Chae et al.	40	0	FMRF	fractional laser (1550 nm)	x			3	20
Cachafeiro et al.	46	4	MN	fractional laser (1340 nm)	x			3	24
Lehata et al.	39	1	MN + TCA	fractional laser	x			6	48
Lehata et al.	30	3	MN	TCA-CROSS	x			4	4
Lehata et al.	24	4	MN + TCA	TCA-CROSS	x			4	32
Min et al.	23	3	FMRF	bipolar RF	x	x	x	2	8
Nofal et al.	45	0	MN + PRP	TCA-CROSS intradermal PRP	x			3	2
CCT									
Asif et al.	50	0	MN + PRP	MN + distilled water	x			3	12
Chawla et al.	30	3	MN + PRP	MN + vC	x			4	1
Fabroccini et al.	12	0	MN	MN + PRP	x			2	32
Jaishree S et al.	30	0	MN	MN + GA peel	x			5	12
Puri et al.	30	0	MN	TCA-CROSS	x			4	16
CT									
Dogra et al.	36	6	MN	baseline	x			5	4
El-Domyati et al.	10	0	MN	baseline	x		x	6	2
Fabroccini et al.	60	0	MN	baseline	x	x		3	40
Fabroccini et al.	32	0	MN	baseline	x	x		2	8
Imrad Majid	37	1	MN	baseline	x			4	8
Lotfi et al.	30	0	MN	baseline	x		x	5	8
Kaftan et al.	25	0	MN	baseline	x			2	4
Burn scars									
RCT									
Busch et al.	20	1	MN + NCASCS	MN, neg co	x	x		1	48
CT									
Aust et al.	16	0	MN	baseline	x		x	4	48
Hypertrophic scars and keloids									
RCT									
Fabbrocini et al.	20	0	MN + Sili Gel	MN alone, SG alone	x	x		3	12
Melasma									
RCT									
Budamakuntla et al.	60	8	MN + TA	injection TA	x			3	12
CCT									
Fabroccini et al.	20	0	MN + depigmn serum	serum	x	x		2	12
Skin rejuvenation									
RCT									
Lee et al.	25	0	MN + hESC-EPC	MN	x	x		5	2

Table 2 (*continued*)

	Participants	Dropouts	Intervention	Comparison	Efficacy measurement			No. of treatments	Follow-up
					Cat	Num	Histo		
CT									
El-Domyati et al.	10	0	MN	baseline	x		x	6	2
Fabroccini et al.	10	0	MN	Baseline	x	x			
Fabroccini et al.	8	0	MN	Baseline	x	x		2	32
Gold et al.	49	4	FMRF	Baseline	x			3	12
Kim et al.	11	0	FMRF	Baseline	x			3	12
Striae									
CCT									
Khater et al.	20	0	MN	Fractional laser (CO_2)	x		x	3	24
CT									
Park et al.	16	0	MN	baseline	x		x	3	12
Total	1083	49			39	12	7	139	
Mean	29,2702	1,5312						3,86111	17,8055

criteria and withdrawal. A performance bias is inevitable because blinding the patients and practitioners for the procedure of microneedling is impossible. Reports that mentioned randomisation without mentioning the used tool were marked with *low(*)* selection bias. Reports that used blinding but based their outcome data only on one assessor without numerical or histological measurement were marked with *low(*)* detection bias. Reports that did not calculate statistical significance of each treatment modality and the difference between the compared modalities were marked with *low(*)* reporting bias. Reports that lacked patient-reported clinical outcomes were marked with *low(°)* reporting bias. Attrition bias was marked high when dropouts affected the validity of the comparison, which is never the case in within-patient controlled trials.

Results

Description of included studies

The search results on PubMed and Google Scholar were screened for duplicates, which resulted in 174 unique records that were screened on the basis of title and abstract. Eighty-six articles were excluded, and the remaining 88 reports were screened on the basis of full text. Fifty-one of these 88 articles were excluded because they did not meet our inclusion criteria. We excluded reviews, letters to editors, expert opinions, case reports, animal studies, in vitro studies, studies in progress and treatment protocols that did not specifically isolate the effects of microneedling in their comparison to a control group. An additional 10 records were identified through reference screening. Five of them were included in this review based on full text. This selection process resulted in 37 included articles and is summarised in Figure 4.

Because of the heterogeneity of the included studies, a meta-analysis could not be executed.

Methods

A total of 37 reports were included in this review, of which 13 randomised controlled clinical trials, 7 controlled clinical trials and 17 prospective clinical trials. There was within-patient control in seven split-face studies and in two split-scar studies, and four of them were randomised. Of the remaining 12 controlled trials, 9 were randomised. Ten reports used a single-blinded evaluation setup by blinding the assessors for the used treatment. Sample sizes varied from 4 to 100 with 1063 participants (393 males, 567 females and 103 unknown) and a mean of 29.3. A total of 49 dropouts were reported, with a mean of 1.53 over all reports. Microneedling was investigated in the literature as a possible treatment for acne vulgaris, androgenetic alopecia, atrophic acne scars, hypertrophic scars, keloid, melasma, skin rejuvenation and striae distensae. The therapeutic effects of microneedling were compared to those of fractional lasers (1550 Er:glass,[8] 1340 Erbium,[9] 1540 nm[10] and CO_2[11]), trichloroacetic acid chemical reconstruction of skin scars (TCA-CROSS),[10,12–15] bipolar radiofrequency,[7] intradermal injection of topical products[14,16] and silicone gel.[17] Methodological data are summarised in Table 2.

Treatment protocol

Treatment protocol variables were needle length (mean: 1.5 mm), number of treatments (mean: 3.86), treatment interval (mean: 4 weeks) and follow-up time (mean: 17.81 weeks).

Twenty-three trials included only microneedling in their treatment protocol. Twelve trials compared it to baseline, one trial compared it to a negative control and 10 compared it to a control group that received a different treatment. Nine trials combined microneedling with topical products such as PRP,[14,18–20] non-cultured stem cell suspension,[21] depigmenting serum,[22] Minoxidil,[23,24] human stem cell conditioned medium,[25] vitamin C[19] and TA.[16]

Six trials investigated the effects of FMRF. One trial compared it to fractional laser,[8] one to bipolar radiofrequency[7] and the others to baseline.[26–29] Microneedling was combined with TCA-CROSS in two trials, with silicone gel[17] and with glycolic acid peel[30] each in one trial.

Efficacy measurement

The clinical changes after a therapeutical intervention can be assessed by the patient and an observer. All studies

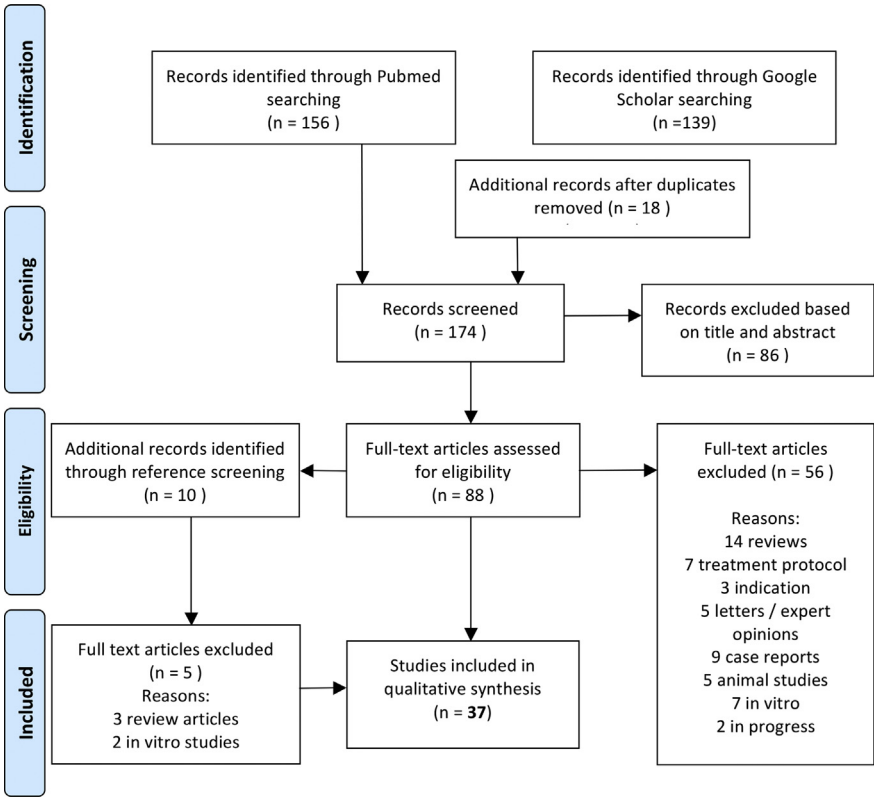

Figure 4 Flowchart.

included a subjective outcome evaluation by the assessor and objectified them with a categorical quantification through the use of scales (Table 3). These provide numeric data that enable statistic weighing of the null hypothesis. The use of an objective measurement tool decreases the risk of bias entailed by subjective assessment.

Seven studies used a numerical measurement tool. Acne vulgaris was evaluated by counting the inflammatory and non-inflammatory lesions and measuring the casual sebum level and sebum excretion rate.[26,31] Lesion count and the sebum level were also used for the evaluation of atrophic acne scars.[7] The changes in skin topography of acne scars and skin ageing were objectified with optical profilometry, a measuring tool that screens the surface irregularities of a silicon imprint from the treated site by Fabbrocini et al.[32–35] Lee measured skin topography with a Visiometer.[25] Fabbrocini also used ultrasound to measure epidermal thickness in skin rejuvenation and keloid scars[17,32] and luminance values to evaluate melasma.[22] The melanin index was an outcome parameter for depigmented hypertrophic scars and skin rejuvenation and was measured using the Mexameter.[21,25]

Seven studies evaluated the effects of the treatment protocol by measuring histological changes.[7,11,36–40] Epidermal thickness, collagen fibres, elastin, tropoelastin and fibroblasts were visualised with several histological stains. Cytokines and growth factors were visualised with immunohistologic colouring and polymerase chain reaction (Table 4).

Outcome parameters

All 37 studies included observer-reported clinical outcomes. Twenty-eight studies included patient-reported clinical outcomes and 29 studies reported adverse effects.

Effects of interventions

The principal summary measures were defined as difference in means. Outcomes are summarised in Table 5 on patient- and observer-reported clinical outcome, numerical outcome, histological outcome and adverse effects.

Risk of bias individual/across studies

Twenty out of 37 included reports in this review used a control group and were evaluated for risk of bias. Seven out of 20 had a risk that was estimated low on all four subdivided risks. It was high on one out of four risks in six reports and on two or more in seven reports. All studies have a high risk of performance bias because microneedling cannot be replaced by placebo treatment. The risk of bias is summarised in Table 6.

Discussion

Microneedling has been the subject of several clinical trials investigating its effects on atrophic acne scars, skin rejuvenation, burn scars, striae distensae, androgenetic

Table 3 Categorical measurement tools.

	Scale	#
Acne vulgaris	Global evolution acne scale	1
	Physician's global assessment	1
	Global aesthetic improvement scale	1
Androgenetic alopecia	Numbered scale (0—7)	2
Atrophic acne scars	Goodman and Baron	8
	Echelle d'evaluation clinique des cicatrices d'acne (ECCA)	3
	Quantitative Global Grading System for Postacne Scarring Instrument	3
	Physicians global assessment (5-point scale)	1
	Investigators global assessment	1
	Numbered scale (0—5; 0—6; 0—10)	11
	Global aesthetic Improvement scale	1
	Scar severity score (3 grades)	2
	Quartile grading scale	7
Hypertrophic scars and keloids	Visual analog scale	1
	Vancouver scar scale	2
	Patient and observer scar assessment scale (POSAS)	2
Melasma	Melasma area and severity index (MASI)	2
Skin rejuvenation	Fitzpatrick wrinkle classification system	2
	Numbered scale (0—5)	1
	Wrinkle severity rating scale	2
	Global aesthetic improvement scale	2
	Quartile grading	1

Table 4 Histological measurement tools.

	Haematoxylin and Eosin	Von Gieson	Pricorius Red	Masson's trichrome	Silver stain	IHC	PCR
Aust et al.	epidermal thickness rete ridge formation	elastin collagen					
El-Domyati et al.	epidermal thickness collagen type I collagen type II collagen type VIII elastin tropoelastin	elastin	new collagen formation				
El-Domyati et al.	epidermal thickness collagen type I collagen type II collagen type VIII elastin tropoelastin	elastin	new collagen formation				
Khater et al.	epidermal thickness collagen fibres fibroblasts			collagen fibres			
Lotfi et al.	epidermal thickness rete ridge formation collagen fibres fibroblasts			collagen fibres	elastin fibres		
Min et al.	collagen fibres					TGFβ1 TGFβ3 IL8 NFkB collagen type I collagen type II	GAPDH TRFβ1 TGFβ3 IL8 collagen type I
Park et al.	collagen fibres	elastin					

Table 5 Outcomes.

	Intervention	Control	Patient-reported clinical outcome	Observer-reported clinical outcome	Numerical outcome	Histological outcome	Adverse effects
Acne vulgaris							
CT							
Kim et al.	FMRF	/	+	+	+ (inflam > non-inflam)	/	bleeding (5), scaling (4), cursting (6), swelling (8), erythema (8) (all less than 1 week)
Lee et al.	FMRF	/	+	+	+	/	mild pain, oedema, bleeding (procedure); pustular eruptions (2) <1 week
Androgenetic alopecia							
RCT							
Dhurat et al.	MN + minox	minox	++	++	++	/	none
CT							
Dhurat et al.	MN + minox	/	+	+	/	/	none
Atrophic acne scars							
RCT							
Alam et al.	MN	negative control	++	++	/	/	minimal pain, transient erythema and oedema
Chae et al.	FMRF	fractional laser	=	=	/	/	FRMF: none significant laser: pain, PIHP, acne vulgaris, prolonged downtime
Cachafeiro et al.	MN	fractional laser	=	=	/	/	both: crusts, pustules, erythema, pain laser: bullae, PIH and prolonged erythema
Leheta et al.	MN + TCA	fractional laser alternating treatment	=	vs laser: = rolling type: ++ boxcar type: - icepick: = vs alternating: -	/	/	both: transient pain, oedema, erythemapeeling: desquamation
Leheta et al.	MN	TCA-CROSS	=	General: = rolling type: ++ icepick type: -	/	/	Pain: - Erythema, downtime: ++
Leheta et al.	MN + TCA	TCA-CROSS	=	General: = rolling type: ++	/	/	=

Min et al.	FMRF	bipolar RF	satisfaction: ++ pain: - convenience: -	++	++ (inflam < non-inflam)	++	Pain: - FMRF: transient erythema, oedema
Nofal et al.	MN + PRP	TCA-CROSS intradermal PRP	=	=	/	/	MN: erythema and oedema, pain TCA: PIH, mild pain PRP: pain, mild bruises (one patient)
CCT							
Asif et al.	MN + PRP	MN + distilled water	++	++	/	/	acne, PIH, milia, persistent erythema, bruising
Chawla et al.	MN + PRP	MN + vC	++	++	/	/	/
Fabroccini et al.	MN + PRP	MN	/	++	/	/	transient erythema and oedema
Sharad et al.	MN + GA peel	MN	/	++	/	/	transient erythema, PIH
Puri et al.	MN	TCA-CROSS	−	=	/	/	MN: transient erythema, pain; oedema TCA: PIH
CT							
Dogra et al.	MN	/	+	+	/	/	postinflammatory hyperpigmentation, tram track, small ecchymosis
El-Domyati et al.	MN	/	+	+	/	= (1 month)+ (3 months)	facial oedema, slight pain, mild erythema
Fabroccini et al.	MN	/	/	+	+	/	erythema, bruising over bony prominence
Fabroccini et al.	MN	/	/	+	+	/	/
Imran Majid	MN	/	+	+	/	/	temporary erythema, postinflammatory hyperpigmentation (one patient), mild crusting
Lotfi et al.	MN	/	+	+	/	/	transient erythema, mild to severe pain during procedure
Kaftan et al.	MN	/	/	+	/	/	/
Burn scars							
RCT							
Busch et al.	MN + NCASCS	MN, neg co	=	=	++	/	/
CT							
Aust et al.	MN	/	+	+	/	+	swelling and bruising
Hypertrophic scars and keloids							
RCT							
Fabbrocini et al.	MN + SG	SG	/	++	=	/	/
Melasma							
RCT							
Budamakuntla et al.	MN + TA	injection TA	/	=	/	/	itching, burning, erythema
CCT							

(*continued on next page*)

Table 5 (*continued*)

	Intervention	Control	Patient-reported clinical outcome	Observer-reported clinical outcome	Numerical outcome	Histological outcome	Adverse effects
Fabroccini et al.	MN + depigmenting serum	depigmenting serum	/	++	++	/	transient erythema and oedema
Skin rejuvenation							
RCT							
Lee et al.	MN + hESC-EPC	MN	=	++	++	/	mild desquamation (one patient) mild pain, transient erythema
CT							
El-Domyati et al.	MN	/	+	+	/	+	slight pain, erythema, oedema
Fabroccini et al.	MN	/	/	+	+	/	mild oedema, erythema and swelling (48—72 h)
Fabroccini et al.	MN	/	/	+	+	/	
Gold et al.	FMRF	/	/	+	/	/	mild-moderate erythema and oedema, pain
Kim et al.	FMRF	/	unclear	+	/	/	minimal pain, bruising (1 week) crusts
Striae							
CCT							
Khater et al.	MN	fractional laser	++	++	/	++	MN: transient mild erythema laser: PIH
CT							
Park et al.	MN	/	+	+	/	+	pain, erythema, spotty bleeding, pruritus

Legend: ++: statistically significantly different in advantage of microneedling; +: statistically significantly better in prospective clinical trial; =: no statistically significant difference between the therapy regiments; -: statistically significantly worse in prospective clinical trial; -: statistical significantly different in disadvantage of microneedling; /: no data; FMRF = fractional microneedling radiofrequency; MN = microneedling; TCA = trichloroacetic acid; PRP = platelet rich plasma; vC = vitamin C; GA = glycolic acid; SG = silicone gel; NCASCS = non cultured stem cell suspension; h-ESC EPC = human embryonic stem cells-endothelial precursor cells; PIH = post-inflammatory hyperpigmentation; CSL = casual sebum level; SER = sebum excretion rate.

alopecia, melasma and acne vulgaris. It has been compared to other treatments such as fractional lasers, topical products and peelings.

To strengthen the validity of the research, some trials used control groups, randomisation and single blinding. Measurement was made through scoring the assessors' and patients' findings on scales, numeric measurement tools and histological evaluation on skin biopsy. Microneedling triggers regenerative mechanisms and activates non-inflammatory wound healing in the treated skin. It activates the release of cytokines and molecules that communicate to induce skin cell proliferation and differentiation, neoangiogenesis and collagen formation. Biopsies of the treated sites showed an epidermal thickening and increased collagen deposition in a normal woven pattern.

The investigated literature lacked the methodological unity to be included in a meta-analysis. However, microneedling has shown to be a safe and effective therapeutic modality for the treatment of atrophic scars, ageing and skin disorders and proved to be useful for the admission of topical products and radiofrequency. It succeeded to deliver results that could complement and, in some cases, replace the more invasive therapeutic regimens while showing less side effects and shorter downtime.

Table 6 Risk of bias.

	Selection bias	Detection bias	Attrition bias	Reporting bias
	Randomisation	Blinding assessor	Exclusion, withdrawal	All outcomes reported
Androgenetic alopecia				
RCT				
Dhurat et al.	low	low	high	low (*)
Atrophic acne scars				
RCT				
Alam et al.	low	low	low	low (*)
Chae et al.	low (*)	low	low	low
Cachafeiro et al.	low	low	high	low
Leheta et al.	low	low (*)	low	high
Leheta et al.	low (*)	low (*)	low	low
Leheta et al.	low	low (*)	low	low
Min et al.	low (*)	low	low	low
Nofal et al.	low (*)	low	low	low
CCT				
Asif et al.	high	unclear	low	low (*)
Chawla et al.	high	high	low	high
Fabroccini et al.	high	unclear	low	low (°)
Jaishree S et al.	high	high	low	low (°)
Puri et al.	high	high	low	high
Burn scars				
RCT				
Busch et al.	low	high	low	high
Hypertrophic scars and keloids				
RCT				
Fabbrocini et al.	low (*)	high	low	low (°)
Melasma				
RCT				
Budamakuntla et al.	low	high	high	low
CCT				
Fabroccini et al.	high	high	low	low (°)
Skin rejuvenation				
RCT				
Lee et al.	low	low	low	low (*)
Striae				
CCT				
Khater et al.	high	high	low	low (*)

(*): statistics incomplete
(°): no patient reported outcome

(*) no randomisation tool mentioned

(*) subjective outcome data by one assessor

Summary of evidence

The use of needles for non-ablative skin treatment was first described by Orentreich and Orentreich in 1995 as subcision surgery, which is the release of depressed scars and wrinkles with a needle from their attachment to the underlying skin. This controlled trauma leads to the formation of connective tissue to fill the created gap.[41] A few years later, in 1997, Camirand and Doucet introduced tattooing without pigment as *Needle Dermabrasion* and proposed it as a technique to improve the appearance of achromic, hypertrophic and unsightly scars.[42] However, this device never gained wide popularity due to the tight grouping of the needles, which made it prone to over-treating and scarring. In 1996, skin needling using a roller device was introduced by Fernandes at the International Society of Aesthetic Plastic Surgery (ISAPS) congress in Taipei.[43] Fernandez designed his pilot roller device as a drum-shaped tool with a cylinder with 3 mm needles that reach the fibroblasts deep in the reticular layer. However, this needle length proved to be way too painful to use in an office setting, and it caused unacceptable bleeding and bruising for the patient. Zeitter et al. confirmed the observation that Fernandes made in 2008 that 1 mm needles show similar results to 3 mm needles, with the extra advantage of less downtime, swelling and pain[3,44]

Methodology of the included studies

The validity of the study results is determined by the methodological setup. Thirteen of the 37 included study setups used randomization, 10 included single-blindation and two performed a power analysis for sample size[9,45] to improve methodological quality.

There was a noticeable difference in treatment regimens. Patients were treated between 1 and 12 times with treatment intervals varying from 1 to 8 weeks. There is no standard treatment protocol available, but Zeitter et al. (2014) performed a study on rats to investigate the effects of repetitive treatments. They observed the best results when the treatment was repeated four times with an interval time of 3 weeks.[44] The choice of needle length depends on the pursued depth of therapeutical intervention (e.g. thick scar tissue) and requires generalised anaesthesia for needles longer than 2 mm.

A second striking difference was observed in the time to follow up, which varied between 1 and 72 weeks. Studies that performed interim follow-up evaluations observed that the effects of microneedling changed over several months to reach a maximum at 12—24 weeks. Fabroccini et al. even reported the most significant results at 8—12 months post treatment.[34] This means that the 25 studies that had follow-up times shorter than 24 weeks might have underestimated the effects of microneedling.

Scales were used to objectify clinical outcomes reported by patients and observers. The heterogeneity in the used scales made it impossible to combine different study samples in a meta-analysis. The Goodman and Baron scale for the evaluation of atrophic acne scars was the most universally used evaluation scale.[46] Second was the use of a numbered scale, like the Visual Analog Scale, but unfortunately there were differences in the numbers given to the maximum score.

Histological measurement was based on the knowledge gained from animal studies about the histological changes that appear after microneedling. The increase in epidermal thickness, increased collagen and elastin deposition and the presence of non-inflammatory cytokines and growth factures like TGF-β3 are measurable to demonstrate efficacy.[2,44,47] Researchers may be reluctant for the labour intensity of a histological evaluation, but the importance of histological outcome parameters is highlighted from the scarceness of objective measurements of changes in skin quality.

Fifty percent of the studies that used a control group did not report a complete statistical analysis. Outcome data from two study groups should be weighed statistically to identify a significant difference compared to baseline and between groups. Only three studies calculated the significance between groups, three other studies calculated only the comparison of each group to baseline and Puri et al. (2015) did not perform either analysis.[15] The remaining three were incomplete because there was no statistical analysis performed on any of their outcome parameters. These shortcomings were accounted for in the estimation of the reporting bias (Table 6, marked with *(*)*).

Outcomes of the included studies

In the current literature, microneedling was investigated in a variety of settings. First, it gained evidence for its use on atrophic acne scars. Compared to lasers and peels, microneedling caused comparable clinical results to these mainstream therapies but with an explicit advantage because of its lower risk of side effects. Hypertrophic scars are less investigated, and a hypertrophic tendency in the patient is often an exclusion criterion in trials that use microneedling. The rationale behind this is that triggering skin formation does not fit in a state of hypertrophic tendency. The few existing trials that did include hypertrophic scars did note the advantages of microneedling especially when combined with topical products that aid repigmentation.

Second, microneedling enhances penetration of topical products. It appeared to increase the effectiveness of topically applied minoxidil on androgenetic alopecia and depigmenting serum on melasma. Other topical products enhanced the percutaneous collagen induction by providing extra growth factors such as PRP for atrophic acne scars and h-ESC-EPC for skin rejuvenation. Badran et al. (2009) investigated the penetration of topically applied radiolabelled mannitol into full thickness human skin grafts spontaneously and combined with microneedling. Hydrophylic compounds like mannitol are expected to have a poor penetration by passive diffusion through the stratum corneum. The authors also noticed differences in penetration between two drug carrier fluids (invasomes or buffer solution), which implicates that the nature of the topical products plays a role in the effectiveness of the combination therapy.[48]

The delivery of radiofrequency through insulated paired microneedles proved to improve the aesthetic appearance of atrophic acne scars, ageing skin and acne vulgaris and showed to be superior compared to the effects of bipolar radiofrequency.[7] It demonstrates beneficial effects on inflammatory lesions, which contradicts the commonly used

exclusion criterion for microneedling, i.e. the presence of active skin infection and inflammation. This criterion excludes patients with active acne, which is often still present in patients with atrophic acne scars. Some studies opted for topical or oral antibiotic prophylaxis,[30,45,49] but none of the reports included in this review mentioned bacterial infections after microneedling. In-vitro studies have shown that there is a transdermal passage of microorganisms through the micropores after microneedling, but there is no increased risk of infection when microneedling is performed with standard hygienic measurements like a sterile device and skin disinfection. It even showed less contamination compared to intradermal needling.[50]

Frequently reported adverse effects are transient erythema, oedema and pain. Very rare cases of post-inflammatory hyperpigmentation,[18,49] a side effect that is commonly reported after the use of lasers and peelings, are assumed to have appeared after not following instructions to protect the treated skin from sunlight for a few days. The appearance of the 'tram track scarring' was described by Dogra et al., and in one case report, the authors concluded that the scarring occurred due to high pressure on the needling and the use of long needles over bony prominences.[51] A second case report described allergic reaction and systemic hypersensitivity after microneedling in three patients. These problems were caused by the use of a topical product that was not suitable for deep administration and the use of a product that had earlier caused hypersensitivity in the patient.[52] These events illustrate that even though microneedling is a simple and non-invasive therapeutical option, there is a need for clear and evidence-based guidelines to avoid these undesired side effects or complications.

Future research

Future research should aim for a strengthening of the current evidence by conducting more qualitative randomised controlled clinical trials with standardised measurement tools and lengthy follow-up times. In addition, the effects of microneedling on hypertrophic scars and keloids have not been examined properly and thus need further research. This could truly establish the evidence that would pose microneedling as a valuable evidence-based treatment option for treating scars, wrinkles and other skin conditions.

Strengths and limitations of this review

The strength of this review lies in the fact that it provides a complete overview of the current use of microneedling. The shortcomings of the current literature involving microneedling were highlighted to serve as a guideline for future research.

The main limitation of this study is the inability to perform a meta-analysis due to the heterogeneity of the included studies. The main objective of this review was to give an overview of the current literature, which includes the mentioning of less qualitative studies. These interfered with the possibility to cluster the qualitative study outcomes into a general conclusion.

Conflict of interest

None.

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