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Research Article

**THE OUTCOME OF USING DIFFERENT SURGICAL
MODALITIES INCLUDING LASER THERAPY IN THE
TREATMENT OF SMALL AND MEDIUM SIZE CONGENITAL
MELANOCYTIC NEVI: A SYSTEMATIC REVIEW**Hanadi Mufakkir ALMutairi¹, Ghadah Ibrahim ALHetheli²¹Medical Intern , College of Medicine , Qassim University., ²Assistant Professor of
Dermatology , College of Medicine , Qassim University.**Article Received:** January 2019**Accepted:** February 2019**Published:** March 2019**Abstract:**

Objectives: The purpose of this study was to review published articles regarding different surgical modalities including laser therapy in the treatment of congenital melanocytic nevi.

Methods: A systematic review was done using several databases including PubMed, Ovid Medline, Google Scholar, and Medline to search for articles related to surgical excisions and different treatment modalities of congenital melanocytic nevi.

Results: Fourteen studies were included according to the inclusion and exclusion criteria. The results have shown that the Q-switched ruby laser therapy was the most commonly used laser therapy to treat CMN. Overall, using laser therapy had positive outcomes in CMN treatment. However, limited knowledge was available regarding patient satisfaction with the outcomes of laser therapy.

Conclusion: We concluded that the most acceptable surgical choice was using excision with tissue expanders. Laser-intense pulsed light (IPL) alone and in combination with erbium: yttrium-aluminum-garnet (Er: YAG) have a risk of reoccurrence. Combination of types of the laser is more effective than a single one.

Keywords: Congenital melanocytic nevi, laser therapy, treatment, outcome, surgical modalities.

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INTRODUCTION:

Congenital melanocytic nevi (CMN) is among the significant dermatological problems worldwide and it is associated with unpredictable outcomes. The CMN can occur as the result of genetic mutations involving mitogen - inactivated protein kinase, especially NRAS (Neuroblastoma RAS Viral) and B-RAF⁽¹⁾. The CMN is associated with psychological stress as well as medical risks for those affected including extracutaneous involvement and malignant transformation. Some of types of the CMN, especially the large one, can lead to severe complications including melanoma as long sequel. There are different modalities of surgical excision and laser therapy used for treatment of congenital melanocytic nevi and they are associated with variable outcomes⁽¹⁾. Overall, all congenital nevi could have a malignant transformation risk, but the risk of malignant transformation is more evident among the large-sized congenital nevi. Clinically, congenital nevi can be divided into three types based on its size: small-sized (SCN, ≤ 1.5 cm), intermediate-sized (ICN, 1.5-20 cm) and large-/giant-sized (>20 cm)⁽²⁾. There are various modalities used in treatment of CMN. These modalities include curettage, dermabrasion, complete surgical excision, and laser therapy. For the management of large-sized or giant CMN, Fresh cultured epithelial autograft (CEA) after curettage or erbium:yttrium-aluminum-garnet (Er:YAG) ablation is considered an innovative option⁽³⁾. However, to date, little evidence is available regarding outcomes of (or patients' satisfaction with) using surgical procedures and laser therapy for small and medium-size CMN. Such evidence is needed to provide a valid conclusion for the patient and the practicing physician regarding the effectiveness of using surgical procedures and laser therapy in treatment of CMN with small and medium size. In this study, we aimed to review published articles regarding different surgical modalities including laser therapy in the treatment of congenital melanocytic nevi with small and medium size. Therefore, our study sheds the light on patients' outcomes and satisfaction with using surgical excision and/or laser therapy for management of CMN based on the currently available evidence.

METHODOLOGY:

Search strategy

To meet the purpose of the current study, a systematic literature review was conducted in accordance with PRISMA guidelines. A systematic review was done using several databases including PubMed, Ovid Medline, Google Scholar, and Medline to search for articles related to surgical excisions and different treatment modalities of congenital melanocytic nevi. The following keywords were included for search

"Congenital Melanocytic Nevi", "Laser Therapy", "Treatment", "Outcome", and "Surgical Modalities". Articles that met the following inclusion criteria were included in the literature review:

(1) Articles describing outcomes of (or patients' satisfaction with) using surgical procedures and laser therapy for small and medium-size CMN, and giant CNN except those which developed malignant transformation.

(2) Articles including a large sample size.

Articles that met the following exclusion criteria were excluded from the literature review:

- (1) Articles with case reports
- (2) Articles not describing the outcome of using surgical excision techniques and laser therapy.
- (3) Articles include the malignant transformation of CMN
- (4) Articles include surgical excisions, followed by laser on the same patients.

These inclusion and exclusion criteria were used to assure reporting relevant articles and to enhance the strength and validity of the conclusions derived from the literature review.

Data extraction

After conducting a literature search, the authors conducting an initial screening for the titles of retrieved articles and their abstracts. Then, the papers that were relevant to the topic of interest were reviewed in full before being considered for inclusion in the systematic literature review. The final list of papers included for review was determined according to the predetermined criteria for inclusion and exclusion of the research studies. A brief description of the articles selected for review was presented in a literature review matrix. As of May 1, 2018, the literature search yielded a total of 247 articles. However, after removing the redundant records and excluding the irrelevant articles, fourteen articles have met the inclusion criteria and included in the current review (Figure 1).

RESULTS:

Congenital melanocytic nevus remains one of the interesting topics in the dermatological field. There are several published articles that addressed the outcome of surgical excision and laser treatment of CMN. We found 14 articles highlighting different modalities of employing laser therapy and surgical removal (Table 1).

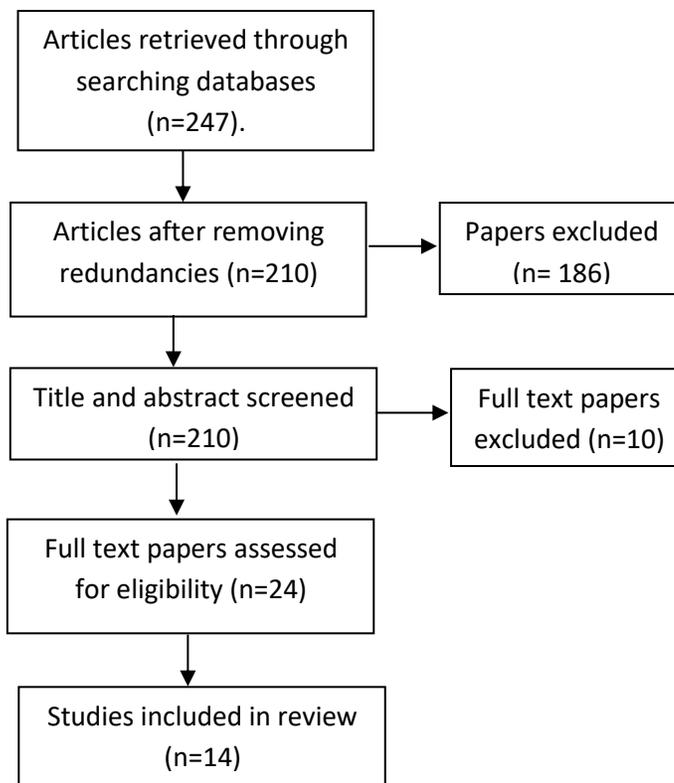


Figure 1. Studies included in literature review.

Table 1: Details of studies included in the systematic review

Reference number	Year of publication	Country	Subjects	Method	Data collection tool	Number of Patients	Objective	Outcome	Limitations
1	2017	Germany	Patients in the German registry between 2005-2012	Prospective cohort study	Questionnaire	100	Clinical course and treatment modalities in CMN by long-term assessment. -Quality of life in patients with CMN.	Most patients are achieving a satisfactory to very good level of psychological adaptation to their conditions. -The decision of the parents regarding surgical treatment can be influenced by the levels of their knowledge regarding the medical risks of CMN	There was no clear relationship between the size or visibility of CMN and impairment among patients.
2	2013	Italy	Clinicians	Nationwide Survey	Interview	250 patients	- Congenital nevi with small and intermediate size undergo frequent clinical observation or surgical	-complete excision is preferred. -The periodic clinical examination is	The frequency of follow up remain controversial

							intervention -Analyzing the management of congenital nevi with small and intermediate size in the Italian hospital network	critical to follow up.	
3	2006	Korea	Patients	Retrospective and prospective	Observation moreover case , note review	18	To look for outcomes of cultured epithelial autograft after curettage or ER:Yag laser ablation	The cultured epithelial autograft after curettage and ER:YAG laser is a safe and effective method and accelerates healing with fewer side effects	Not recorded
4	2002	Japan	Patients	Prospective study	Photographic assessment and histological examination Comparative study	15	-To assess the usefulness of using normal mode ruby laser and combined normal mode plus the q-switched ruby laser in the treatment of congenital nevi.	-The combined laser more effective than NMRL alone, there is no scarring.	-Need multiple sessions of treatment because there is no clearance from single sessions.

5	2010	UK	Patients	Prospective cohort study	Questionnaire moreover case , note review	55	Treatment of 55 congenital nevi using pigment-specific lasers and carbon dioxide.	Upper trunk and mamillated CMN had the better response	A high risk of repigmentation was found as a result of using laser treatment of congenital nevi despite employing multiple treatments with initial clearance.
6	2005	UK	Patients	Retrospective chart review	Chart review	12	-To identify the outcome of using CO2 laser in the treatment of congenital nevi	-CO2 laser is an effective method to reduce pigmentation	Not recorded
7	2016	China	Patients	Prospective cohort study	Observation	8	-Treatment of nasal nodular CMN by CO2 laser and Q-switched Nd:YAG laser	-The CO2 laser has an excellent cosmetic outcome but Q-switched Nd: YAG laser not recommended	Not Recorded
8	2006	the Netherlands	Neonates	Prospective cohort study	Observation	10	-To identify histopathological and clinical results of using erbium:YAG (Er:YAG) laser resurfacing for	-Few complications and minimal scarring	Not recorded

							treatment of congenital nevi		
9	1-	Norway	Children	case series	Case study	14	-To look for results of ruby laser treatment	-Ruby laser not recommended in the treatment of CMN because it could associated with malignant potential.	Not recorded
10	2012	UK	Patients	Retrospective chart review	Chart review	52	-To identify the frequency of doubled Q-switched Nd-YAG laser and efficacy of UPCO2 for a period of 15 years.	-Minimal complications and it is recommended.	Not recorded
11	2017	Korea	Patients	Retrospective cohort study	Chart review	26	-To evaluate the clinical outcome of small-medium sized CMN IPL when it is used alone or in combination with ER:YAG laser	-Not effective treatment and is not used the first line of treatment	- Sample size is small and included Asians only. Thus, the generalizability of the outcomes is limited. -the effect of intense pulsed light (IPL) alone on CMN was not presented in some cases due to the limited efficacy

									of using IPL alone -The study lacked a control group
12	2015	Korea	Patients	Prospective study	Clinical examination	24	-To assess the outcome of using combined short pulsed ER:YAG and long-pulsed alexandrite laser for both medium and large congenital nevi	-This method is effective and had shown minimal side effects.	-Lack of histopathologic examination of nevi -A short period of follow up
13	1999	California	Patients	Prospective study	Observational		-The Q-switched ruby laser in the treatment of CMN in general	-After five years of observation, there is no recurrence of CMN and the complications like scarring not observed	-No limitations
14	2017	China	Patients	Case Series	Patients with congenital nevi during period between June 2007 and	11	-Use of tissue expansion in the treatment of CMN in three stages -look for advantages	- complications in the first stage. -in the second stage, one patient develop	Not recorded.

					December 2015		over traditional modalities.	distal tip necrosis. -no malignant transformation. -good functional result.	
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First of all, we want to see if the CMN had an impact on quality of life. There is a study conducted in this area. In this study, eighty three patients or instead their parents responded to questions of the survey⁽¹⁾. The study concluded that 73 of patients underwent surgery (78%) reported no or minimal effect of CMN on their quality of life (Figure 2).

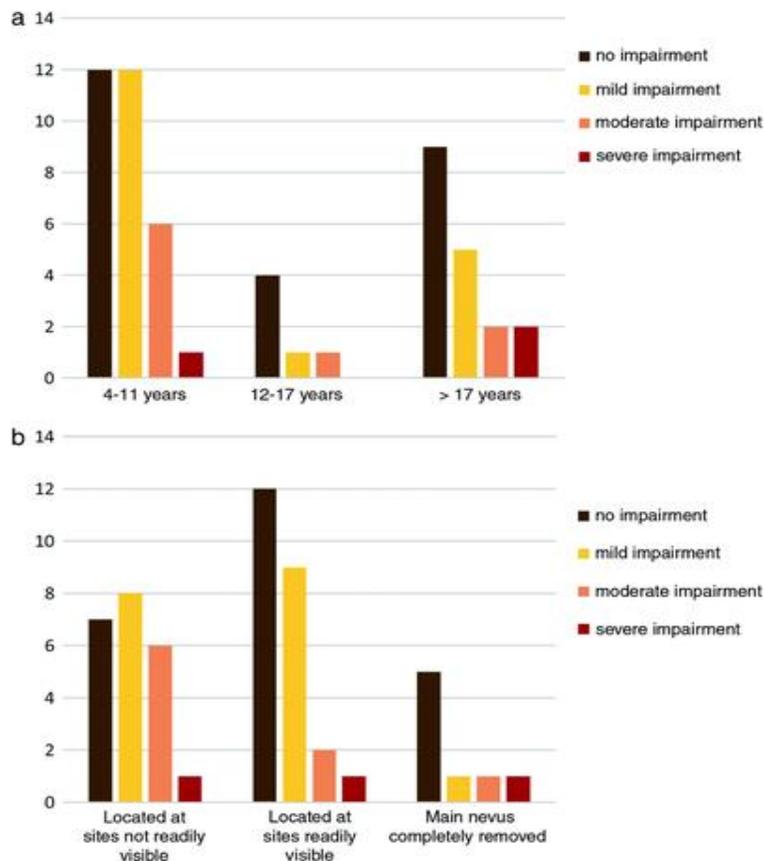


Figure 2. Effects of a surgical intervention for CMN on patients' quality of life

monitoring or surgical excision. This study concluded that the complete surgical removal is a preferred option.

Another study based on a nationwide survey (including multiple representative centers around the country) was done in Italy⁽²⁾. The main objective of the study was to analyze the treatment of small and intermediate CMN which undergo periodic clinical

sample of 52 patients with 314 CMN and patients who have nodular CMN of the nasal ala and treated with UltraPulse Carbon Dioxide (UCO₂) laser and FDQS Nd-Yag laser(10). The authors concluded that using UCO₂ and FDQS Nd-Yag lasers is effective in treatment of CMN with minimal complications.

Ten children were enrolled in another study that used Erbium:YAG laser (Derma K) laser (8). The main objective of this study was to identify the clinical and histopathological outcomes after treatment. The results have shown that the laser ablation was tolerated by all children and the immediate results were good (8). The period of follow-up ranged from 3-36 months. Recurrence percent was only 2%

A total of 14 children (age between 2 and 16 years) with medium – sized CMN were involved and treated by Ruby laser(9). Because all nevi had a facial distribution, these cases were unsuitable for surgical intervention. Ten children (age range 2-5 years) were managed under general anesthesia and four under local anesthesia. Twelve patients treated with Q-switched and normal mode ruby laser and only two with normal mode. The duration of treatment done at the interval (2 – 20 months). The results were followed by clinical photographs, and none of the patients demonstrated a satisfactory outcome. So, treatment with a ruby laser in children is not recommended. This study concluded that laser treatment has malignant potential (9).

A retrospective chart review of twenty six small to medium sized CMN was also conducted (11). The purpose of this study was to assess the clinical outcomes by using intense pulsed light (IPL) alone and in combination with ER:YAG laser. The result showed the treatment with IPL alone or in combination with ER:YAG laser has not to be considered first-line therapy.

The treatment of acquired and small congenital melanocytic nevi was done by using combined ER:YAG laser and long-pulsed alexandrite(12). Prospective studies showed that this method is effective and had few side effects.

Risk of bias

The authors assessed all articles regarding the risk of bias before including them in the literature review. The items included in Cochrane Collaboration were used as guide for assessment of the bias risk including allocation concealment, random sequence generation blinding of outcome assessment, participants, and personnel, selective reporting, and incomplete outcome data. Overall, the results indicated unknown risk of bias for the reviewed articles.

Another study was completed by ten patients who have giant CMN; One patient was treated with curettage, four patients were treated with Er:YAG ablation, and five patients treated with both curettage and Er:YAG ablation, followed by cultured epithelial autograft (CEA). In addition, eight patients were treated with curettage (two patients), Er:YAG ablation (one patient), or both (five patients) without CEA(3). The result of this study showed reduced pigmentation in both groups of patients but the group who had CEA demonstrated a shorter duration of complete healing than the non-CEA group and fewer side effects occur after in the CEA group. The study indicated a favorable outcome of CEA combined with curettage or Er:YAG laser ablation in the treatment of CMN. Therefore, using CEA was found to have fewer side effects in addition for being safe and effective (3).

Another prospective study employed photographic assessment and histological examination demonstrated the efficacy of the combined (normal-mode plus q-switched) ruby laser in the treatment of congenital melanocytic nevi (4). Q-switched ruby laser treatment of a congenital melanocytic nevus was very effective(4), because after five years of the follow up there was no recurrence and the scarring was not observed.

Another study was conducted with 55 patients who have medium – sized CMN and treated with CO₂ and FDQS Nd-Yag laser(5). Thirty-six of the 55 CMN were macular, and 19 were mammillate. The outcome of truncal macular CMN was better while the scarring and pallor were seen in the three lower limbs CMN. On the other hand, Mammillated CMN on the head and neck showed the best improvement. The recurrence had shown 6% of macular and 21% of mammillated CMN.

Another retrospective study was performed in 12 patients with CML treated with CO₂ laser(6). There was minimally visible pigmentation, and six patients developed hypertrophic scarring more in special places like torso, flanks, or arms than on the back or buttocks. This study concluded that CO₂ is an effective treatment for visible pigmentation but the risks for hypertrophic scarring can be limited if this therapy is used in the areas where the dermis is thinner. In addition, cautious use of paint mode or prophylactic use of pressure or silicon was also found to be helpful.

Because the CMN had an increasing risk of malignancy and caused cosmetic and psychological problems, the surgery is considered the best approach. However, the laser was recently used to treat CMN. This study used retrospective research design with a

erbium: yttrium-aluminum-garnet (Er: YAG) laser. The study included seventeen patients and had proven that both types of the laser should not be used as a first line treatment for CMN due to the risk of reoccurrence, even if the gross results seemed to be negative. Another study investigates the use of carbon dioxide and Q-switched neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser to treat facial CMN located in the nasal ala. This study demonstrated the superiority of carbon dioxide laser over Nd:YAG. The study involved eight patient with nodular CMN, and although the Nd:YAG laser does not manage the pigmentation, it doesn't remove the hyperplastic tissue(11). Nevertheless, the use of both ultra-pulse carbon dioxide, and frequency doubled Q-switched Nd-Yag located in the face did prove to be effective leaving only a grayish hue(7) .

The use of combination laser was seen in most of the studies included in our review. For example, a study for Lee SE in South Korea included 24 patients with acquired and small CMN that were treated with Er:YAG laser followed by long-pulsed alexandrite laser. The results proved to be effective. All CMN had loss of pigmentation after eight weeks of treatment, all side effects caused by the treatment – except scarring - had resolved within a few months(12). In another study, carbon dioxide and Q-switched lasers were used in the treatment of medium-sized congenital melanocytic naevi. However, in this study, Q-switched lasers; which include frequency-doubled Nd:YAG, Nd:YAG and alexandrite showed no additional benefit to carbon dioxide. Outcomes were better to only truncal mamillated CMN(13) .

Some studies used only one type of laser in a sample of patients. A study of ten neonates with giant CMN treated by Er:YAG laser had shown benefit, but some side effects like scar formation complicated the laser treatment(8). Another example is a retrospective chart review study on twelve patients. In this study, CO2 laser was used, and six out of twelve patients had hypertrophic scarring especially on the anterior torso, flanks, and arms(6). Another study had also shown that combined ruby laser (normal-mode plus q-switched) was more effective in penetrating deep into the dermis and removing nevomelanocytic nests than the use of a normal-mode ruby laser(4).

CONCLUSION:

The most acceptable surgical choice was using excision with tissue expanders. Laser-intense pulsed light (IPL) alone and in combination with erbium: yttrium-aluminum-garnet (Er: YAG) carries a risk of reoccurrence. Combination of types of the laser is

DISCUSSION:

Recently, addressing the effectiveness of medical interventions is considered a concern for many researchers worldwide ⁽¹⁴⁻¹⁸⁾. The current study highlighted the role of different surgical modalities including laser therapy as medical interventions used in the treatment of congenital melanocytic nevi. The result section includes many points regarding the outcomes of surgical and laser treatment of CMN. These outcomes had a wide range of variability and had various aspects including procedure complications, patient satisfaction and the effect on the patient quality of life, and using single or more than one type of laser therapy. These interventions were important to prevent the development of subsequent melanoma.

Studies on Procedure Complications and Patient Satisfaction

A study was conducted to assess the role of tissue expansion in the treatment of CMN had revealed only a few complications and excellent patient satisfaction with using this type of treatment(19). The tissue expansion technique is done using a silicone balloon placed in the subcutaneous tissue for three to four months. The expanded tissue is then used to close a defect created by excisional surgery. The rate of complications related to the use of this technique had varied from 13% to 20% (15).

Regarding the use of other surgical modalities, it was found that the most common procedures to be done were serial excision and dermabrasion according to a cross-sectional study done in Germany. However, data from this study represent only the German population(1) . Most patients in this study undergo these procedures before the age of one year old, and the most common reasons were to prevent melanoma and also for cosmetic improvement. Among the 100 patients involved in this study, the highest satisfaction rate was among patients who were treated with the tissue expansion technique. Nevertheless, these results can't be generalized owing to that fact that those patients represent only 5.5% of the sample. Dermabrasions had the lowest level of satisfaction and was mostly due to the repigmentation following the procedure. This also confirms that the most acceptable surgical choice was using excision with tissue expanders.

Combination of Different Laser Types versus Using Only One Type of Laser

A retrospective chart review done by Lee MS have investigated the use of specific type of laser-intense pulsed light (IPL) alone and in combination with

- Vermeulen AHM, Bertleff MJOE, Venema AW, et al. Congenital naevi treated with erbium:YAG laser (Derma K) resurfacing in neonates: Clinical results and review of the literature. *Br J Dermatol*. 2006;154(5):889–95.
9. Helsing P, Mørk G, Sveen B. Ruby Laser Treatment of Congenital Melanocytic Naevi. *Acta Derm Venereol* [Internet]. 2006 [cited 2018 Sep 17];86(3):235–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16710582>
 10. Al-Hadithy N, Al-Nakib K, Quaba A. Outcomes of 52 patients with congenital melanocytic naevi treated with UltraPulse Carbon Dioxide and Frequency Doubled Q-Switched Nd-Yag laser. *J Plast Reconstr Aesthet Surg* [Internet]. 2012 April [cited 2012 August]; 65(8):1019-28. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/22525254>
 11. Lee MS, Jun HJ, Cho SH, Lee JD, Kim HS. Intense Pulsed Light Alone and in Combination with Erbium Yttrium-Aluminum-Garnet Laser on Small-to-Medium Sized Congenital Melanocytic Nevi: Single Center Experience Based on Retrospective Chart Review. *Ann Dermatol* [Internet]. 2017 Feb [cited 2018 Sep 17];29(1):39. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28223745>
 12. Lee SE, Choi JY, Hong KT, Lee KR. Treatment of Acquired and Small Congenital Melanocytic Nevi With Combined Er. *Dermatologic Surg* [Internet]. 2015 Apr [cited 2018 Jul 21];41(4):473–80. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25760556>
 13. Nelson JS, Kelly KM. Q-switched ruby laser treatment of a congenital melanocytic nevus. *Dermatol Surg* [Internet]. 1999 Apr [cited 2018 Sep 17];25(4):274–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/10417581>
 14. Almulhim AS, Alotaibi FM. Comparison of broad-spectrum antibiotics and narrow-spectrum antibiotics in the treatment of lower extremity cellulitis. *IJHS*. 2018 Oct 7;12(6).
 15. Farooqui SI, Siddiqui PQ, Ansari B, Farhad A. Effects of spinal mobilization techniques in the management of adolescent idiopathic scoliosis-A meta-analysis. *IJHS*. 2018 Oct 7;12(6).
 16. Ibrahim IA, Ting HN, Moghavvemi M. The effects of audio stimuli on auditory-evoked potential in normal hearing Malay adults. *IJHS*. 2018 Sep;12(5):25.
 17. Ertürk EB, Ünlü H. Effects of pre-operative individualized education on anxiety and pain severity in patients following open-heart surgery. *IJHS*. 2018 Jul;12(4):26.
 18. Rizk HM, Al-Ruthea M, Habibullah MA. The

more effective than a single one. Future research studies should overcome the limitations existed in the studies that have been included in our systematic review regarding several aspects including demographic data, genetic diseases and skin type, and the use of recognized and validated outcome measures.

REFERENCES:

1. Wramp ME, Langenbruch A, Augustin M, Zillikens D, Krenzel S. Clinical course, treatment modalities, and quality of life in patients with congenital melanocytic nevi—data from the German CMN registry. *JDDG*. 2017 Feb;15(2):159-67.
2. Stanganelli I, Ascierio P, Bono R, De Giorgi V, Pimpinelli N, Chiarion-Sileni V, Palmieri G, Pizzichetta MA, Testori A. Management of small and intermediate congenital nevi: a nationwide survey in Italy. *Dermatology*. 2013;226(Suppl. 1):7-12.
3. Whang KK, Kim MJ, Song WK, Cho S. Comparative treatment of giant congenital melanocytic nevi with curettage or Er: YAG laser ablation alone versus with cultured epithelial autografts. *Dermatol Surg*. 2005 Dec;31(12):1660-7.
4. Kono T, Erçöçen AR, Chan HHL, Kikuchi Y, Nozaki M. Effectiveness of the normal-mode ruby laser and the combined (normal-mode plus q-switched) ruby laser in the treatment of congenital melanocytic nevi: a comparative study. *Ann Plast Surg* [Internet]. 2002 Nov [cited 2018 Jul 21];49(5):476-85. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12439014>
5. August PJ, Ferguson JE, Madan V. A study of the efficacy of carbon dioxide and pigment-specific lasers in the treatment of medium-sized congenital melanocytic naevi. *Br J Dermatol* [Internet]. 2011 May [cited 2018 Jul 21];164(5):1037–42. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21275945>
6. Horner BM, El-Muttardi NS, Mayou BJ. Treatment of congenital melanocytic naevi with CO2 laser. *Ann Plast Surg* [Internet]. 2005 Sep [cited 2018 Jul 21];55(3):276–80. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16106167>
7. Al-Hadithy N, Al-Nakib K, Quaba A. Outcomes of 52 patients with congenital melanocytic naevi treated with UltraPulse Carbon Dioxide and Frequency Doubled Q-Switched Nd-Yag laser. *J Plast Reconstr Aesthetic Surg* [Internet]. 2012 Aug [cited 2018 Jul 20];65(8):1019–28. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22525254>
8. Ostertag JU, Quaedvlieg PJF, Kerckhoffs FEMJ,

Tissue expansion in the treatment of giant congenital melanocytic nevi of the upper extremity. *Medicine (Baltimore)* [Internet]. 2017;96(13):e6358. Available from: <http://insights.ovid.com/crossref?an=00005792-201703310-00009>

effect of three lining materials on microleakage of packable composite resin restorations in young premolars with cavity margins located on enamel and dentin/cementum-An In vitro study. *IJHS*. 2018 Oct 7;12(6).
19. Ma T, Fan K, Li L, Xie F, Li H, Chou H, et al.