Evaluation of Applied Protocols by Sudanese Dermatologists for Treatment of Non-Segmental Vitiligo

Ahmed Kamal Aldaw[1], Omer Yahia El-Hussein Mohamed[2], Bakry AL-Agra[3]

Abstract: There are different guidelines applied in the treatment of Vitiligo around the world. They are varied from immunosuppressant, antioxidants and melanogenesis enhancers to bleaching remedies in the spread type of disease.

Aim: To reflect the practice of treating non-segmental vitiligo in Vitiligo- Clinic of Khartoum Hospital for dermatological and venereal diseases.

Method: The survey was designed as two parts: "Part one" studying the medicine from different categories that are mostly prescribed for the subdivisions of non-segmental vitiligo and "Part two" was designed as 20 questions in which we evaluated the Phototherapy applied by dermatologists with or without medicine. The two parts were then filled by 21 out of 28 dermatologists working in Vitiligo-Clinic of Khartoum hospital with at least one year experience in dermatology according to their actual practice in Vitiligo-Clinic in Khartoum hospital for dermatological and venereal diseases during the period from October 2012 to February 2013. The data were then analyzed using Statistical Package for Social Sciences (SPSS) version 14.

Results: Topical corticosteroids Grade 2 are the most prescribed steroid for adults (25%) with different types of vitiligo. In Acrofacial vitiligo the doctors prescribed topical Tacrolimus and Pimecrolimus more than often (17.7%, 15.5% respectively). Unlike in other subtypes of vitiligo, doctors prefer Melanogenesis enhancers like methoxsalen and Psoralen in adults with generalized (30%) and universal vitiligo (25%). However, physicians in this survey usually prescribe depigmentation therapy only for universal vitiligo (20%). First choice phototherapy for focal and generalized vitiligo is BB-UVB (57.14% for both). The commonest method to determine the starting dose for NB-UVB and PUVA is to give fixed starting dose to all skin type then minimal erythemal dose (57.4%). The results showed that dermatologists equally suggest that both PUVA and NBUVB phototherapies give better color matching, or they cannot say which is better (33.3% 3,33% 33,3% the same percent). 52.38% of dermatologists think PUVA give the fastest, effective and stable repigmentation. 42.86% think NBUV is sometimes effective against acral vitiligo. 47.86% of dermatologists recommend adjuvant to phototherapy in the

beginning or if there is no response after one month and 47.62% prefer highly potent topical steroids as an adjuvant. They prescribed multivitamins and antioxidant mainly as an oral medication (42.86% 32.10% respectively), and they notice purities and mid burn as a major side effect on their patients (52.38% 33.33% respectively). They prefer emollient if there is an accident overdose of UVB.

Conclusion:

We recommend establishing registry and evaluation program of current protocols applied in Non-segmental vitiligo in Sudan so as to reflect the patient's variability in compare to the world record.

Introduction:

Vitiligo is a disease characterized by hypomelanosis due to a defect in the melanocytes. Although many shreds of evidence supporting the autoimmune nature of vitiligo pathogenesis, until now there is no accurate etiology for this disease[1].

In vitiligo, the defect of melanocytes causes the appearance of the white patches on different parts of the body. According to the distribution of white patches, vitiligo is divided into two categories: Generalized (non-segmental) and segmental vitiligo. While the segmental vitiligo affects one side of the body and has no autoimmune nature, the generalized (bilateral) vitiligo is characterized by a symmetric distribution of white color on both sides of the body that typically started around the mouth and on the fingers and feet. It is common in Koebner's phenomena; in which depigmentation occurs in lines of trauma [2].

Vitiligo responds to general immunosuppressants like Corticosteroids, Calcineurin inhibitors, Vitamin D3 and Ultraviolet light. However, patients varied in their response to those medicines [3]. Stable pigmentation was registered in melanocytes grafting, which made intense pressure on the rule of the pathogenic microenvironment in the disease resistance to medications [4].

Upon study done in Khartoum hospital for dermatological and venereal diseases in 2007 the prevalence of vitiligo was approximately 3 to 4 % of total patients who come to refer clinics. Male patients were (42%). Children were (11%), adults were (80%), and elderly were (9%). The mean age of onset of the disease was found to be 11.5 yrs in 22.5% of the patients.

In this study, we survey the medications prescribed for non-segmental vitiligo issued by Sudanese dermatologists in Khartoum hospital for dermatological and venereal diseases. We considered subtypes of non-segmental vitiligo as Focal, Acrofacial, Generalized and Universal Vitiligo and we supplied the questionnaire with definitions for every term [3,5]. . Also, we studied the outcome of the Applied Phototherapy by the Sudanese dermatologists and their use with or without chemotherapeutic medicine in the treatment of non-segmental vitiligo.

Material and Method:

Study design:

The study was designed as Descriptive hospital–based study. Based on a questionnaire designed as two parts: "Part one" studying the medicine from different categories that are mostly prescribed for the subdivision of non-segmental vitiligo (as in figure 1). In this type of question we considered 3 types of patients: Adults, Children (12 years old and above), pregnant and patients with vitiligo and other common autoimmune diseases like SLE and Diabetes type 1. In "Part two" was designed as 20 questions in which we evaluated the Phototherapy applied by dermatologists with or without medicine. The questionnaire was filled by doctors with at least one year experience in dermatology according to their actual practice in dermatology and work in Vitiligo-Clinic in Khartoum hospital for dermatological and venereal diseases during the period from October 2012 to February 2013.The data were then analyzed using Statistical Package for Social Sciences (SPSS) version 14.

		Focal	Acrofacial	mucosal	Generalized	Universal
1	Topical steroids grade 1					
2	Topical steroids grade 2					
3	Topical steroids grade 3					
4	Topical steroids grade 4					
5	Topical Tacrolimus					
6	Topical pimecrolimus					
7	Antioxidants					
8	Vitamins B12 + folic acid					
9	Depigmentation					

10	Anthelmintics					
11	Psoralen/Methoxsalen					
12	Vitamin D3					
13	Total number of respondent					

Figure 1: This figure describes the design of part one of the questionnaire. In this figure, we include the different types of medicine that usually prescribed by dermatologists in Khartoum hospital for dermatological and venereal diseases according to a separate study (Data not shown) beside other applied treatments for the diseases. This part of the questionnaire was supplied with definitions for the subdivisions of non-segmental vitiligo and characterization for the different categories of medicine included in the survey e.g. the types of steroids belonging to each grade from 1 to 4.

Results:

Out of 28 dermatologists working in Vitiligo-Clinic of Khartoum hospital for dermatological and venereal diseases, 21 returned the questionnaires (response rate 75%). Two questionnaires were excluded as they were incomplete. Thus, we finally included 19 dermatologists 23.8% of which saw from 5 to 10 vitiligo patients per week, and 14.28% saw more than ten patients per week.

First choice therapies for Adult:

First choice therapies for Adult:

For the clinical types: focal, acrofacial, mucosal, generalized, and Universal vitiligo 47.15 %,26.66%, 56.98%, 33.1%and 19.91% of the dermatologists, respectively, prescribed topical corticosteroids. The most prescribed corticosteroid was grade 2 (mid-potent).

Topical tacrolimus was prescribed by 9.25%, 17.7%, 2.38%, 0%and 0% for Focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively. Topical pimecrolimus was prescribed by 9.25%, 15.5%, 4.7%, 2.7% and 0%, for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Antioxidant was prescribed by 11.11%, 13.33%, 16.6 %, 5.5%and 14.2% for Focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Vitamin B12&folic acid prescribed by 14.81%, 15.5%, 11.9%, 22.2%and 20% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively

Depigmentation was prescribed by 1.85%, 2.22%, 2.38%, 5.5%and 20% for Focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Anthelmintics was prescribed by 1.85%, 0%, 0%, 2.7%and 0% for Focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

methoxsalen/Psoralen was prescribed by 3.7%, 8.8%, 4.7%, 30.5%and 25.7% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Vitamin D3 was not prescribed by Sudanese dermatologist in all type of nonsegmental vitiligo.

First choice therapies for children:

For the clinical types: focal, acrofacial, mucosal, generalized, and Universal vitiligo 37.5 %,27%, 59.4%,30.6%and 24.9% of the dermatologists, respectively, prescribed topical corticosteroids. The most prescribed corticosteroid was grade 2 (mid-potent).

Topical tacrolimus was prescribed by 10%, 5.4%, 8.1%, 0%and 4.16% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively. Topical pimecrolimus was prescribed by 20%, 8.1%, 5.4%, 3.8% and 4.16%, for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Antioxidant was prescribed by 2.5%, 16.2%, 5.4%, 7.6%and 12.5% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Vitamin B12&folic acid prescribed by 10%, 27%, 24.3%, 38.4%and 33.3% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Depigmentation was prescribed by 2.5%, 2.7%, 0%, 0%and 8.3% for Focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Anthelmintics was prescribed by 10%, 2.7%, 0%, 11.5%and 8.3% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Methoxsalen/Psoralen was prescribed by 5%, 2.7%, 2.7%, 3.8%and 4.16% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Vitamin D3 was prescribed by 2.5%, 2.7%, 0%, 0%and 0% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

First choice therapies for pregnant:

For the clinical types: focal, acrofacial, mucosal, generalized, and Universal vitiligo 53.12%, 46.5%, 49.99%,24%and 32.8% of the dermatologists, respectively, prescribed topical corticosteroids. The most prescribed corticosteroid was grade 2 (mid-potent).

Topical tacrolimus was prescribed by 0%, 3.3%, 0%, 0%and 0% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively. Topical pimecrolimus was prescribed by 6.25%, 10%, 0%,

0% and 0%, for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Antioxidants were prescribed by 12.5%, 13.3%, 17.85%, 20%and 33.3% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

Vitamin B12&folic acid prescribed by 28.12%, 26.6%, 32.14%, 52%and 42.85% for focal, acrofacial, mucosal, generalized, and Universal vitiligo, respectively.

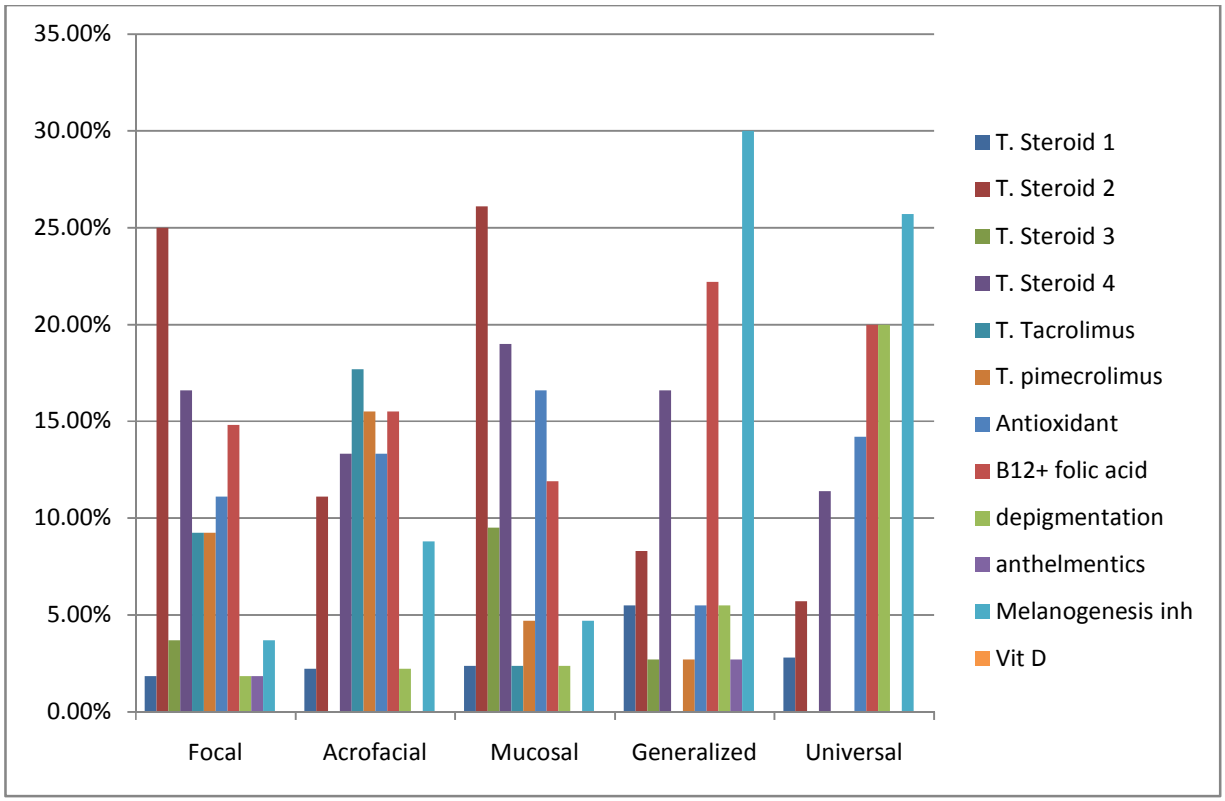


Figure 2: Medication of choice for the treatment of Nonsegmental Vitiligo in adults among dermatologists in Khartoum hospital for dermatological and venereal diseases.

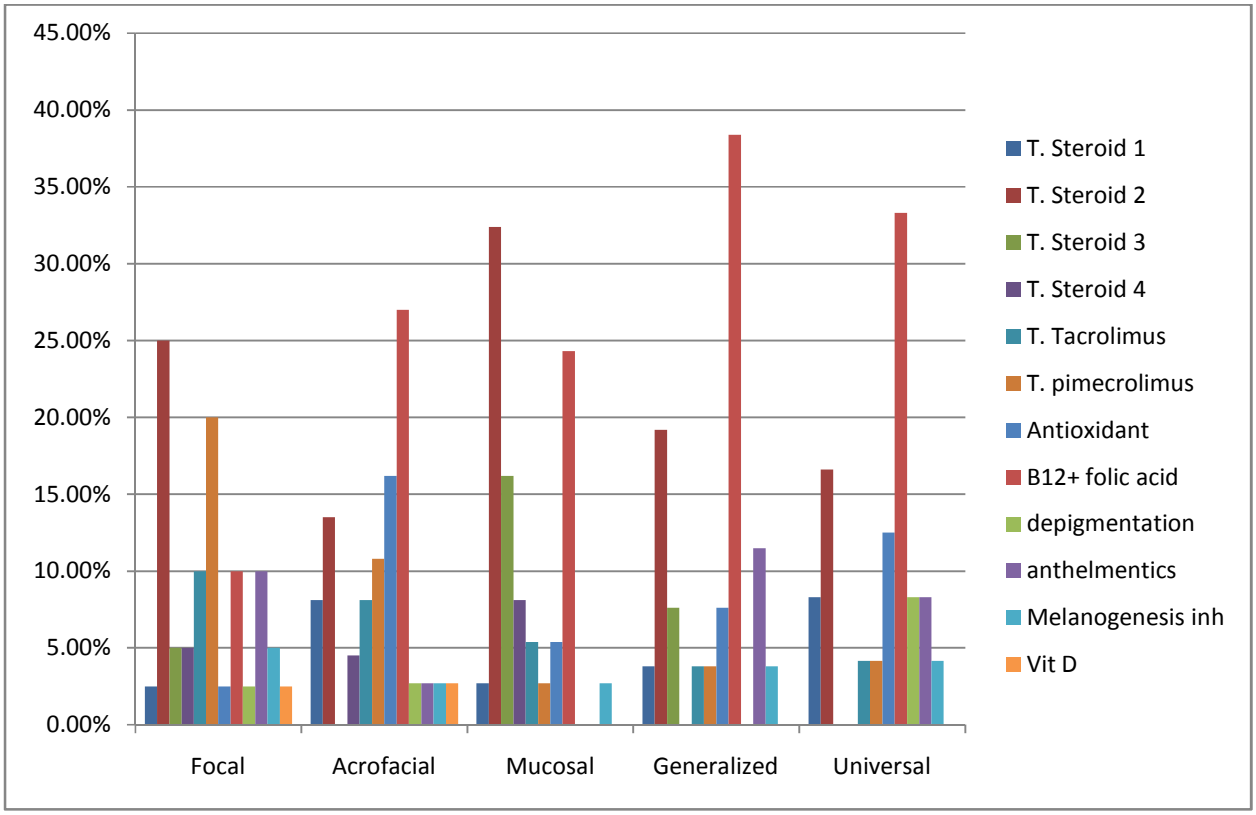


Figure 3:

Figure 3: Medication of choice for the treatment of Nonsegmental Vitiligo in children (under 12 years old) among dermatologists in Khartoum hospital for dermatological and venereal diseases.

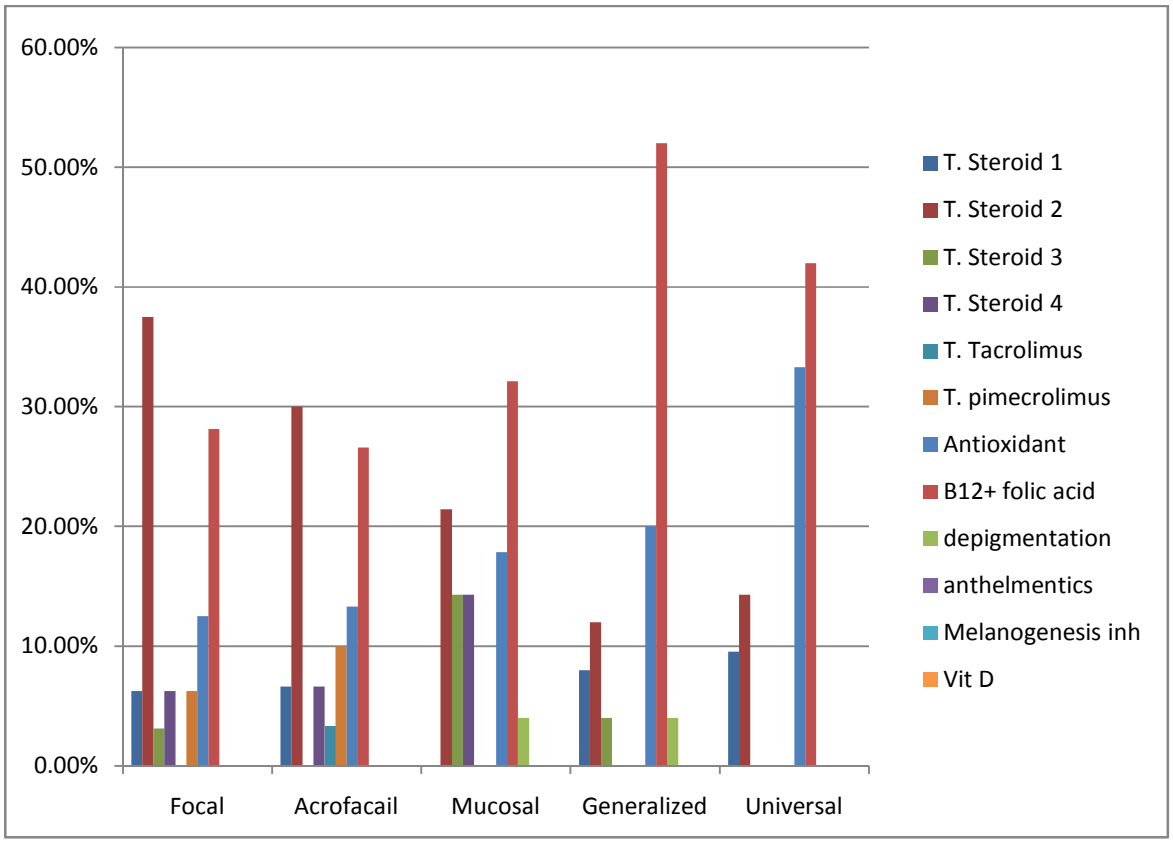


Figure 4: Medication of choice for the treatment of Nonsegmental Vitiligo in pregnant ladies among dermatologists in Khartoum hospital for dermatological and venereal diseases.

Phototherapy Evaluation:

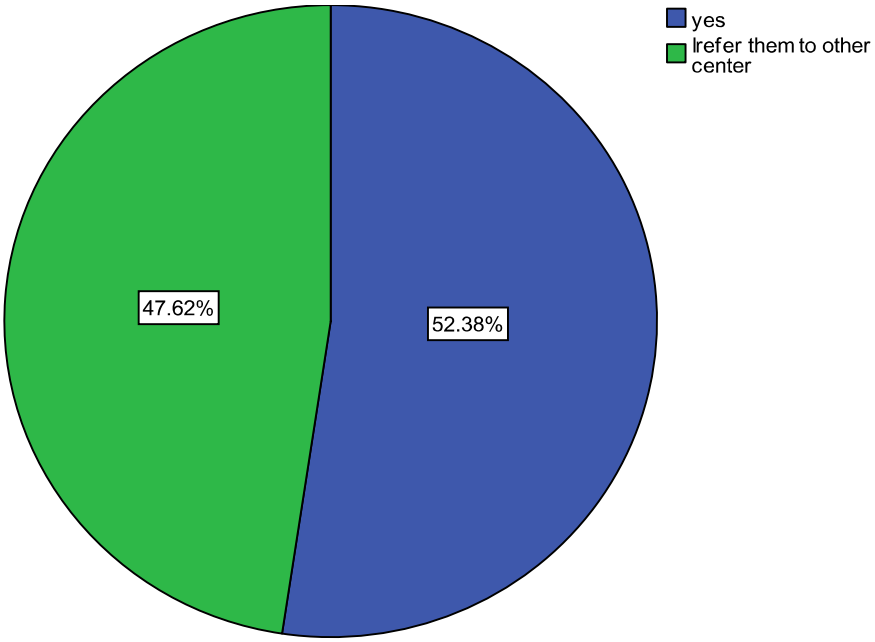


Figure 5: the concept of dermatologists about using phototherapy..

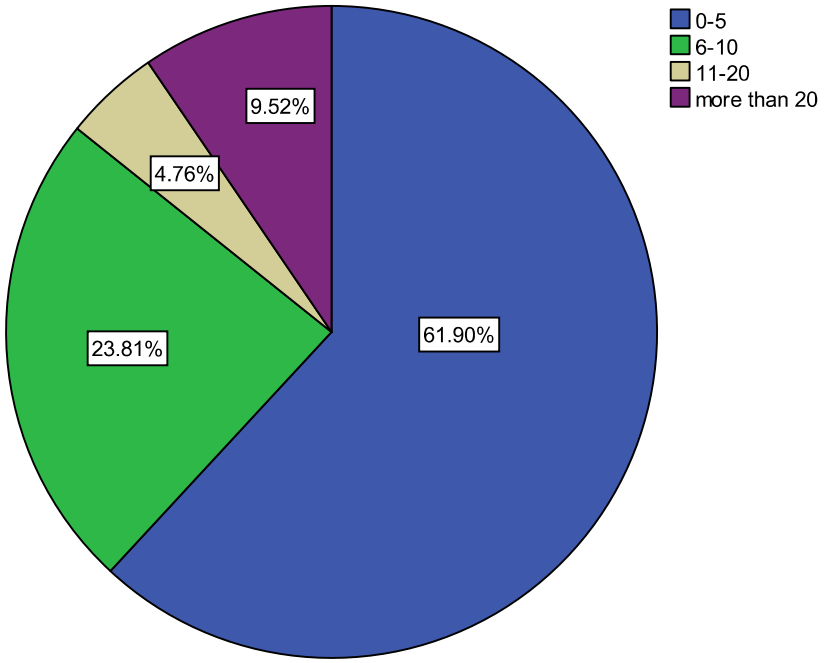


Figure 6: the average of vitiligo patients using phototherapy per week.

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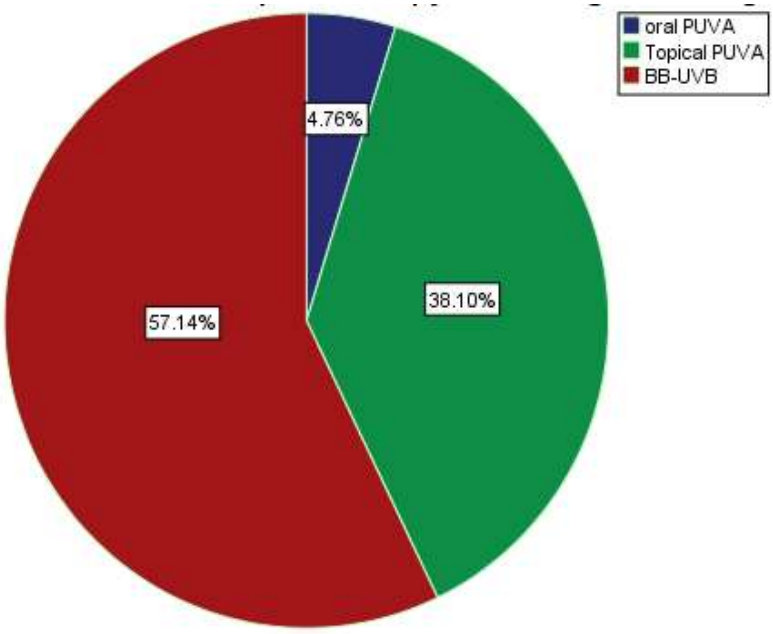


Figure 7: the first choice phototherapy for treating local vitiligo.

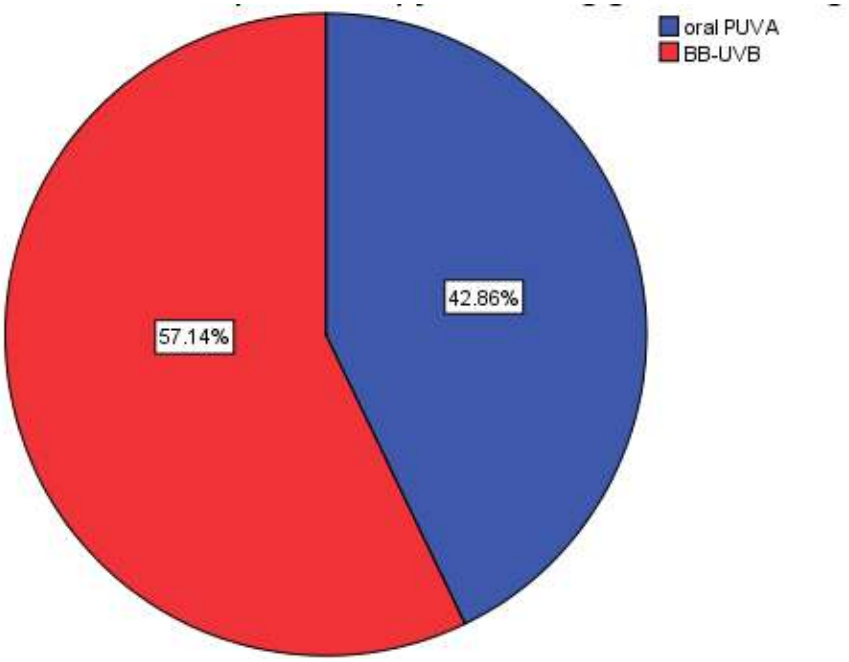
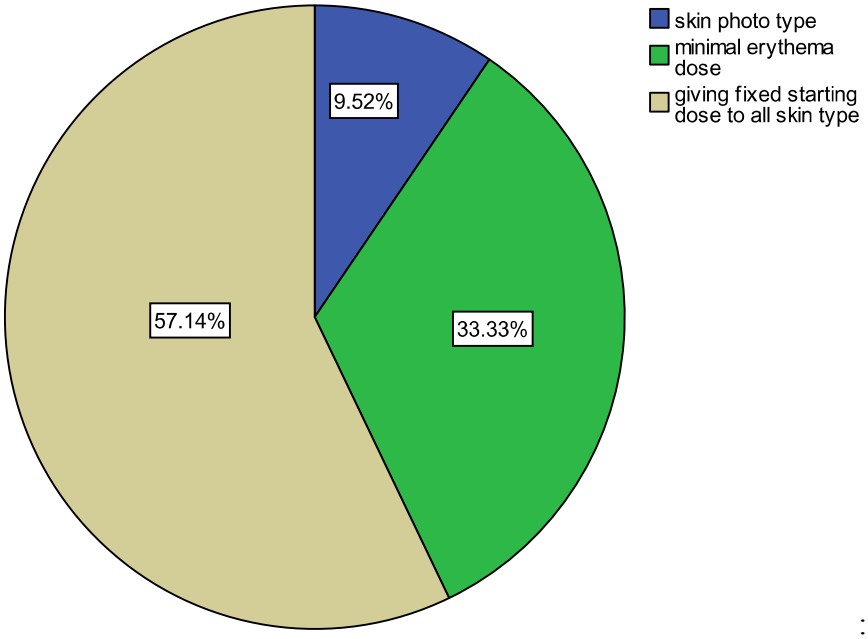


Figure 8: the first choice phototherapy for treating generalized vitiligo.



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Figure 9: the commonest method to determine the starting dose for NB_UVB.

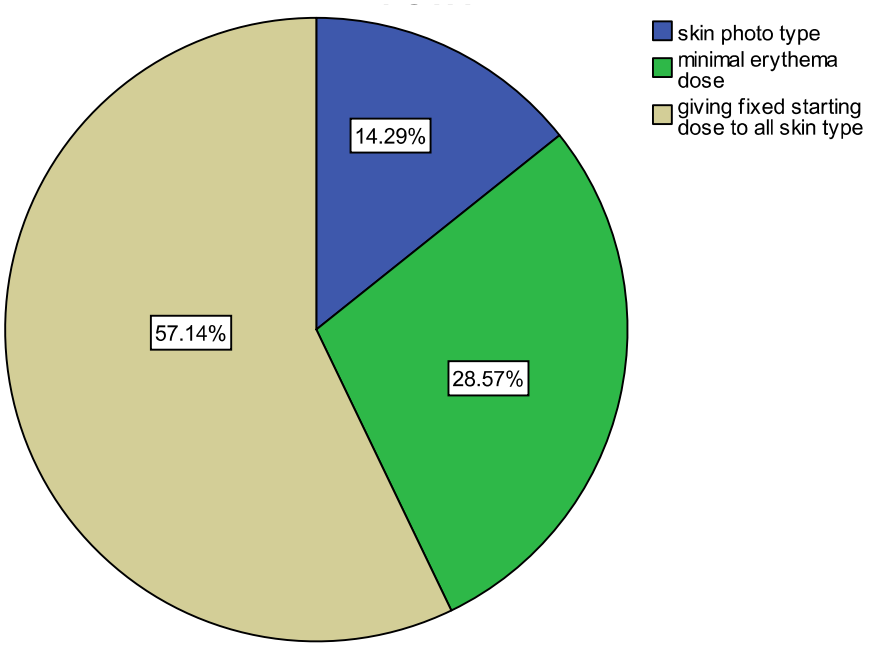


Figure 10: the most convenient way to determine the starting dose for PUVA.

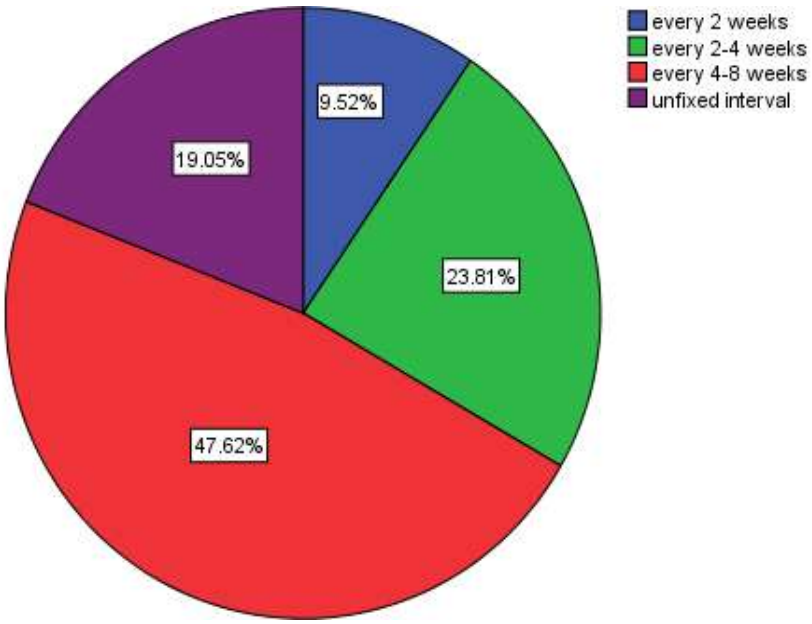


Figure 11: the period of doctor evaluation for vitiligo patients during phototherapy.

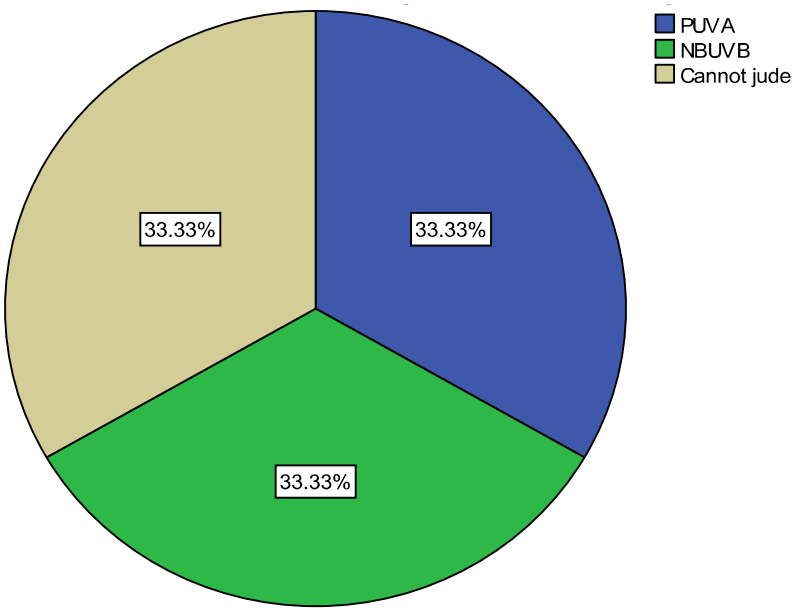


Figure 12: the comparison between PUVA & NB_UVB in which is better color matching with surrounding skin.

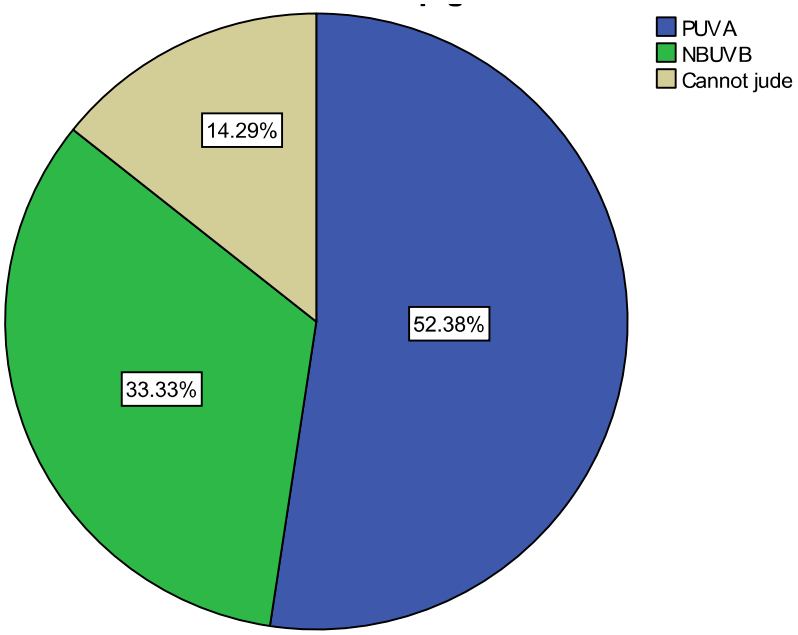


Figure 13: the comparison between PUVA & NB_UVB in which is the most stable pigmentation.

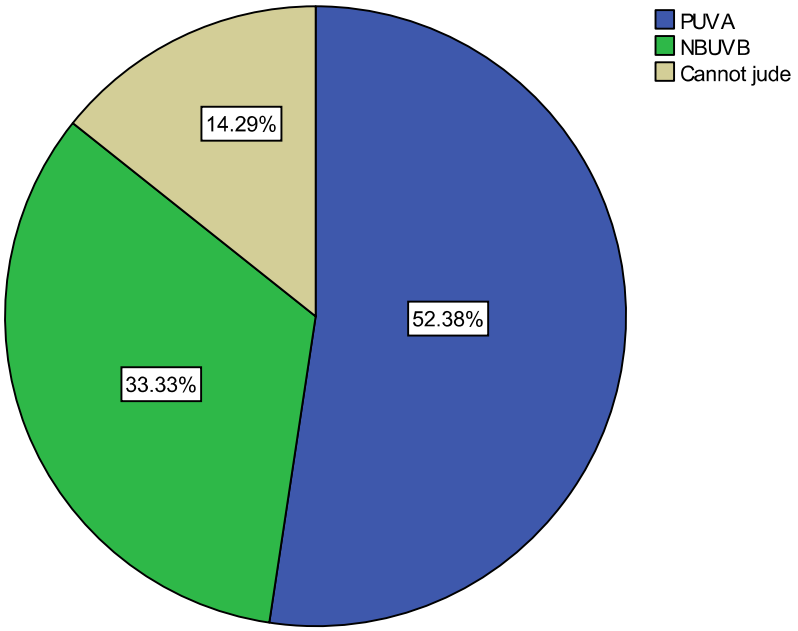


Figure 14: the comparison between PUVA & NB_UVB in which is the faster pigmentation.

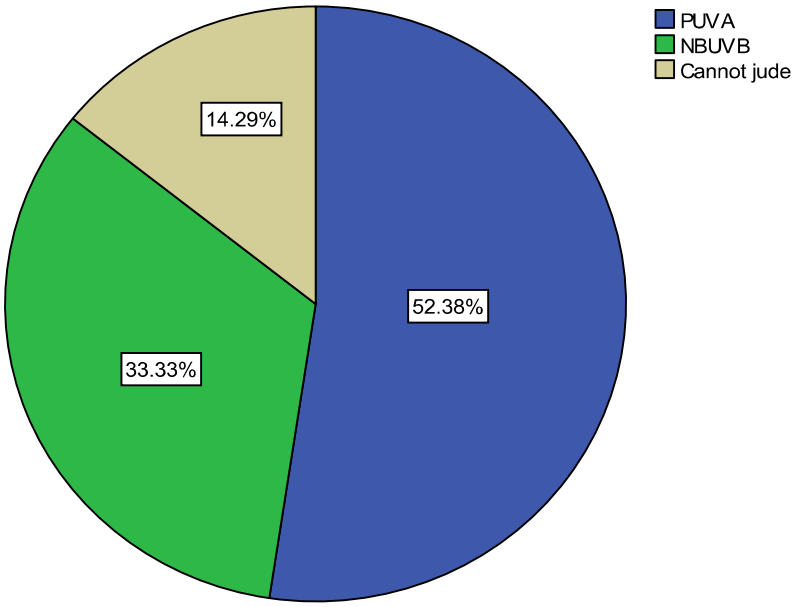


Figure 15: the comparison between PUVA &NB_UVB in their effectiveness.

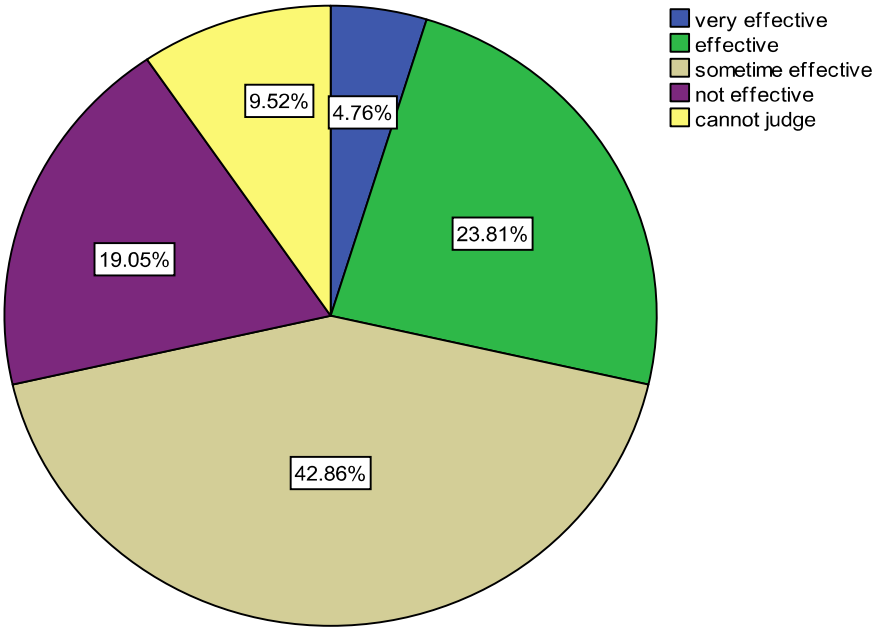


Figure 16: the efficacy of local NBUVB in treating acrofacial vitiligo.

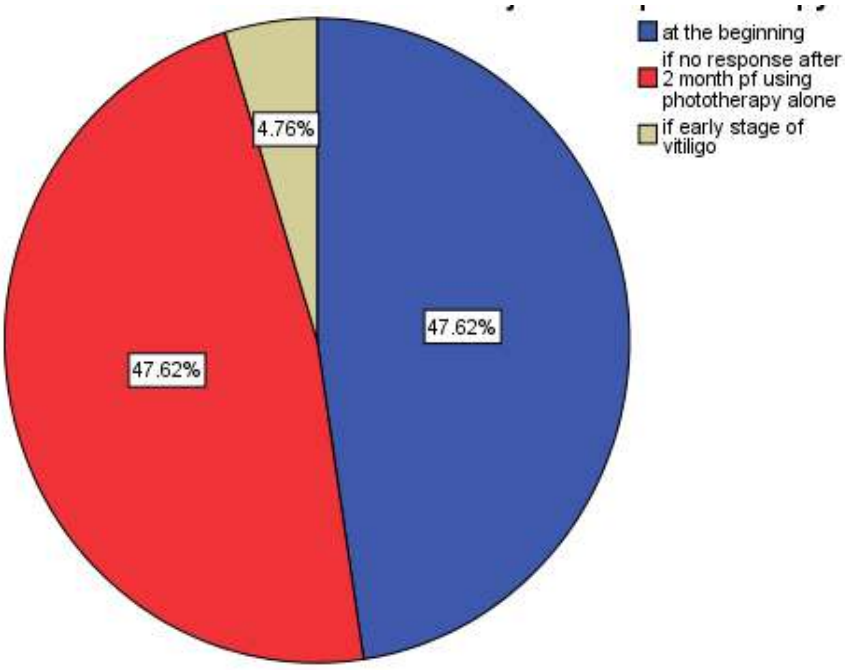


Figure 17: the consideration to add an adjuvant to phototherapy.

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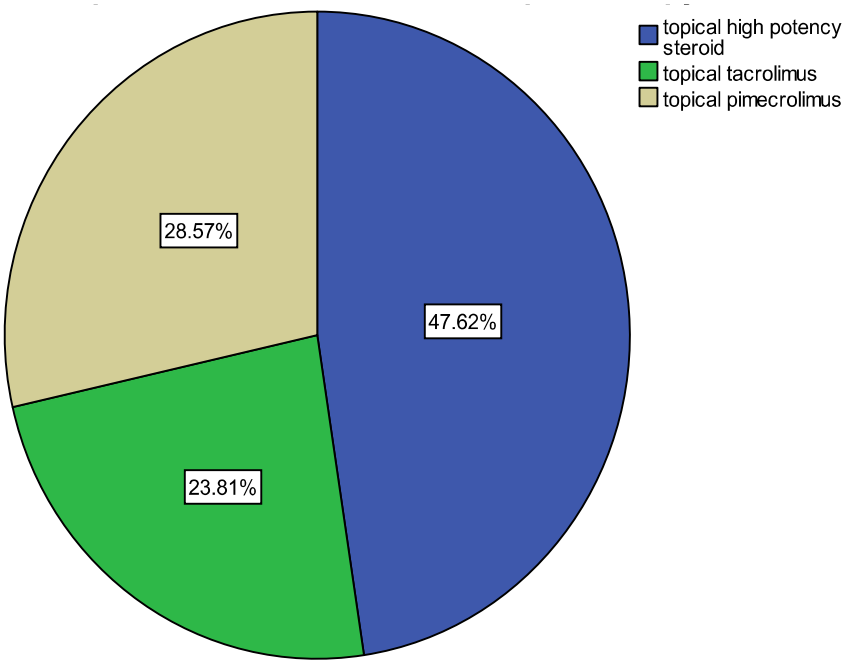


Figure 18: the addition of topical medication to phototherapy.

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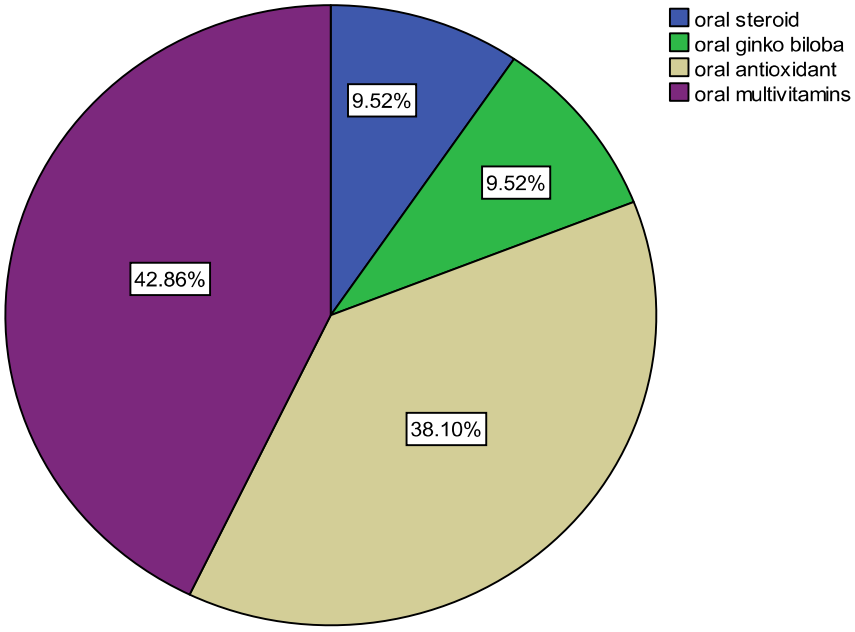


Figure 19: the oral medication in addition to phototherapy treatment.

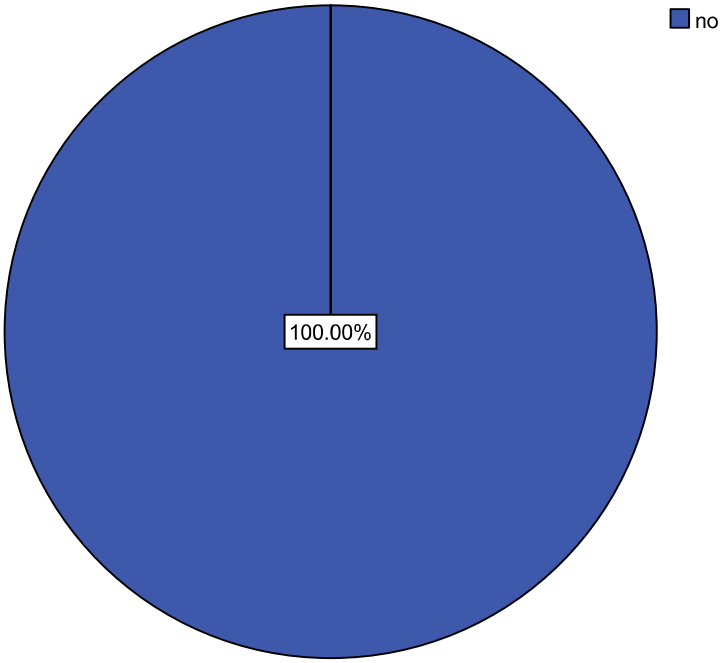


Figure 20: the percentage of developing skin cancer after phototherapy.

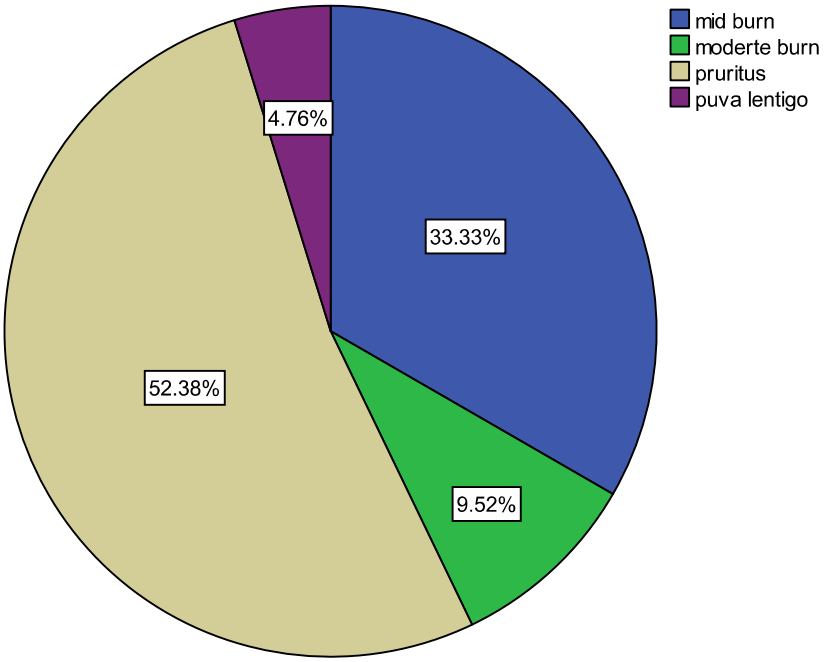


Figure 21: the most common side effects from phototherapy.

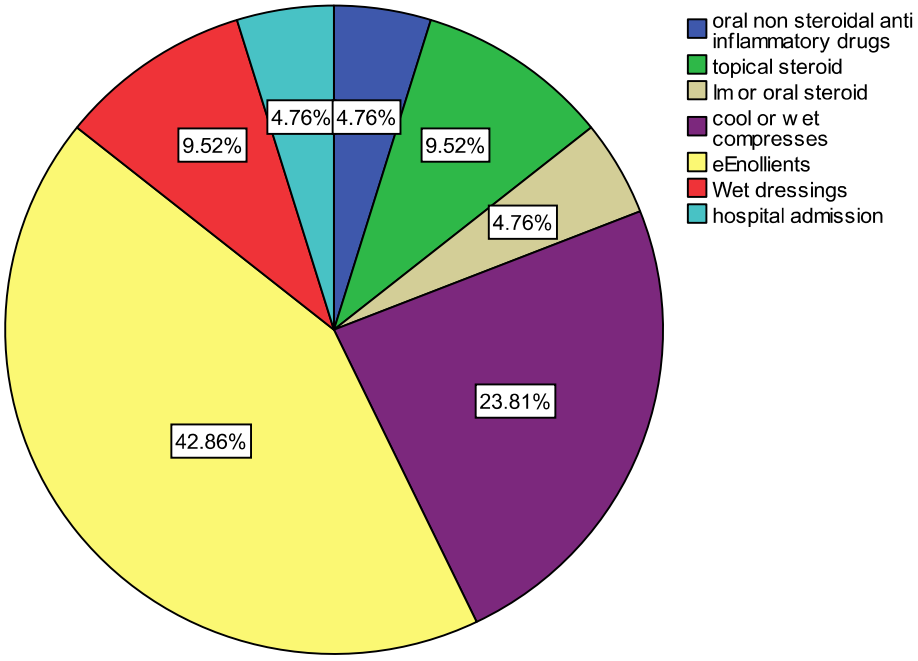


Figure 22: the treatment recommended for sever accidental UVB overdose.

Discussion:

In the current protocol applied in Khartoum Hospital for dermatological and Venereal diseases, the diagnosis, classification and treatments of Vitiligo are depending only on the phenotypic feature of the disease which makes the outcome of the personal health care varied extremely. For this reason, many centers tried to establish an evidence-based guideline for diagnosis and management of vitiligo depending on the evaluation of data from meta-analysis studies, case control cohort studies, besides case reports, case series and expert opinions[5]. Here in this study, we try to survey the practice of dermatologists of Vitiligo-Clinic in managing of non-segmental vitiligo in the Khartoum hospital for dermatological and venereal diseases. As a preliminary step, we made a survey of the types of medications usually prescribed for different types of vitiligo (data not shown).We included the drugs stated in that study plus other remedies like depigmenting medications and vitamin D analogs.

We compare our results to the guideline for the diagnosis and management of vitiligo [5] and a similar study in Saudi Arabia[6]

Adults:

Topical corticosteroids Grade 2 (triamcinolone acetonide, mometasone, budesonide, fluocinolone acetonide) are the most prescribed steroid for adults (25%) with different types of vitiligo or with vitiligo associated

with other autoimmune diseases like SLE, Diabetes type 1 and Alopecia mainly mucosal vitiligo. With the exception for skin atrophy, topical steroids are considered as a safe drug in Adult, pregnant ladies or children. And their use alone or in combination with other medications for management of different categories of vitiligo-like phototherapy where 47.62% of total medication prescribed by responders in addition to phototherapy (figure:18.) this result match what was also found by Al-Ghamdi [6] .

In Acrofacial vitiligo the doctors prescribed topical Tacrolimus and Pimecrolimus beside Vitamin B12, folic acid more than often. Unlike in other subtypes of vitiligo, doctors prefer Melanogenesis enhancers like Oxoralen & methoxsalen in adults with generalized (30%) and universal vitiligo (25%) beside Topical corticosteroids grade 4 (16%), VitB12 and folic acid (22%) in generalized vitiligo. Antioxidants are usually prescribed in focal (11%), Acrofacial (13%), and mucosal vitiligo (16%) and they are not commonly prescribed in generalized and universal vitiligo. However, doctors in this survey usually prescribe depigmentation therapy only for universal vitiligo (20%).

Children:

In general, the most prescribed medication for vitiligo in children is topical corticosteroid grade 2 and vitB12 plus folic acid. However, in focal vitiligo, the doctors prefer topical pimecrolimus beside Topical steroids grade 2 (25%) than the other medications. Pimecrolimus which

is more expensive but used for a shorter time compared to topical steroids which were used for two months as maximum [5].

It is clear that there is very limited use of melanogenesis enhancers in children due to their toxicity.

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Pregnant ladies:

The most used medication for focal and Acrofacial vitiligo in pregnant women is topical corticosteroid grade 2, VitB12 and folic (figure: 4). However, doctors prescribe VitB12, folic acid, and antioxidants more for pregnant ladies with mucosal, generalized and universal vitiligo. It seems that doctors suggest that there is an association between the cases of acrofacial vitiligo and pernicious anemia because of generous accommodation for vitamin B12 + folic acids. While the use of antioxidant was approved as patients with vitiligo, have law Catalase levels with high levels of hydrogen peroxide which was associated with the theory for vitiligo pathogenesis [7].

It was noticed that dermatologists do rarely prescribe Vit.D3 or Anthelmintics for vitiligo, and they are not part of their protocols. Parenteral corticosteroids were not included in the survey provided to dermatologists.

Phototherapy:

Our results of Phototherapy showed that 52% of dermatologists Follow patients using phototherapy and 47.62% refer them to another center. 61.90% Of dermatologists See from 0-5 patients per week.

First choice phototherapy for focal vitiligo is BB-UVB (57.14%) and topical PUVA (38.10%). Whereas the first choice phototherapy for generalized BB-UVB (57.14%) Oral PUVA (42.86%), The commonest method to determine the starting dose for NB-UVB and PUVA is to give fixed starting dose to all skin type then minimal erythemal dose (47.14%). 47.62% of the doctors evaluate vitiligo patients every 4-8 weeks, 23.81% every 2-4 weeks and 19.05% in unfixed time, The results showed that dermatologists were not sure if PUVA and NBUVB phototherapies give better color matching (33.33% for each). and (33.33%) cannot say which is better. 52.38% of dermatologists think PUVA is more efficient than NBUVB (33.33%), and 14.29% cannot judge. 42.86% think NBUVB is sometimes effective in acral vitiligo,23.81% believe it is efficient and 19.05% believe that it is ineffective. 47.62% of dermatologists Add adjuvant to phototherapy at the beginning, and the same percentage of dermatologists add the adjuvant after two months of using phototherapy alone if there is no response. As a topical medication, 47.62% of dermatologists added topically high potency steroid to phototherapy, 23.81% add topical tacrolimus and 28.57% add pimecrolimus. As oral medication supplement, 42.86% of dermatologists add an oral multivitamin, 38.1%

add an oral antioxidant, but only 9.25% add either oral steroid or Ginko Biloba. The data showed that dermatologists had seen no development of skin cancer after phototherapy.

The most common side effect seen by dermatologists is pruritus (52.38%), mid burn (33.33%), moderate burn (9.52%) and PUVA lentigo (4.76%). For accidental UVB over dose, 42.86% of dermatologists recommend emollient, 23.81% of dermatologists recommend cool or wet compresses, 9.52% either wet dressing or topical steroid and 4.76% recommend oral non-steroidal anti-inflammatory drug, I.m or oral steroid or prefer hospital admission.

Conclusion:

Many approaches to the treatment of vitiligo have been studied in the last few years, some of them show a noticeable effectiveness along given period, but no clear protocol is applied.

Choosing a particular treatment for vitiligo is almost always difficult, because it is a multi-factorial disease with an unpredictable course, adding to these factors the patient's compliance as a significant influence in treatment success.

This research highlighted the individual experiences of most Sudanese dermatologists in choosing the topical steroid grade II as the first line with calcineurin inhibitors for most of them.

Introducing of the PUVA and micro-phototherapy as a new treatment option with antioxidants considering age, the distribution of lesions, the associated autoimmune disease.

The NBUVB, anti-helminths, vitamin D, B12 and folic acid, de-pigmentating agents and surgery were of lesser proven efficacy in Sudan.

We recommend recording the use of different trials in treating vitiligo with regular follow-up to avoid the lack of reliable evidence in the future.

We also recommended to the increase of patient's awareness about the approximate period required for treating vitiligo, and the difficulties that can face the success of treatment.

We recommended also applying vitamin D for its potent therapeutic value with or without corticosteroids.

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