

A photograph of a middle-aged couple standing on a beach at sunset. The woman, on the left, has dark hair tied back and is wearing a black tank top. She is smiling and looking at the man, holding a rolled-up grey yoga mat. The man, on the right, has grey hair and a beard, and is wearing a grey t-shirt. He is also smiling and looking at the woman, with his hand resting on her shoulder. The background shows the ocean and a warm, golden sunset sky.

Beauty & Skin

Beauty & Skin Case Studies

“Looking good helps you feel good. Improving the appearance and health of the skin or hair is a common reason people use IV drip therapy in their beauty routines. Liquivida’s scientific team have been exploring this for many years, across several conditions affecting the skin.”

Dr Michael Barnish

➤ [Hyperpigmentation Case Study](#)

➤ [Eczema Case Study](#)

➤ [Rosacea Case Study](#)

➤ [Acne Case Study](#)

Response of a Multi-Nutrient Intravenous Infusion on Hyperpigmentation and Skin Quality

Dr Michael J.A. Barnish MBChB

Clinical Case Studies Liquivida

Global Ltd.

Abstract

Hyperpigmentation is a common condition affecting all ethnicities, in particular those with darker skin tones. Current treatment interventions are topical hydroquinone and oral tranexamic acid. Due to their potential interaction with melanin production, glutathione, vitamin C have been studied as potential interventions for this condition and also as a cosmetic skin lightening

therapy. Whether these are successful interventions on their own is inconclusive. This case study explores combined glutathione and vitamin C, intravenous injection and observes the skin, following an eight-week protocol. Although firm findings cannot be ascertained from this study, a perceived effect is noted, with no reported adverse events, and further study would be required.

Introduction

Melanocytes, in the skin's basal epidermal layer, produce melanin, the pigment responsible for producing skin colour and providing photoprotective protection to the skin.¹

Melanogenesis occurs in organelles, within the melanocytes, called melanosomes where dopaquinone is formed when tyrosinase oxidises tyrosine as the first step to forming both eumelanin (brown) and pheomelanin (red) pigments.² Melanin production, induced by the sun's ultraviolet (UV) results in the production of reactive oxygen species (ROS).¹

Hyperpigmentation, or melasma, of the skin, is a local and acquired hypermelanosis of the skin. It is a common condition affecting all ethnicities, however epidemiological studies report higher prevalence in higher pigmented phenotypes.³ The aetiology of this condition is still not fully determined.⁴ Hyperpigmentation often appears as brown macules of the face, often affecting quality of life, even in individuals with a small area of pigmentation.⁵ Hypermelanosis is not fully understood, however it could occur following excessive inflammation to the skin, or from an inability to successfully clear ROS's, built up from melanin production.¹

Gold standard treatment of hyperpigmentation has been topical hydroquinone, but this has been superseded by tranexamic acid (TA), in recent years, following clinical trials that have revealed its effectiveness and safety for treating the condition.⁵

Glutathione and vitamin C both play a role in melanin production, in different ways and therefore could provide a potential intervention for treating this condition. Glutathione is thought to play a potential role in changing skin colour because in its reduced form it is essential for pheomelanin formation, mediating the switch from eumelanin production to pheomelanin production.⁶ Reduced glutathione (GSH) is also thought to bind to the copper containing active site of tyrosinase, therefore proposing that glutathione could also inhibit melanin production, via this method.⁶ Despite these potential mechanisms of action, glutathione's efficacy for skin lightening skin colour or for improving hyperpigmentation conditions is not proven. A randomized control trial of 60 women, from Bangkok, measuring oral glutathione supplementation on melanin index found no statistically significant difference between

those taking it and the placebo group.⁷ An alternative method of measuring skin colour may have found a different result. There were no serious adverse events throughout this study, involving 250mg oral supplementation. Oral supplementation of glutathione may not be an efficacious route for administration of glutathione as it can be easily degraded by the intestinal enzyme gamma-glutamyl transpeptidase (GGT), making cellular bioavailability potentially challenging and may have accounted for the result.⁸ In general, glutathione supplementation has been observed in several clinical trials, with no serious adverse events being recorded.⁷

Sonthalia et al, in 2018, argue the safety and efficacy of glutathione use parenterally for cosmetic use around cosmetic skin whitening treatments, suggesting evidence for these, in particular parenteral glutathione, was limited to one study of poor design and concluded that there was little convincing evidence in favour of glutathione use for hyperpigmentation, calling for more evidence to explore glutathione's efficacy and safety for this condition.⁹ The authors appear to have a clear bias tone against intravenous glutathione use, focusing on the negative aspects of the one study that they explored for this IV intervention. They reported that this study did not show an effective or lasting treatment for skin tone lightening.⁹ However, the authors explore the studies faults and limitations in detail. This negative outcome could therefore be down to poor study design and not representative of a true outcome. The authors do not suggest this.

Wantanabe et al share the results of a randomized control trial assessing the effect of topical glutathione on melanin index value, moisture content, smoothness, wrinkle formation and elasticity of the skin. Their findings revealed a significantly lower skin melanin index in the 30 women, as well as significant increases in moisture content, suppression of wrinkle formation and improvement in skin smoothness. None of the case subjects reported adverse events, hinting at its safe use.¹⁰ Vitamin C, a potent antioxidant exerts several roles supporting skin physiology, including collagen synthesis

and photoprotection.¹¹ It is currently a controversial topic, that vitamin C can inhibit melanogenesis. Studies have demonstrated its ability to do this, but some have only revealed weak effects, especially in the absence of vitamin E.¹² Vitamin C also has antioxidant properties, which helps to counteract the accumulation of ROS species caused from melanin production and UV radiation.¹¹

A study of 17 patients, measuring the efficacy between tranexamic acid vitamin C showed that independently they both improved melasma statistically significantly, however there was no statistically significant difference observed between the two interventions.⁵

There are several methodologies for measuring interventions for hyperpigmentation in individuals. High resolution cross polarized digital photographs at different profiles can be taken and can be an effective way of observing the result.¹³ However, there are also several scores that can be determined for measuring a whitening effect. Calculating the individual typology angle (ITA°) using a spectrophotometer, utilizing a white ceramic plate is one methodology for measuring whitening effect in clinical study. Alternatively, many studies measure either melasma area and severity scoring (mMASI) or Taylor hyperpigmentation scale. Individuals in studies are often scored using the Fitzpatrick methodology to assess baseline skin type. Scoring methodologies will be subjectivity and therefore, computed and systematic methodologies are more favourable to reduce the chance of subjectivity with these outcomes.

Case Presentation

The case in this study was a 49-year-old, Caucasian female who presented with post-inflammatory hyperpigmentation, diagnosed at a specialist aesthetic clinic. The case is of Greek heritage. Alongside examination, Mediterranean skin type and chronic excessive sun exposure, without SPF protection, were the two risks that helped to establish diagnosis. The case also complained of dark circles under her eyes and a dull skin tone. The case had not previously received any topical or oral treatment for this condition.

Fig. 1 (below) highlights the hyperpigmentation observed and the main areas of concern for the case. The case had been wearing SPF sun protection on the face for 2 years prior to the study and had a baseline skin care routine that had been long standing for more than 1 year.



Figure 1: Unedited case photo prior to the treatment displaying significant hyperpigmentation of the lower face and freckling on the mid face. Arrows demarking main areas of concern.

The case received a weekly, multi-nutrient, intravenous (IV) infusion over the course of an eight-week period, having 8 treatments in total. The multi-nutrient IV infusion contained key ingredients such as glutathione and vitamin C. Rationale for this IV formulation was based upon a full literature review of potentially relevant nutrients for hyperpigmentation. An independent laboratory assessment for pharmacodynamics, particulates and endotoxins was also performed, prior to use.

The case did not change any skin care or SPF habits, keeping them static, as they had been for a long time prior to this study. There were no other treatment interventions, during this study. Prior to and during the treatment schedule, the case's blood pressure, heart rate, temperature, oxygen saturation and respiratory rate fell within normal limits. The case reported no side effects from the treatments throughout the study.

High resolution, cross polarized photography was not available for this case experiment and the method of measuring the intervention was via standard high-resolution photography and patient perceived effect.

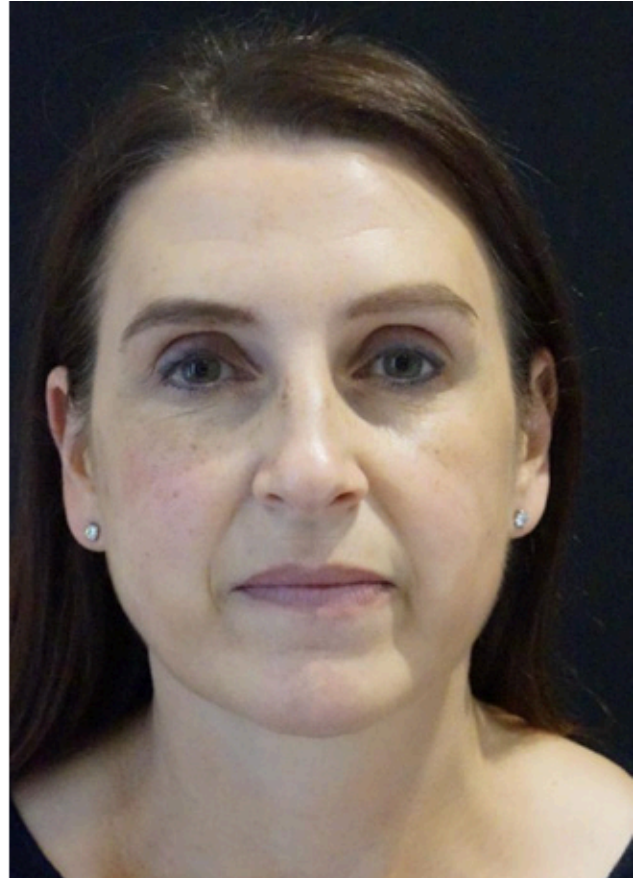


Figure 2: Unedited case photo following the eight-week treatment schedule, displaying a reduction in hyperpigmentation of the lower face and freckling on the mid face with improved under eye skin quality.

The post-treatment image's lighting is slightly different from the pre-treatment image, despite using the same location and camera for the image, at a similar time of day with the window being covered by a blind. However, the image does highlight several improvements. Firstly, the skin tone is more even. The hyperpigmentation is still present around the lower face, bilaterally, but it is softer with a less marked difference between the two skin tones on the first image. The lighting may account for some of this difference. Secondly, the under-eye region of this case appears improved with reduction of fine lines and improved tone. The freckles are also improved and more blended with the surrounded skin tone. Finally, fine lines on the upper lip are also reduced.

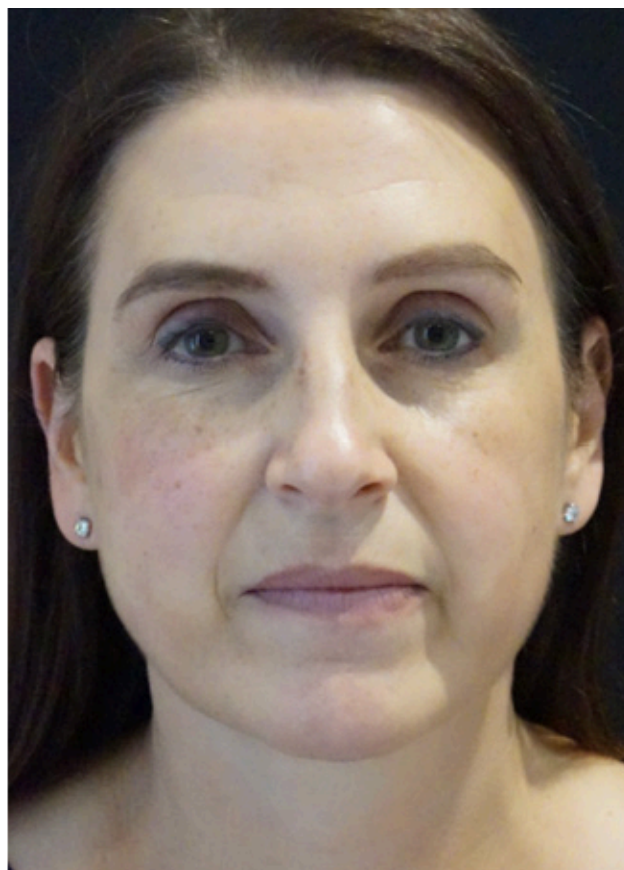


Figure 3: Comparative photos of the case pre and post treatment schedule.

Following the treatment schedule, the case reported a significant improvement in the skin's tone and quality and was content with her perceived reduction of the hyperpigmentation.

Discussion

The current literature suggests that glutathione and vitamin C may be helpful stand alone or adjunctive interventions for improving conditions involving hypermelanosis. To date there has been only small scale clinical trials to look into this with only marginal evidence of its efficacy.

Combining these two interventions, in different forms (NAC & glutathione, for example) and providing them to the case in larger, intravenous doses, was tested during this case study, with perceived improved outcomes. With the lack of standardised calculations of skin colour or advanced photographic methods for recording findings, this case is limited in its ability to make a firm judgment, however the perceived result is apparent, following the intervention. It would be appropriate to explore the same experiment considering cross polarized photography, mMASI scoring, skin melanin index scoring and spectrophotometer use, to measure pigmentation outcomes. Additionally skin

moisture, wrinkle definition, skin smoothness and firmness could be quantified via several specialist sensors or devices, manufactured for these purposes. Testing the safety of this multi-nutrient infusion by monitoring renal and liver function throughout the experiment would also be beneficial when intravenous glutathione is used. Comparing these interventions with placebos will also be beneficial to establish potential efficacy of this intervention.

References

1. Lu, Yaoying, Kathryn F. Tonissen, and Giovanna Di Trapani. 'Modulating Skin Colour: Role of the Thioredoxin and Glutathione Systems in Regulating Melanogenesis'. *Bioscience Reports* 41, no. 5 (28 May 2021): BSR20210427. <https://doi.org/10.1042/BSR20210427>.
2. Hearing, Vincent J., and Mercedes Jiménez. 'Mammalian Tyrosinase—The Critical Regulatory Control Point in Melanocyte Pigmentation'. *International Journal of Biochemistry* 19, no. 12 (January 1987): 1141–47. [https://doi.org/10.1016/0020-711X\(87\)90095-4](https://doi.org/10.1016/0020-711X(87)90095-4).
3. Handel AC, Miot LDB, Miot HA. Melasma: a clinical and epidemiological review. *An Bras Dermatol*. 2014 Sep;89(5):771
4. Iraj, Fariba, Mojtaba Nasimi, Ali Asilian, Gita Faghihi, Samaneh Mozafarpour, and Hossein Hafezi. 'Efficacy of Mesotherapy with Tranexamic Acid and Ascorbic Acid with and without Glutathione in Treatment of Melasma: A Split Face Comparative Trial'. *Journal of Cosmetic Dermatology* 18, no. 5 (October 2019): 1416–21. <https://doi.org/10.1111/jocd.12874>.
5. Zhao, Huijuan, Mengna Li, Xiaofeng Zhang, Li Li, Yan Yan, and Baoxi Wang. 'Comparing the Efficacy of Myjet-assisted Tranexamic Acid and Vitamin C in Treating Melasma: A Split-face Controlled Trial'. *Journal of Cosmetic Dermatology* 19, no. 1 (January 2020): 47–54. <https://doi.org/10.1111/jocd.13112>.
6. Chung, Bo, So Choi, Ik Moon, Chun Park, Young-Hoon Kim, and Sung Chang. 'The Glutathione Derivative, GSH Monoethyl Ester, May Effectively Whiten Skin but GSH Does Not'. *International Journal of Molecular Sciences* 17, no. 5 (27 April 2016): 629. <https://doi.org/10.3390/ijms17050629>.
7. Weschawalit, Sinee, Siriwan Thongthip, Phanupong Phutrakool, and Pravitt Asawanonda. 'Glutathione and Its Antiaging and Antimelanogenic Effects'. *Clinical, Cosmetic and Investigational Dermatology Volume 10* (April 2017): 147–53. <https://doi.org/10.2147/CCID.S128339>.
8. Schmitt B, Vicenzi M, Garrel C, Denis FM. Effects of N-acetylcysteine, oral glutathione (GSH) and a novel sublingual form of GSH on oxidative stress markers: A comparative crossover study. *Redox Biology*. 2015 Dec;6:198–205.
9. Sonthalia S, Jha A, Lallas A, Jain G, Jakhar D. Glutathione for skin lightening: a regnant myth or evidence-based verity? *Dermatol Praat Concept*. 2018 Jan 31;15–21.
10. Watanabe F, Hashizume E, Chan GP, Kamimura A. Skin-whitening and skin-condition-improving effects of topical oxidized glutathione: a double-blind and placebo-controlled clinical trial in healthy women. *CCID*. 2014 Oct;267.
11. Sanadi, RizwanM, and RevatiS DeshmUSAh. 'The Effect of Vitamin C on Melanin Pigmentation – A Systematic Review'. *Journal of Oral and Maxillofacial Pathology* 24, no. 2 (2020): 374. https://doi.org/10.4103/jomfp.JOMFP_207_20.
12. Wang, Kaiqin, Hui Jiang, Wenshuang Li, Mingyue Qiang, Tianxiang Dong, and Hongbin Li. 'Role of Vitamin C in Skin Diseases'. *Frontiers in Physiology* 9 (4 July 2018): 819. <https://doi.org/10.3389/fphys.2018.00819>.
13. Duperray, Joël, Renaud Sergheraert, Kunyanatt Chalothorn, Preeyanuch Tachalerdmanee, and Fabrice Perin. The Effects of the Oral Supplementation of L-Cystine Associated with Reduced L-Glutathione-GSH on Human Skin Pigmentation: A Randomized, Double-blinded, Benchmark- and Placebo-controlled Clinical Trial'. *Journal of Cosmetic Dermatology*, 22 April 2021, [jocd.14137](https://doi.org/10.1111/jocd.14137). <https://doi.org/10.1111/jocd.14137>.

Demographic Information

Gender:	Ethnicity:	Age:
Female	Caucasian	22

Customer testimonial:

I have had eczema for 3 ½ years now. My eczema mostly affects my legs and arms, but it has also been across my belly, my back, on my scalp and on my chest, even around my ears. It got so bad that I couldn't always go into work and I work at a desk in an office. I lived in bandages, my fiancé had to dress me and I barely slept. My skin was raw. I could barely move. Wearing clothes and having bedsheets touch me was painful and my skin was constantly weeping. Showering and bathing reduced me to tears as it felt like my skin was burning. I only wanted to leave the house if I had to go to the doctor. From my first treatment I felt awake and energised and over that first weekend if I had a flare up of eczema, it calmed down quicker than it had done before. I feel like my skin looks normal and I'm not limited to where I can go, what I can do or wear. I know the eczema may never fully go away but the treatment makes me feels and look like it has! It is definitely something I am going to carry on doing.



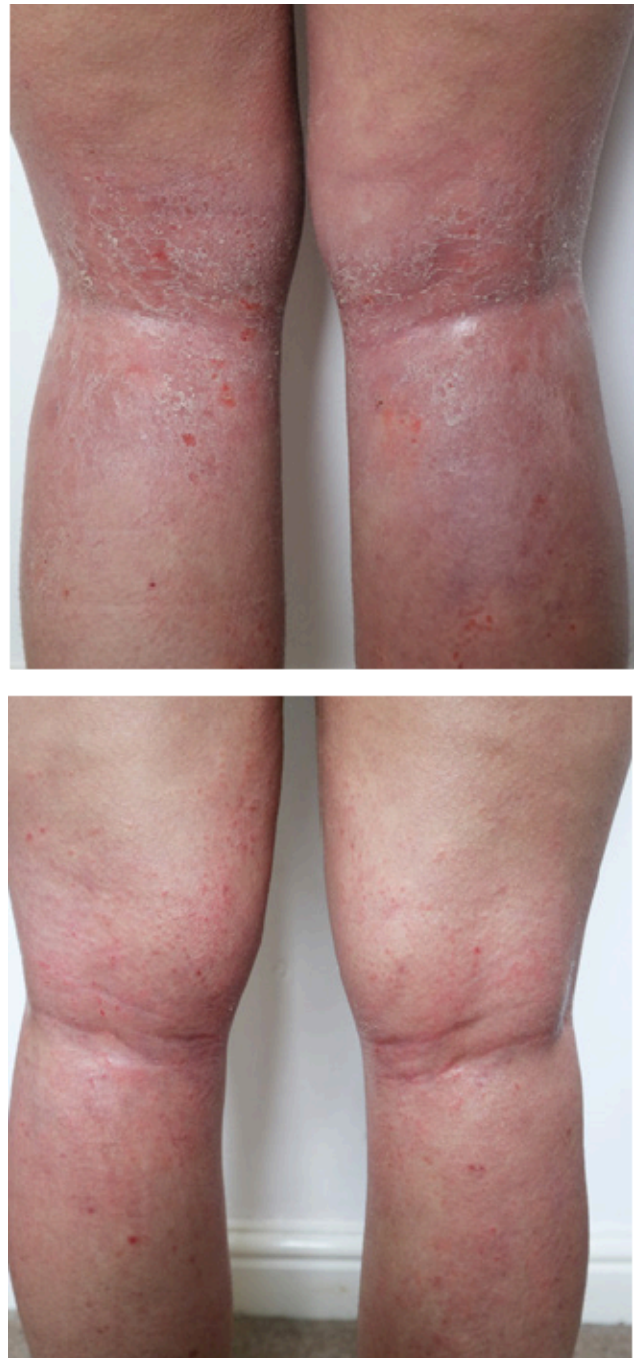
By exploring the customer's medical history, eczema's natural history, her potential triggers, and lifestyle, we were able to establish what her potential nutritional requirements were, that may have been compromising her skin's health and altering the normal, natural skin cycle. In-depth analysis of the existing literature for different nutrients and eczema was undertaken and stratified to an IV formulation. The infusion had undertaken laboratory testing, prior to administration, to ensure safety. The intravenous infusion contained several nutrients, delivered at 2-weekly intervals, for the duration of 12 weeks, representing 2 normal skin cycles. The results show an almost complete resolution of symptoms, something that conventional dermatological management (moisturising creams, steroids and antibiotics) had been unable to offer the patient over her 3 ½ year presentation.

Treatment schedule:

2x Glutathione Pushes, administered every 2 weeks, for a 12 week period.

Patient photographs:

Before and after photographs of case study following 6x personalized IV nutritional therapies, spanning 12 weeks.



References

1. Oxidative stress in atopic dermatitis. Hongxiu et al. Oxidative medicine & cellular longevity. 2016. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4781995/pdf/OMCL2016-2721469.pdf>
2. Role of vitamin C in skin diseases. Wang et al. Frontiers in Physiology. 2018 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6040229/pdf/fphys-09-00819.pdf>
3. Evaluation of topical vitamin B12 for the treatment of childhood eczema. Januchowski. Journal of alternative & Complimentary medicine. 2009. <https://pubmed.ncbi.nlm.nih.gov/19368512/#:~:text=Objectives%3A%20Topical%20vitamin%20B12,through%20reducing%20nitric%20oxide%20production.>
4. Oxidative stress and apoptosis. Kannan K et al. Pathophysiology. 2000. <https://pubmed.ncbi.nlm.nih.gov/10996508/>

The Use of Intravenous Glutathione in the Management of Rosacea

John Tebbutt RN
Clinical Case Studies
Liquivida Global Ltd.

Dr Michael J.A. Barnish MBChB
Clinical Case Studies Liquivida
Global Ltd.

Introduction

Oxidative stress is the imbalance of free radical particles and antioxidants throughout the body. Immunological mechanisms in autoimmune disorders have been shown to increase oxidative stress, leading to aggravation of pathophysiology in a variety of conditions, including rosacea. These molecules are highly reactive throughout the body and can damage vital proteins and lipids which can lead to the breakdown of Deoxyribonucleic acid (DNA).

Given that acne rosacea appears to have autoimmune features we can hypothesise that oxidative stress could worsen the condition and propose antioxidant support as a potential solution for the condition. Rosacea is a common skin condition affecting the face. It is categorised by frequent episodes of transient or continuous erythema, caused by swelling to superficial blood vessels and resulting in a localised pyrexia and erythema, sometimes leading to pain. Sebaceous gland hyperplasia can lead to papule and pustule formation. Phymatous changes, from chronic connective tissue regeneration resulting in fibrosis can occur, which may to fibrosis scar tissue development, in severe cases. Sebaceous gland hyperplasia most commonly affects the nose, resulting in it appearing bulbous in nature. Initially rosacea affects the forehead, the bridge of the nose and the cheeks, with periorbital and perioral areas being spared. Rosacea typically presents as a fluctuating pattern, before disease progression leads to continuous symptoms. Symptom intensification, from exacerbating factors and UV light exposure is typical with the condition. Exacerbating factors that can intensify symptoms include emotional triggers, temperature changes and hot food or drink consumption.

The aetiology of rosacea is unknown, however the precipitating factors, listed above, suggest a potential

theory for a lack of normal homeostatic control of the blood vessels that supply the pilosebaceous follicles. Speculative associations with the mite, demodex folliculorum, found in large numbers on the face, is also a prominent theory of aetiology.

Recent research has shown there could be a potential genetic link to the condition. Further studies have discussed genetic variant relationships with almost half of cases with rosacea. These variants are associated with autoimmune diseases, in general, proposing a potential autoimmune link to the condition. Treatment of rosacea depends on symptomology, but typically includes topical antibiotic, topical antiparasitic (Ivermectin) or azelaic acid as a first line treatment, in primary care. Topical retinoids are commonly used by dermatologists for management of symptoms. There is no known cure for the disease. Resistant individuals are commonly prescribed oral antibiotics.

Diagnosing rosacea presents a variety of difficulties as a range of dermatology conditions identify with the same clinical indicators.

Rosacea is often misdiagnosed and studies have shown that incorrect diagnosis and use of medications could induce rosacea. This can lead to incorrect management of the condition, for instance with topical corticosteroids. The incorrect use of potent topical steroids was found to worsen the effects of rosacea. Treatment for steroid induced rosacea is typically oral antibiotics as first line treatment. Notably, it is also worth considering topical steroid withdrawal syndrome when there is a history of inappropriate use of topical steroids for a significant period of time in patients with rosacea.

With oxidative stress and autoimmunity both considered in the cause or exacerbation of rosacea, Wozniacka et al explored the antioxidant properties of nicotinamide adenosine dinucleotide (NAD) as a potential treatment for the condition.

They found the topical application of NAD flattened papules and the reduced in erythema with a 75% success rate. This pilot study provides some evidence that antioxidant therapy may have a role in the management of rosacea. However, it is important to note that NAD has 100s of roles in cellular metabolism, so the mechanism of action, for this noted improvement, cannot be firmly concluded to be through its antioxidant effects. Further to this, Dalloglio et al 2020 found applying topical glutathione to participants with rosacea reduced the number and size of lesions on their skin. Glutathione is one of the body's principal antioxidants.

Case Results

Glutathione is a major antioxidant, found in almost all cells of the body. It can neutralise free radical and reactive oxygen species, that can accumulate and lead to oxidative stress. Glutathione is also a cofactor for antioxidant enzymes and is a key component in the regeneration of other antioxidants, such as vitamins C and E. As a cleaner the case had higher than normal exposure to exogenous chemicals and could mean that there was more oxidative stress present and therefore, a higher demand for antioxidants.

We explored a multi-antioxidant intravenous infusion, containing glutathione, vitamin C and N-acetyl cysteine to monitor its effectiveness for reducing the symptoms of rosacea in the case. The proposed antioxidant intravenous infusion underwent laboratory analysis for pH, osmolarity, specific gravity, endotoxin formation and particulate formation to assess for agreeable pharmacodynamic properties prior to utilising this infusion. All parameters were acceptable. See Appendix 1: Certificate of Analysis. The case did not want to explore the topical or oral antibiotic therapy, outlined by national guidance, and wanted to explore intravenous nutrition prior to further review for her symptoms with her general practitioner (GP). Prior to this she had been given topical steroids, which she used and symptoms exacerbated, and therefore was reluctant to re-engage with her GP, despite advice from us. Due to the steroid exacerbation she wanted to avoid medication.

A clear discussion was undertaken with the case explaining the rationale, safety and existing evidence, alongside potential benefits of the intervention, when compared to conventional treatment. The case did not want to explore topical or oral antibiotic therapy, due to concerns of long-term antibiotic use. Prior to presentation the case received topical steroids, which she used for a long period of time and had exacerbated her symptoms.

The intervention was carried out in a specialist intravenous (IV) nutrition clinic, Liquivida, registered with the Care Quality Commission (CQC) and prescribed by a qualified and registered medical prescriber and administered by a registered medical professional.

Case Background

41-year-old caucasian woman who presented with a two-year history of intermittent facial maculopapular erythema with papules and pustules present. This was present bilaterally, on the cheeks and there was peri-oral and peri-orbital sparing. There was notable xerosis over the erythematous region. There was also some involvement on the chin. See Fig 1.

The erythema was positive for itching and burning type sensations, particularly aggravated if there was exposure to UV light. Skin care could not be tolerated and exacerbated the condition. There was no sign of infection. There was no ocular involvement. Systemically she was otherwise well with no symptoms. Her menstrual cycle was normal and regular. Sleep was affected by the burning and itching symptoms, particularly in warmer weather. The case cannot recollect an initial causal event, two years ago, and had no past medical history. She reported taking no regular medication, but supplements daily with oral vitamin D, vitamin C and magnesium. Her general practitioner, in Poland, initially prescribed topical steroid (Mometasone 0.1% cream), which the patient used regularly with some initial improvement. However, the condition persisted, and symptoms returned with more severity, following the course of steroids. There was no further medical intervention and her symptoms have intermittently occurred with no predictability, including no menstrual pattern. The current exacerbation of the rosacea was continuous and had been present for almost one year.

A diagnosis of rosacea was made based on clinical examination and the nature of symptoms and exacerbating factors. For this paper, it is important to bear this in mind as the patient had incorrectly been administering topical steroids. The patient was made aware that oral antibiotics would have been the first line treatment, for her particular

presentation. However, she wanted to avoid regular antibiotic use, for the preservation of her microbiome.



Figure 1 : Case photos (front & lateral) prior to the intervention.

The case cannot recollect an initial causal event, two years ago, and had no past medical history. She reported taking no regular medication, but supplements daily with oral vitamin D, vitamin C and magnesium. Her general practitioner, in Poland, initially prescribed topical steroid (Mometasone 0.1% cream), which the patient used regularly with some initial improvement. However, the condition persisted, and symptoms returned with more severity, following the course of steroids. There was no further medical intervention and her symptoms have intermittently occurred with no predictability, including no menstrual

pattern. The current exacerbation of the rosacea was continuous and had been present for almost one year.

A diagnosis of rosacea was made based on clinical examination and the nature of symptoms and exacerbating factors. For this paper, it is important to bear this in mind as the patient had incorrectly been administering topical steroids. The patient was made aware that oral antibiotics would have been the first line treatment, for her particular presentation. However, she wanted to avoid regular antibiotic use, for the preservation of her microbiome. The case had been practising a vegan diet for six and a half years, avoiding animal proteins and products. She received occasional vitamin B12 injections because of this and had no symptoms of vitamin B12 deficiency. The case also reported that she ate one meal a day on average and consumed limited coffee. The case's occupation, as a cleaner resulted in daily exposure to multiple cleaning products that potentially harboured harmful chemicals. The exposure to these chemicals remained largely static throughout the study, with a change to the window cleaning product only to a vinegar-free product. The remaining exposure stayed the same.

Intervention

The case received six multi-nutrient intravenous infusions. The frequency of these infusions was once weekly.

The case was asked to not alter any aspect of her life, including diet and continued not to use skin care. Supplementation was continued, as before as had been on these supplements for several years.

Outcome measures were observed through standard clinical photography and patient feedback questionnaire. Photographs were taken using mobile photography.

Safety outcomes were measured by obtaining the following blood biomarkers:

- Urea & electrolytes (renal function)
- C-reactive protein (CRP) (inflammatory marker)

These bloods were obtained prior to the intervention and repeated one week after the final infusion.

A superior technique for clinical photography would be high resolution cross polarized photography, however this was not available during the time of intervention.

Outcomes



Figure 2: Case photo following intervention. 7 weeks after the initial photography.

As demonstrated in figure 2 highlights the results following the intervention, showing improved symptoms of rosacea and appearance of healthier looking skin. There is a marked reduction in erythema and improved skin texture and tone.

The xerosis has vastly improved overall. Upon further examination there is minimal dry skin towards the upper right side of the cases lips. Papules and pustules appear visibly reduced in number and size, bilaterally. Some erythema still persists, particularly on the nose region.

Measurable outcomes were conducted using patient surveys upon each visit. Symptoms such as burning, itching, redness, sleep, hair quality and energy levels were given a subjective score from 0 to 10.

- For burning, itching and redness a score of 10

represented the most severe score and a score of 0 represented no symptom present.

- For sleep quality, hair quality and energy levels, the score of 10 represented optimal hair quality, sleep quality or energy levels and a score of 0 represented the highest severity.

Each symptom was analysed on the cases weekly visit to the clinic, prior to each intervention and reported by the patient. The patient was also asked to report any other perceived benefits as well as adverse events. Figures 5 and 6 reveal the results of these outcomes.

From these scores there is a clear reduction in symptoms prior to the third infusion. There is an exacerbation of all symptoms prior to the fourth infusion and was potentially due to a period of sunny weather. Following that week, and despite the weather being summer weather for the following weeks, the symptoms continued to fall until they were no longer present by the 7th week.



Figure 3: Visual comparisons of pre-therapy (left) and post-therapy (right) frontal face assessing the effectiveness of the intervention.



Figure 4: Visual comparisons of pre-therapy (left) and post-therapy (right) lateral face assessing the effectiveness of the intervention.

Symptom	Pre-trial	Post-trial
Burning	3/10 in cold weather 10/10 in warm weather	0
Itching	5/10	0
Redness	5/10	0

Figure 5: Severity of symptom scores throughout the intervention highlighting a reduction in perceived symptoms by the patient for erythema (redness), itching and burning sensation.

Lifestyle	Pre-trial	Post-trial
Sleep quality	1/10	10/10
Energy levels	4/10	10/10
Hair quality	10/10	10/10

Figure 6: Severity of symptom scores throughout the intervention highlighting an improvement in perceived symptoms by the patient for hair quality, sleep quality and energy levels.

As demonstrated in figure 6, hair quality was noted to be significantly improved, as was sleep quality. Energy levels were also improved. These factors show how the intervention improved the quality of life of the case, alongside rosacea symptom resolution.

Another perceived benefit, reported by the case, but not formally assessed were noticeable improvements in finger and toe nail quality, strength and growth rate.

No adverse events or negative experiences were noted by the case or observed in clinic during any or following the treatment schedule.

Safety of the intervention was also assessed through blood biomarker analysis. As demonstrated in figure 7, Biomarkers included urea, creatinine and high sensitivity C-reactive protein (HsCRP).

Blood	Pre-trial	Post-trial
Sodium	139	136 4.5
Potassium	4.7	99 26 3
Chlorine	101	50 0.3
Bicarbonate	28	
Urea	3.7	
Creatine	44	
CRP	8.8	

Figure 7: Table outlining the biomarkers prior and after the intervention. Initial results reveal a high HsCRP and normal urea and creatine.

The results demonstrate that the treatment schedule did not alter renal function and there was a significant fall of HsCRP into optimal ranges. The HsCRP has been raised prior to the intervention.

Upon discovery of the initial raised HsCRP, the case was clinically assessed and examined, with the absence of any other inflammatory signs or symptoms prior to the intervention. Therefore, it was thought to be linked to the exacerbation of rosacea. The fall in HsCRP and preservation of renal function, alongside the absence

of adverse events and experiences gives reassurance on the safety of the intervention in this case.

The management of rosacea with multi-nutrient intravenous therapy.

Further research is required to explore the clinical effectiveness of multi-nutrient intravenous therapies for rosacea in other cases with the disease. This can further be investigated assessing responses in different cohorts, both phenotypic and genotypic, with the disease.

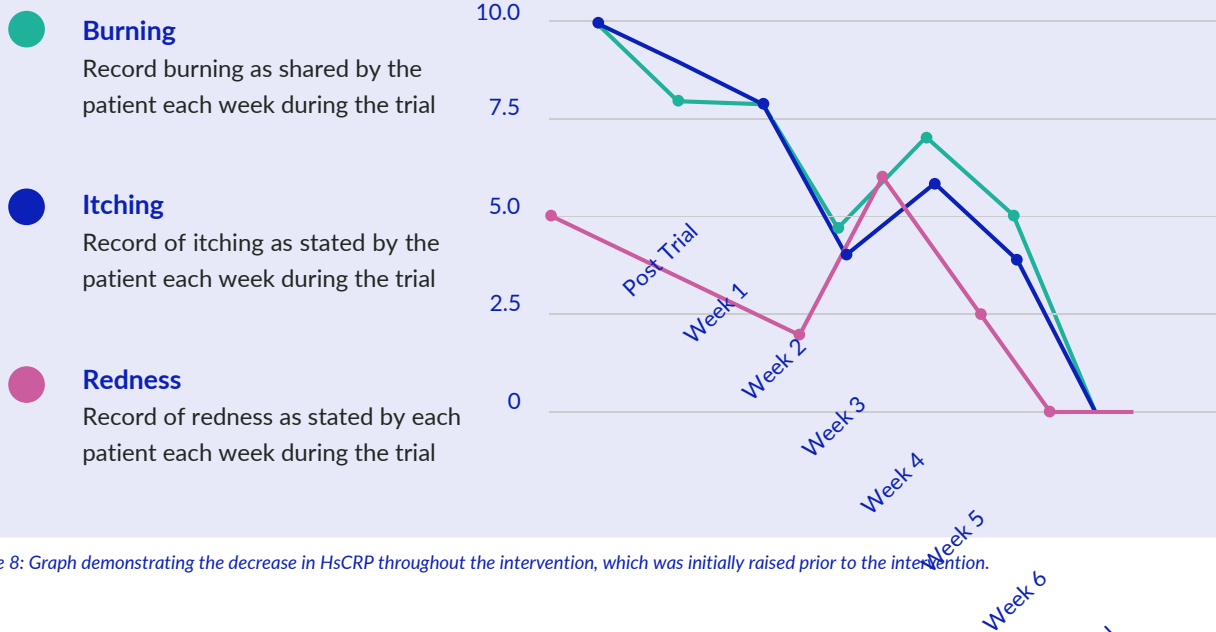


Figure 8: Graph demonstrating the decrease in HsCRP throughout the intervention, which was initially raised prior to the intervention.

Discussion

Present literature is scanty when outlining the role of antioxidant therapy in a variety of skin conditions, including rosacea. There is a theoretical rationale for antioxidants to play a positive role in the management of rosacea, through a potential reduction of oxidative stress. Oxidative stress could have a negative impact on the condition, particularly if the disease has autoimmune origins. Occupational exposure to chemicals daily also may add to the case's oxidative burden. Antioxidants such as glutathione, its precursor N-acetyl cysteine and vitamin C help to neutralise free radical toxins and reactive oxygen species that accumulate, essential for oxidative stress processes.

This case demonstrates that intravenous multi-nutrient therapy, with a focus on nutrients that exert antioxidant effects, was significantly effective at reducing symptoms and appearance of rosacea, alongside reducing associated raised inflammatory markers (HsCRP). Although some erythema was present, the patient reported the resolution of the burning sensation and itching that was associated with her rosacea. It also demonstrates that the intervention was safe, anti-inflammatory, with no side effects, in this individual case. The patient was followed up several months following the intervention and reported no return of her symptoms or worsening of the appearance. The treatment of rosacea, using multi-nutrient intravenous therapy, has been effective in this one case and improved several measurable outcomes, as well as reducing severity of symptoms. Further case studies, cohort studies or

randomised controlled trials are required to investigate this relationship further. However, for a disease process with no identifiable cure and management of symptoms requiring potent medication such as antibiotics and steroids.

Further investigations could utilise high resolution cross polarised photography for outcome measures, which provide a more systematic and clearer type of clinical photography for skin conditions, such as rosacea.

Conclusion

This case demonstrates that intravenous multi-nutrient therapy, with a focus on nutrients that exert antioxidant effects, was significantly effective at reducing symptoms and appearance of rosacea, alongside reducing associated raised inflammatory markers (HsCRP).

There may be a role in the management of rosacea with multi-nutrient intravenous therapy.

Further research is required to explore the clinical effectiveness of multi-nutrient intravenous therapies for rosacea in other cases with the disease. This can further be investigated assessing responses in different cohorts, both phenotypic and genotypic, with the disease.

References

1. <https://www.nhs.uk/conditions/rosacea/>
2. <https://emedicine.medscape.com/article/1071429-differential-diagnosis-of-rosacea>
3. <https://www.guidelinesinpractice.co.uk/skin-and-wound-care/rosacea-newer-treatments-can-avoid-antibiotics/352882>
4. article.
5. <https://cks.nice.org.uk/topics/rosacea/management/rosacea-management>
6. <https://www.hopkinsmedicine.org/health/conditions-and-diseases/rosacea>
7. <https://www.healthline.com/health/skin/maculopapular-rash#:~:text=A%20maculopapular%20rash%20is%20made,red%20and%20can%20merge%20together>
8. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2702150/>
9. <https://www.ncbi.nlm.nih.gov/books/NBK562148/>
10. <https://cks.nice.org.uk/topics/rosacea/diagnosis/diagnosis/>
11. <https://www.guidelinesinpractice.co.uk/skin-and-wound-care/rosacea-newer-treatments-can-avoid-antibiotics/352882>
12. <https://onlinelibrary.wiley.com/doi/full/10.1111/ddg.13139>
13. Error! Hyperlink reference not valid.
14. <https://cks.nice.org.uk/topics/rosacea/management/rosacea/>
15. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4580655/#:~:text=Brimonidine%20tartrate%20topical%20gel%20is,adrenergic%20receptor%20on%20endothelial%20cells>
16. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4807898/>
17. <https://emedicine.medscape.com/article/1071429-differential-diagnosis-of-rosacea>
18. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3088930/>
19. https://www.rosacea.org/rr/2013/summer/article_2.php
Rosacea Review Summer 2013.
20. Chang AL, Chung PI, Chen YJ, et al. Assessment of the genetic basis of rosacea by genome-wide association study. *J Invest Dermatol* 2015;135:1548-1555.
21. Chang AL, Chung PI, Chen YJ, et al. Assessment of the genetic basis of rosacea by genome-wide association study. *J Invest Dermatol* 2015;135:1548-1555.
22. Ramani S, Pathak A, Dalal V, Paul A, Biswas S. Oxidative Stress in Autoimmune Diseases: An Under Dealt Malice. *Curr Protein Pept Sci.* 2020;21(6):611-621. doi: 10.2174/1389203721666200214111816. PMID: 32056521.
23. Wozniacka A, Jedzejowska S, Adams J, Gebicki J. Topical application of NADH for the treatment of rosacea and contact dermatitis 2003. Department of dermatology, medical university and the institute of applied radiation chemistry, technical university Lodz Poland
24. Dall'Oglio, F. Puviani, M. Milani, M. Micali, G. Efficacy and tolerability of a cream containing modified glutathione (GSH-C4), beta-Glycyrrhetic and azelaic acids in the mild-to-moderate rosacea: A pilot, assessor-blinded, VISIA and ANTERA 3-D analysis, Two-center study (The rosazel Trial), Published by the dermatology clinic university of catania, dermatology service medica plus moderna, catabrialabs difa cooper medica departments, Italy 2020
25. Error! Hyperlink reference not valid.
26. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4684116/>
27. <https://cks.nice.org.uk/topics/rosacea/management/rosacea/>