VITAMIN C INJECTION FOR COSMETIC

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DISCLAIMER

Technology review is a brief report, prepared on an urgent basis, which draws on restricted reviews from analysis of pertinent literature, on expert opinion and / or regulatory status where appropriate. It has been subjected to an external review process. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of this review.

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DISCLOSURE

The author of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia.

EXECUTIVE SUMMARY

Introduction

Vitamin C which is also known as ascorbic acid (AA) has been widely employed in pharmaceutical and cosmetic preparations. The preparations included semisolid topical preparation and tablet dosage forms. The formulation is for protection against oxidation and to exert physiological/biological activities.

The antioxidant function of vitamin C and its function as a cofactor in prolyl and lysyl hydroxylation reactions of collagen production is said to be important in the maintenance of healthy skin. In that regards, vitamin C is also considered as an anti-ageing ingredient due to its potential to promote collagen production. However, the relationship between vitamin C in the regulatory mechanism of collagen production is not well known.

This technology review was requested by the Head of Department and Consultant Specialist from Department of Dermatology, Hospital Kuala Lumpur, Ministry of Health, Malaysia, to look into the effectiveness and safety of vitamin C injection either alone or in combination with collagen and glutathione as anti-ageing, anti-wrinkles and whitening agent.

Objective/aim

To assess the safety, efficacy/effectiveness and cost-effectiveness of vitamin C injection for cosmetics, purposes such as anti-ageing, anti-wrinkles and whitening agent.

Results and conclusions

There was no significant clinical evidence to prove that vitamin C injection either single or in combination with glutathione and collagen can improve skin elasticity (anti-ageing and ait-wrinkle) and whiten the skin. Although there was a laboratory study that showed the potential effect of vitamin C to improve skin elasticity, the study was low level of evidence. In additions, the safety of vitamin C injection for cosmetic purposes such as anti-ageing, anti-wrinkle and whitening agents was inconclusive due to lack of clinical data retrieved. No cost effectiveness study was retrieved from the scientific databases.

Recommendation

From the above review, the vitamin C injection can not be recommended to be used for cosmetic purposes suchas anti-ageing, anti-wrinkles and whitening agents due to lack of clinical evidence and safety data. Moreover, the NPCB of Malaysia prohibited any kind of vitamin C injections to be used as anti-ageing, anti-wrinkles and whitening agent in Malaysia.

Methods

Electronic databases were searched through the MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, EBM Reviews - Cochrane Central Register of Controlled Trials-4th Quarter 2010 and EBM Reviews - Health Technology Assessment - 4th Quarter 2010. Other database was PubMed, National Horizon Scanning and FDA website. Besides that, additional articles from bibliographies of retrieved articles and requestor lists were also included. There was no limit in the search. Relevant articles were critically appraised using Critical Appraisal Skills Programme (CASP) and the studies were graded according to US/Canadian Preventive Services Task Force (Harris 2001).

1. INTRODUCTION

Vitamin C which is also known as ascorbic acid (AA) has been widely employed in pharmaceutical and cosmetic preparations. The preparations included semisolid topical preparation and tablet dosage forms. The formulation is for protection against oxidation and to exert physiological/biological activities. The vitamin C major biologic activity is said to be related to the maintenance of the organism oxidation-reduction potential.[1]

Vitamin C is also known as naturally occurring antioxidant obtained from certain fruits and vegetables. It is believed that it can cause skin lightening by interacting with copper ions at the tyrosinase active site and by reducing oxidized dopaquinone; a substrate in the melanin synthetic pathway.[2] Besides such antioxidant property, the vitamin C is also believed that it can act on the free-radical inactivation, work as enzymatic co-factor, inhibit the nitrosamines formations, participate in collagen synthesis, involved in iron and histamine metabolism, skin depigmentation and immunological reactions.[1]

The antioxidant function of vitamin C and its function as a cofactor in prolyl and lysyl hydroxylation reactions of collagen production is said to be important in the maintenance of healthy skin. Hence, vitamin C is also considered as an anti-ageing ingredient due to its potential to promote collagen production.[3] Collagen is the primary structural component of the dermis and the most abundant protein found in humans. The collagen is responsible to confer strength and support to human skin.[4] However, the relationship between vitamin C in the regulatory mechanism of collagen production is not well known.[3]

Therefore, the Head of Department and Consultant Specialist from Department of Dermatology, Hospital Kuala Lumpur from Ministry of Health Malaysia requested for a technology review to look into the used of vitamin C injection either alone or in combination with collagen and glutathione as anti-ageing, anti-wrinkles and whitening agent.

2. OBJECTIVE/AIM

To assess the safety, efficacy/effectiveness and cost-effectiveness of vitamin C injection either alone or in combination with collagen and glutathione for cosmetic purposes such as anti-ageing, anti-wrinkles and whitening agent.

3. TECHNICAL FEATURES

Pharmacokinetics of Intravenous Vitamin C

Study conducted by Padayatty SJ *et al*. found that peak plasma vitamin C concentrations were higher after administration of intravenous doses than after administration of oral doses (P<0.001). The difference increased according to the dose. Vitamin C at a dose of 1.25g administered orally produced mean (± SD) peak plasma concentrations of 134.8 ± 20.6µmol/L compared with 885 ± 201.2µmol/L for intravenous administration. For the maximum tolerated oral dose of 3g every 4 hour, pharmacokinetic modelling predicted peak plasma vitamin C concentrations of 220µmol/L and 13400µmol/L for a 50g intravenous dose. Peak predicted urine concentrations of vitamin C from intravenous administration were 140-fold higher than those for maximum oral dose.[5]

Figure 1: Vitamin C Injection

Glutahione

Glutahione (GSH) is a tripeptide of glutamic acid, cysteine, and glycine. In both reduced and oxidized forms, the glutathione has important functions such as involved in various redox reactions including destruction of peroxides and free radicals. The glutathione also acts as a cofactor for enzymes, and detoxify harmful compounds.[6]

Collagen

Collagen is a group of naturally occurring proteins found in animals, especially in the flesh and connective tissues of mammals. It is the main component of connective tissue, and is the most abundant protein in mammals. The collagen, in the form of elongated fibrils, is mostly found in fibrous tissues such as tendon, ligament and skin, and is also abundant in cornea, cartilage, bone, blood vessels, the gut, and intervertebral disc. The fibroblast is the most common cell which creates collagen. The

collagen has been widely used in cosmetic surgery, as a healing aid for burn patients for reconstruction of bone and a wide variety of dental, orthopedic and surgical purposes.[7]

4. METHODS

4.1. Searching

Electronic databases were searched through the MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, EBM Reviews - Cochrane Central Register of Controlled Trials-4th Quarter 2010 and EBM Reviews - Health Technology Assessment - 4th Quarter 2010. Other database was PubMed, National Horizon Scanning and FDA website. Besides that, additional articles from bibliographies of retrieved articles and requestor lists were also included. The search term used can be referring to Appendix.

4.2. Selection

A reviewer screened the titles and abstracts against the inclusion and exclusion criteria and then evaluated the selected full-text articles for final article selection.

The inclusion and exclusion criteria were:

Inclusion criteria

Population	Vitamin C Injection for cosmetic used (anti-ageing, whitening skin and increase skin collagen)
Interventions	Vitamin C Injection Vitamin C + glutathione and collagen
Comparators	None
Outcomes	Whiten skin, increase skin collagen, improved wrinkles Side effects of vitamin C alone and in combination with glutathione and collagen.
Study design	Vitamin C injection for cosmetic only (RCT, laboratory study, case study)
Type of publication	English language

Exclusion criteria

Study design	Other than vitamin C injection for cosmetic used, vitamin C in topical and oral used (RCT, laboratory study)
Type of publication	Other than English language

Relevant articles were critically appraised using Critical Appraisal Skills Programme (CASP) and evidence graded according to the US / Canadian Preventive Services Task Force (Appendix 2).

5. RESULTS AND DISCUSSION

No clinical study was found for injection of vitamin C as anti-ageing, whitening agent and anti-wrinkles either in single used or in combination with glutathione and collagen. However, only one study was included in this review but it was a laboratory study which is considered as low level of evidence.

5.1. EEFICACY/ EFFECTIVENESS

Park HJ *et al*. (2010) conducted a laboratory study to investigate the regulatory effects of vitamin C and LL-37 on collagen production and the cellular signalling between vitamin C and LL-37 in human dermal fibroblasts. The study was conducted in South Korea. LL-37 is antimicrobial peptide that plays a crucial role at many levels in the wound healing process. Cells that were used in this study were prepared by extracting proteins through specific process. During the study, the cells were treated with human LL-37 and/or vitamin C. After the treatment time was completed, the cells that were treated with 0.5 mM of vitamin C for 2 hours prior to addition of 10nM of LL-37 had increased expression of COL1A1, COL1A2 and COL1A31 compared with treated only with 10nM of LL-37. COL1A1, COL1A2 and COL1A3 are collagen genes that involved in skin strengthening in human. The authors also found that, the vitamin C independently enhanced collagen expression and offset the reduced production of collagen by LL-37 in both cells (HDFs and HKFs). In addition, the study showed that there was no significant difference in the fibrotic effect of vitamin C between human dermal fibroblasts (HDFs) and human keloid fibroblasts (HKFs).[3, Level II-2]

5.2. SAFETY

There was no USFDA approval of vitamin C injection for cosmetic especially as anti-ageing, whitening agent and anti-wrinkle. In Malaysia the National Pharmaceutical Control Bureau (NPCB) did not approve any vitamin C injection for cosmetic used.

However in 2010, there was a survey conducted by Padayatty SJ *et al*. to assess the trend of vitamin C intravenous (IV) used by Complementary and Alternative Medicine (CAM) practitioners and adverse effects. The survey was conducted during CAM conferences in 2006 and 2008. The study was reviewed by the Human Subjects Committee/Institutional Review Board at the University of Kansas Medical Center. Within that

survey time, 300 survey forms in 2006 and 250 survey forms in 2008 were distributed. However, only a total of 199 responded both surveys. Out of 199 survey respondents, 172 practitioners stated that they administered vitamin C where only 27 stated that they did not use IV vitamin C. All the patients were treated for infections, cancers and other conditions which were not stated in the study. The adverse events reported by the survey respondents were minor. No side effects were reported for 9227 patients while 59 reported to have lethargy of fatigue. A single practitioner listed change in mental status in 10% of his patients (20 patients) but provided no details. One patient with pre-existing renal impairment and cancer metastases to kidneys was reported to have developed unconfirmed renal failure. The most common adverse events reported were lethargy, and fatigue (reported by 27 practitioners), vein irritation (by 9 practitioners), and nausea and vomiting (by 9 practitioners).[8]

The studies reported few toxic effects on the use of vitamin C which were related to the dose. Diarrhea or abdominal bloating can occur when several grams are taken orally at once (≥250grams). However, with intravenous administrations there is possibility of hyperoxalemia induced with intravenous vitamin C.[9]

5.3 COST/COST-EFFECTIVENESS

There are various types of vitamin C injection products claimed to be effective for whitening agent and anti-ageing at prices ranging from RM200 to RM900 per pack of 10 to 50 ampoules.

5.4 LIMITATIONS

This technology review has several limitations. The selection of studies was done by one reviewer. Although there was no restriction in language during the search but only English full text articles were included in this report. Any abstracts without a full text articles were also excluded. Some of the studies were conducted retrospective instead of prospective.

6. CONCLUSION

There was no significant clinical evidence to prove that vitamin C injection either single or in combination with glutathione and collagen can improve skin elasticity (anti-ageing and ait-wrinkle) and whiten the skin. Although there was a laboratory study that showed the potential effect of vitamin C to improve skin elasticity, the study was low level of evidence. In additions, the safety of vitamin C injection for cosmetic purposes such as anti-ageing, anti-wrinkle and whitening agents was inconclusive due to lack of clinical data retrieved. No cost effectiveness study was retrieved from the scientific databases.

7. RECOMMENDATION

From the above review, the vitamin C injection can not be recommended to be used for cosmetic purposes suchas anti-ageing, anti-wrinkles and whitening agents due to lack of clinical evidence and safety data. Moreover, the NPCB of Malaysia prohibited any kind of vitamin C injections to be used as anti-ageing, anti-wrinkles and whitening agent in Malaysia.

8. REFERENCES

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9. APPENDIX

9.1. Appendix 1: LITERATURE SEARCH STRATEGY

Ovid MEDLINE® In-process & other Non-Indexed citations and OvidMEDLINE® 1948 to present

1. Ascorbic Acid/
2. acid ascorbic.tw.
3. sodium ascorbate.tw.
4. magnorbin.tw.
5. ferrous ascorbate.tw.
6. acid l-ascorbic.tw.
7. magnesium ascorbicum.tw.
8. l-ascorbic acid.tw.
9. vitamin c.tw.
10. (ascorbate adj2 (ferrous or sodium)).tw.
11. l ascorbic acid.tw.
12. (ascorbic adj2 (acid or monosodium salt)).tw.
13. hybrin.tw.
14. Glutathione/
15. gamma l glu l cys gly.tw.
16. gamma-l-glu-l-cys-gly.tw.
17. glutathione.tw.
18. glutathione reduced.tw.
19. gamma-l-glutamyl-l-cysteinylglycine.tw.
20. reduced glutathione.tw.
21. gamma l glutamyl l cysteinylglycine.tw.
22. Collagen/
23. avicon.tw.
24. pangen.tw.
25. alpha collagen.tw.
26. microfibril collagen hemostat.tw.
27. (collagen adj3 (fleece or felt or hemostat microfibril)).tw.
28. zyderm.tw.
29. collastat.tw.
30. dermodress.tw.
31. alpha-collagen.tw.
32. avitene.tw.
33. collagen.tw.

OTHER DATABASES	
EBM Reviews - Cochrane Central Register of Controlled Trials	Vitamin C Injection
EBM Reviews - Database of Abstracts of Review of Effects	
EBM Reviews - Cochrane database of systematic reviews	
EBM Reviews - Health Technology Assessment	
PubMed	Vitamin C Injection
NHS economic evaluation database	
INAHTA	Vitamin C Injection
FDA	Vitamin C injection

9.2. Appendix 2

HIERARCHY OF EVIDENCE FOR EFFECTIVENESS STUDIES

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)