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INFORMED CONSENT AND RESEARCH AUTHORIZATION

UVB-Induced Microvesicle Particle Release in Human Skin

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Staff Physician

Sponsor(s) name and address:
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

Site where study is to be conducted:
Wright State Physician's Building- 2nd floor
725 University Blvd
Dayton Ohio 45435

Phone number for subjects to call for questions:
(937) 245-7500 or 775-2463

Introduction and Background Information

You are invited to take part in this research study. This study does not involve any particular diagnosis. This study is only to obtain skin biopsy samples from MALE humans. The study is being conducted under the direction of Dr. Jeffrey Travers, Principal Investigator. The study procedures/visits will all occur at the Wright State Physician Health Center, Dermatology Clinic on the 2nd floor. The total number of subjects will be 12 or less.

Purpose

This study is designed to test whether localized UVB (burning rays of sunlight) treatment will result in increased skin levels of pieces of skin cells called microvesicle particles (MVP) and if use of antioxidants vitamins (vitamin C and vitamin E) that have been demonstrated to block UVB-induced production of a product we hypothesize is involved in MVP release block UVB-induced MVP release.

Introduction

Sunlight exerts many effects on the body. We have evidence that in response to ultraviolet B radiation, which are the burning rays of sunlight, skin cells will release small pieces of themselves, known as microvesicle particles(MVP). We think that MVP could be how sunlight can send signals to the entire body. We also have evidence that MVP release can be blocked by agents that act as "anti-oxidants", that is, they decrease the levels of agents that release oxygen, like hydrogen peroxide. Examples of antioxidants include vitamin C and vitamin E. These vitamins also have been reported to decrease UVB-induced redness. Thus, we will test if UVB will make MVP in your skin, then, you

will be given vitamin C and vitamin E to take and we will repeat the testing to see if the antioxidants block the MVPs.

Procedures

Your participation in this study will last for 9 days. If you consent to participate, you will have the following procedures while you are in this study.

DAY 0. (5-6 hrs)
1. Following informed consent, you will work with Ms. Cates/Williams to define all follow up appointments. The protocols will need to begin (Day 0) on a Monday, Tuesday, Wednesday, with Day 1 being on a Tuesday-Thursday and Day 8 being a Tuesday-Thursday and Day 9 being a Wednesday-Friday.

2. Volar (inner) forearm skin will be photographed, and a 5 x 5 mm area of skin (1/5th inch) area will undergo treatment with UVB irradiation blocked off with a 5 x 5 mm hole to allow UVB radiation to focus on the small area of skin. The areas will be treated with 1000 J/m2 (less than three minimal erythema dose [MED; ~350 J/m2] of UVB using a Philips F20T12/UV-B bulb. An MED is the amount of UVB able to induce a mild red response by 24 h, which would be the same as a very, very mild sunburn (just redness). The amounts we plan to use are similar to being out in direct sunlight approximately 1.3 h in June/July in Bethesda MD (estimated from the UV-B Monitoring and Research Program of the United States Department of Agriculture (USDA) headquartered at Colorado State University; see http://uvb.nrel.colostate.edu/UVB/index.jsf).

3. On your back (same side as the forearm used) we will also test UVB levels of 100 J/m^2, 200 J/m^2, 400 J/m^2, 600 J/m^2, 800 J/m^2 with our portable UVB light unit. This provides phototesting, and will be used to confirm the effects of vitamin C/E on UVB-induced redness. We expect that this treatment will result in small areas of increasing amounts of redness by 24 hours, resulting in localized areas of mild sunburns.

4. You will return to clinic in 4 h to allow us to measure erythema of the UVB-treated areas on forearm and back with a mexameter (non-invasive instrument that emits light to measure redness). The mexameter measures the redness by calculating the amount of light absorbed by the skin. The area on the forearm treated with UVB and area approximately 8 cm away that did not receive UVB will be photographed and 5 mm (1/5th inch) skin biopsies will be obtained from these two areas.

For the skin biopsies, the skin will be prepared in the usual sterile manner and anesthetized with 1% lidocaine with 1:100000 epinephrine. The lidocaine is a numbing medication and the epinephrine is used to decrease bleeding from the skin. The punch biopsy consists of cutting a round hole 5 mm across in the top layer of skin. If needed, a suture will be placed. If sutures placed, then we will ask you to return for suture removal in 10-14 days. Wound care will be discussed and a sample of bacitracin ointment and bandaids supplied. The biopsies will be taken to our laboratory and placed into enzymes and MVP measured.

DAY 1. (30-60 minutes)
1. The next day, you will return to our clinic. The UVB-treated areas on the back will be photographed to document the redness response. We will again use a mexameter to measure erythema.

2. The subjects will then be provided over-the counter commercially available (Spring ValleyTM) vitamin C (1000mg capsules) and Vitamin E (1000 IU capsules) and will be instructed to take two Vitamin C and one Vitamin E tablets daily for 8 days, starting that day. The subjects will be given an unopened bottles containing 110 vitamin C and 60 vitamin E, and will be instructed to bring the bottles back at Day 8 to allow us to count remaining vitamins.

DAY 8. (5-6 hrs)
1. You will bring in vitamins to allow staff to count them to ensure compliance.

2. You will undergo photography and UVB treatment of contralateral arm with a 4 h later two skin biopsies (as per Day 0).

3. You will undergo UVB treatment to back for phototesting (as per Day 0).

4. You will return to clinic in 4 h to allow us to measure erythema of the UVB-treated areas on forearm and back with a mexameter (as per Day 0).

DAY 9. (1 hr)
1. You will return to clinic to have the areas on back subjected to mexameter to allow non-invasive erythema measurements.

Suture Removal. If sutures were placed for the skin biopsies, then you would be scheduled to have them removed from 10-14 days after their placement.

Potential Risks

1. UVB treatment: risks to the UVB protocol include an exaggerated response to UVB (sunburn). This in theory could result in a localized rash, pain and scarring. Our experiences thus far with using UVB at similar doses in other protocols has not resulted in any problems, which is to be expected given the doses (1000J/m2) and small area (5 x 5 mm) of UVB irradiation. **Please note that our patients who are undergoing UVB treatments for their skin diseases (eg, psoriasis) end up getting much higher doses (>1000 J/m2) over their entire body. Thus, these doses of UVB are likely quite safe.**
2. Skin biopsies: risk of allergic reaction to the local anesthetic lidocaine, risk of small scar at the biopsy sites, risk of wound infection at the biopsy sites, risk of bleeding from the biopsy site.
3. Photography - the risk of photography is the possible loss of confidentiality. Pictures will not be of recognizable body parts or markings. Photos will be labeled with the study number and a code that does not identify the subject. Photos will not include any identifying information.
4. Mexameter readings- there is no risk to this non-invasive device.
5. Vitamin use- ingesting 2g/day of vitamin C and 1000 IU of vitamin E are considered safe, especially for a short period of time (8 days) [6]. Side effects of vitamin C include

nausea/diarrhea/headaches. As noted in Mayo Clinic website, 2g/day is felt to be the upper limit of ingestion (http://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/expert-answers/vitamin-c/faq-20058030). Similarly, Vitamin E doses below 1500 IU per day are considered safe (http://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/expert-answers/vitamin-c/faq-20058030).

6. There is also the potential risk of loss of confidentiality, but this will be minimized as photos of the wounded/UVB-treated sites will not allow the person to be identified, and will not expose buttocks or genitals. Samples will be labeled with numeric numbers --001, 002, 003 etc. and the study number (XXXX). Example 001-XXXX.
7. In addition, you may suffer harms that we have not seen before.

Benefits

You may not benefit by participating in this study. The information collected may not benefit you directly; however, the information may be helpful to others by providing us with an understanding of how sunlight can have effects on the human body.

Alternatives

This study is not a treatment study. Your alternative is to not participate.

Compensation & Treatment for Injury:

You will be paid for taking part in this study. You will be paid for each completed visit as follows:

- DAY 0 - $25 for the UVB procedures and $50 for the two small skin biopsies
- DAY 1 - $50 for returning on for the mexameter measurements and taking the vitamins.
- DAY 8 - $25 for the UVB procedures and $50 for the two small skin biopsies.
- DAY 9 - $100 for the repeat mexameter and completing the study.

If you complete all study visits, you will receive a maximum payment of $300.00. If you don't complete all study visits, you will be paid for the visits you do complete.
Checks for the appropriate amount will be given to you or mailed after the end of the study (Day 9).
There is no cost for parking at the Wright State Physician's Building.

If you are injured by being in this research study, the investigator will arrange for you to get medical treatment from Dr. Travers. The most likely adverse reaction would be a biopsy site infection, which would manifest as increased pain and pus in the biopsy site approximately 4-7 days after the procedure. If that happens, Dr. Travers will provide you with a tube of the prescription antibiotic mupirocin ointment. If that is not effective, then, Dr. Travers will prescribe an oral antibiotic. You or your insurance company would then be responsible for paying for the cost of the prescription oral antibiotic, but Dr. Travers services will be free. If you are injured, there is no money set aside for lost wages, discomfort, disability, etc. You do not give up your legal rights by signing this form. If you think you have a research related injury, please call Elizabeth Cates (study coordinator) at (937) 245-7500 or Dr. Travers at (937) 775-2463. Should an adverse event occur, please contact Dr. Travers who will provide treatment as outlined above.

Research Subject Costs:
There will be no costs to you for any of the procedures or testing done as part of this research study.

Confidentiality

Total privacy cannot be guaranteed. We will protect your privacy to the extent permitted by law. If the results from this study are published, your name will not be made public. Once your information leaves our institution, we cannot promise that others will keep it private.

Identifiers might be removed from your identifiable private information (or/and identifiable biospecimens). After such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without your (or your legally authorized representative's) consent.

Data Security

All conversations and procedures will take place in the Wright State Physician's building in the dermatology clinic in a private examining room. The data will be kept in the locked office of the PI. Samples and pictures from subjects will be coded by numbers as outlined above. Photos will not be of recognizable body parts or markings.

Voluntary Participation

Taking part in this study is completely voluntary. You may choose not to take part at all. If you decide not to be in this study, you won't be penalized or lose any benefits for which you qualify. If you decide to be in this study, you may change your mind and stop taking part at any time. If you decide to stop taking part, you won't be penalized or lose any benefits for which you qualify. You will be told about any new information learned during the study that could affect your decision to continue in the study.

Termination

The investigator, the IRB or the study sponsor has the right to stop this study at any point. The investigator may take you out of this study with or without your permission. Reasons why this may occur include: malfunction of study equipment such as the Mexameter.

Participation in Other Research Studies

You may take part in this study if you are currently in another research study. It is important to let the investigator know if you are in another research study.

Research Subject's Rights, Questions, Concerns, and Complaints

If you have any questions, concerns, or complaints about the research study you may contact the principal investigator, Dr. Travers, or Elizabeth Cates at 937-245-7500 or 937-775-2463.

If you have any questions about your rights as a study subject, questions, concerns or complaints, you may call the Wright State University Institutional Review Board (IRB) at (937) 775-4462. You may discuss any questions about your rights as a subject with a member of the IRB or staff. The IRB is an independent committee composed of members of the University community, staff of the institutions, as well as lay members of the community not connected with these institutions. The IRB has reviewed this study.

Authorization to Use and Disclose Your Health Information

State and Federal laws, including the Health Insurance Portability and Accountability Act (HIPAA), require researchers to protect the privacy of your health information. This section of the consent form describes how researchers, with your authorization (permission), may use and release (disclose or share) your protected health information (PHI) for this research study. **Please read this section of the consent form carefully.**

If you sign this document, you give permission to Dr. Travers and his Wright State Physicians Pharmacology Translational Unit research team to use or disclose (release) the following protected health information:

- Your medical records for past medical conditions and medications related to your skin conditions
- All information (research records and medical records) created during your participation in this research study

The research team needs this information to conduct the study. This is a study to test if taking vitamin C and vitamin E will block the increased levels of pieces of skin cells call microvesicle particles (MVP) produced from localized ultraviolet B radiation (UVB; burning rays of sunlight) treatment.

To maintain the integrity of this research, you might not have access to any health information developed as part of this study until it is completed. At that point, you generally would have access to your health information.

Disclosure of your protected health information

If you sign this form, the researchers may share your health information during the conduct of the study with:

- Non-Wright State Physicians researchers or organizations working with Wright State Physicians researchers.
- Law enforcement or other agencies, when required by law
- WSU's Institutional Review Board (or other IRB of record), which oversees our research
- The sponsor (the organization paying for) of this research study: National Institute of Health (NIH)

- Representatives of government agencies in the United States and other countries (i.e. Food and Drug Administration and the Office of Human Research Protection)
- Other authorized Wright State University/Physicians Officials who oversee research and clinical care

The people listed above will use and share your health information to review the quality, safety, and results of the research and may also do additional research.

Please understand that these persons/organizations who may receive your health information may not be required by U.S. Federal privacy laws (such as HIPAA) to protect it and may share your information with others without your permission.

This authorization does not have an expiration date.

However, you can change your mind and cancel this authorization at any time. To cancel this authorization, you must write the study investigator listed at the beginning of this consent form.

If you cancel this authorization, you will no longer be allowed to take part in the research study. If you cancel this authorization, health information you had already allowed us to obtain may still be used and disclosed by researchers in order to maintain the integrity and reliability of the research, and to report any adverse (bad) effects that may have happened to you.

Right to refuse to sign this Authorization

You have the right to refuse to sign and give your authorization. If you do not sign this form, your non-research related treatment, payment or enrollment in any health plans, or your eligibility for other medical benefits at Wright State Physicians will not be affected in any way.

However, if you do not sign this form, you will not be able to participate in this research study.

Signature of Subject

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to participate in this research and authorize the use and disclosure of my protected health information for this study. I will be given a copy of this signed and dated form.

_____ _____
Signature Date

_____
Printed Name

_____
Signature of Person Obtaining Consent and Authorization

_____
Date

_____
Printed Name of Person Obtaining Consent and Authorization