The NCS

Roles within the team

Laraib Kashif: Used her interest in biology to research Raynaud's (risk factors, symptoms and importance) and poster design layout

Sumayyah Hussain: Research on transdermal patches, graphics and used her A Level economics knowledge to research feasibility and affordability

Zerwa Asad: Research on drug logistics, testing and clinical trials, and used her artistic background to produce original drawings and graphics

PATCH IT ON

By Laraib Kashif, Sumayyah Hussain and Zerwa Asad

OUR PROPOSAL

The alpha-blocker, phenoxybenzamine, and beta-blocker, sotalol, coupled in a heated transdermal patch. Both of these blockers dilate arteries and vessels, increasing blood flow and counteracting the vasospasm that leads to Raynaud's.

WHAT IS RAYNAUDS?

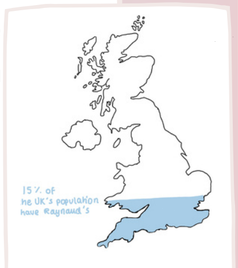
- Raynaud's disease is a vascular disorder which affects the blood vessels, mainly in the fingers and toes. This is caused by reduced blood flow to these areas, leading to changes in skin colour and sensation.
- It is often triggered by exposure to cold temperatures or emotional stress where blood vessels shut down and constrict more than usual. This is known as a vasospasm.
- Constriction of blood vessels can cause changes in skin colour, typically resulting in pale appearance, followed by cyanosis (bluish tint) and erythema (redness).

IMPORTANCE OF TREATING RAYNAUDS

Raynaud's is a chronic condition which can take a toll on a person's mental and emotional well-being because episodes can be uncomfortable and interfere with daily activities. Physical symptoms can lead to depression, anxiety and social isolation. This can lead to a reduced quality of life.

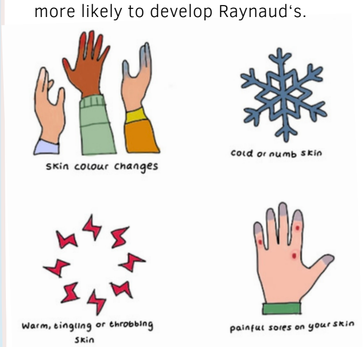
Currently, there is no specific cure in treating Raynaud's so it is vital to focus on managing symptoms which can help reduce the frequency and severity of episodes to enhance a person's overall wellbeing.

Overall, treating Raynaud's disease is vital to alleviate symptoms, prevent complications, enhance functionality, improve quality of life and minimize the impact on overall health and well-being



RISK FACTORS + SYMPTOMS

Risk factors for Raynaud's include family history, smoking, colder climate and gender, where women are more likely to develop Raynaud's.



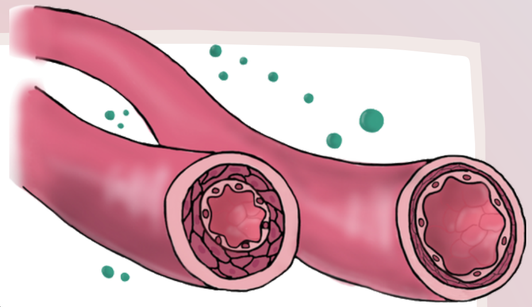
Thermal image of a Raynaud's hand

REFERENCES:

https://blog.radiology.virginia.edu/new-treatment-for-raynauds-syndrome/ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3304686/ https://www.healthline.com/health/general-use/how-to-use-transdermal-patch Raynaud's phenomenon – Illnesses & conditions | NHS inform Complications | Background information | Raynaud's phenomenon | CKS | NICE https://onlinelibrary.wiley.com/doi/full/10.1002/mds3.10069 https://pubmed.ncbi.nlm.nih.gov/6141750/ https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-quality-transdermal-patches-rev_en.pdf https://onlinelibrary.wiley.com/doi/abs/10.1002/qj.5566#:~:text=Hybrid%20transdermal%20drug%20delivery%20patch%20made%20from%20poly(2%2Dphenylene controlled%20by%20an%20electric%20field https://www.ems1.com/ems-products/education/articles/receptors-and-the-autonomic-nervous-system-5tR9qroX60aHqrf0/ https://www.rxlist.com/beta-blockers-drugs-by-activity/drug-class.htm https://www.bensnaturalhealth.com/blog/alpha-blockers-vs-beta-blockers/#:~:text=It%20is%20a%20medicine%20type layer%20and%20overlapped%20releasing%20liner.

HOW DO THE DRUGS WORK ?

We will be using Alpha and Beta Blockers to treat Raynaud's.

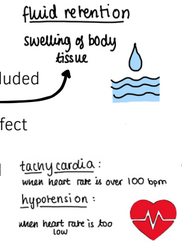


What are Alpha and Beta Blockers?

- These are drugs which are commonly used to treat hypertension (a factor which can cause secondary Raynaud's)
- Alpha-blockers block the hormone Norepinephrine. By inhibiting this hormone, the muscles in the walls of smaller arteries and veins are prevented from tightening so the blood vessels can remain dilated.
- Beta-blockers block the effect of adrenaline, helping to treat high blood pressure
- These blockers also help widen veins and arteries by binding to alpha-1 and beta receptors and preventing their stimulation, improving blood flow.

Why we are using them together?

- Following a published study on the use of alpha and beta blockers, we concluded that alpha blockers are effective at treating vasoconstriction.
- However, alpha-blockers by themselves can lead to fluid retention, a side effect which can counteracted by the addition of beta blockers
- Beta-blockers also reduce the heart rate, preventing alpha-blocker-induced tachycardia whilst simultaneously not causing hypotension.

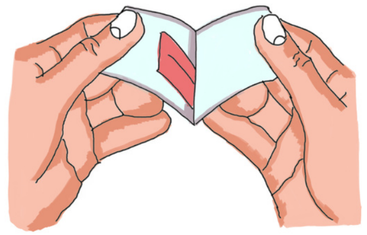


How does this help with Raynaud's?

- Alpha and beta blockers dilate vessels to counteract the vasospasm which occurs in a Raynaud's attack
- The widening of vessels, specifically in the hands and feet can reduce the symptoms of a Raynaud's attack (such as the swelling and colour changes) by allowing more blood flow to these areas and allowing them to return to their natural red colour.

APPLICATION

1. Wash hands with soap and water
2. Open the package carefully, and avoid tearing the patch itself. If you do tear the patch, don't use it and throw it away in a waste bin.
3. Take the patch out of the packaging and remove the protective liner
4. Apply the exposed sticky part of the patch on the wrist above the hand that is suffering from a Raynaud's attack
5. Peel back the second part of the liner and press the entire patch down



TRANSDERMAL PATCH

How does the transdermal patch work?

The transdermal patch is designed to release drugs in a controlled manner, maintaining steady levels of the drug in the body.

- The drug is dissolved into the adhesive layer of the patch, which is firmly attached to the skin.
- The drug diffuses across skin layers and enters capillaries where it is transported throughout the body via the bloodstream.
- It is delivered consistently over a specific period.
- The patch is heated by the oxidation of iron powder, which generates heat. The iron powder is sealed in the patch and then exposed to air after the adhesion of the patch to the target area .

Why is the patch heated?

- To help ease a Raynaud's attack - when placed on the wrist the heat helps to open blood vessels leading to the hands and fingers.
- For most drugs, solubility can be significantly enhanced by an increase in temperature - studies have shown that heating transdermal patches improves drug penetration.
- Self-heating patch is cost-effective and can be produced easily by modifying the production process of existing patches

PROS AND CONS

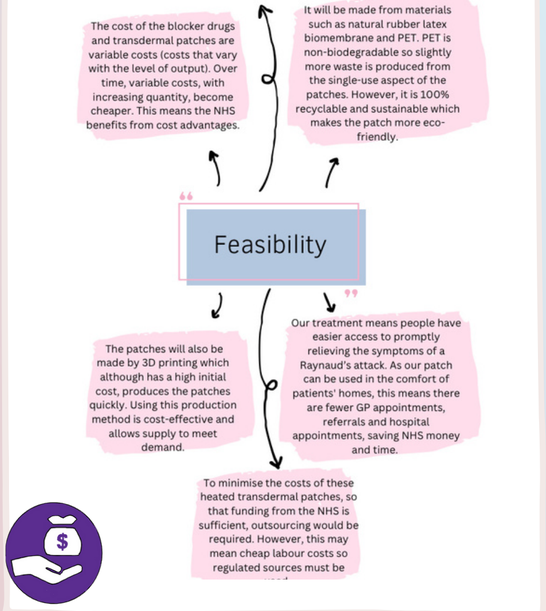
Pros

- ✓ Patches are more convenient
- ✓ Ease of use and application >> Raynaud's sufferers don't have to struggle to put on other treatments such as gloves
- ✓ Controlled and steady drug delivery
- ✓ Well tolerated, with little skin reactions, even in elderly populations.
- ✓ Medication is supplied gradually and constantly, rather than in a large single dose
- ✓ Easier for the elderly who may find it harder to swallow pills or refuse to / better than use of invasive needles
- ✓ The heat from the patch helps additionally to ease a Raynaud's attack

Cons

- ✗ May still be difficult for some patients to apply during an attack
- ✗ Can cause skin reactions in some patients (e.g. rashes, itching, redness)
- ✗ Not suitable for delivering large doses of medication
- ✗ May be unused drug left in the patch after patch is removed from skin (waste)

FEASABILITY



TRIALS

Ethics

- Trials in the early stages of development will not be done on humans due to ethical, practical and economic reasons
- In later phases when testing is more widespread, patient consent will be required.

Initial Testing (Phase 0)

In vitro drug release, permeation and adhesion testing:

- In vitro release test: evaluates the rate of release of an active substance from a transdermal patch, through a dissolution test or a release test, using a non-rate-limiting membrane.
- In the dissolution test: the transdermal patch should be tested under various conditions e.g. pH and media
- In vitro permeation studies are used to reflect the quality of the patch and the thermodynamic activity of the drug
- In vitro adhesion tests for the adhesive properties of the patch

Further Testing: