The effect of subcutaneous glyceryl trinitrate on radial artery diameter and the utility in radial access coronary angiography

Project Summary

A transradial arterial approach is being used more frequently for coronary angiography due to the lower vascular complications and lower bleeding rates reported in recent large trials. Radial artery spasm, subclavian tortuosity and the increased technical difficulty of puncturing a smaller and more mobile artery are causes for access failure. This trial aims to look at the role of subcutaneous glyceryl trinitrate, as a vasodilatory agent, and whether this increases radial artery diameter and subsequent improvement in arterial puncture success rates as well as overall patient satisfaction.

Principal Investigator: Dr Alexander Binnie

Sub/Associate Investigators: Dr Peter Stewart, Dr Sam Hayman, Dr Krystian Guppy-Coles, Dimity Williams

Correspondence:
Dr Alexander Binnie
Cardiology Advanced Trainee,
Royal Brisbane & Women's Hospital
Alexander.Binnie@health.qld.gov.au

Acronyms

GTN – glyceryl trinitrate

USS – ultrasound scan

RRA – right radial artery

LRA – left radial artery

TRA – transradial approach

TFA – transfemoral approach

ECG – electrocardiogram

TTE – transthoracic echocardiogram

Background

A transradial artery approach for coronary angiography is being used more frequently due to the lower bleeding and vascular complications reported in recent large trials[1,2,3]. The commonest cause for failed transradial access is radial artery spasm followed by subclavian tortuosity[1,2,3]. Accessing the radial artery is more technically difficult compared to transfemoral artery access due to the size and mobility of the artery[1,2,3].

Glyceryl trinitrate has been used widely in the management of angina due to the vasodilatory effects. Previous trials have suggested that using subcutaneous glyceryl trinitrate locally enlarges the size of the radial artery diameter at the point of injection, reduces the amount of radial artery spasm and increases the success rate of arterial puncture[4].

This trial aims to provide further information on the use of subcutaneous glyceryl trinitrate in transradial approach coronary angiography, paying close attention to objective measures of radial artery dilatation, puncture success and patient satisfaction.

Objectives

We seek to assess the role of subcutaneous GTN in TRA coronary angiography. We hypothesise that the use of the vasodilatory agent GTN will cause the radial artery diameter to increase and subsequently decrease the number of attempts required to successfully puncture the artery.

This trial will also aim to gauge if there is a systemic effect from local GTN injection by assessing the right radial artery diameter pre and post injection. We will also aim to see if there is a change in overall patient experience by comparing pain scores post procedure.

Methods

Study Design:

Prospective, double-blinded, randomised placebo-controlled trial.

Inclusion criteria

- Patient attending for a planned coronary angiogram – outpatient or inpatient
- Planned for transradial approach

Exclusion Criteria

- Presentation requiring emergent coronary angiography including ST-elevation myocardial infarction (STEMI)
- Cardiogenic shock
- Requiring inotropic support or intra-aortic balloon pump insertion
- Known severe aortic stenosis
- Known left ventricular outflow tract obstruction (including hypertrophic cardiomyopathy)
- No transthoracic echocardiogram in the month prior to procedure
- Systolic blood pressure <90mmHg at the time of the procedure
- Previous intolerance or reaction to glyceryl trinitrate
- Known history of glaucoma or stroke or significant head trauma
- Phosphodiesterase inhibitor (e.g. Sildenafil / Tadalafil) use in the preceding 4 days
- Have been on regular long-acting nitrates in the previous 48 hours

Method:

Data collection for patients who are eligible for enrolment will include: age, gender, body mass index (BMI), reason for coronary angiogram, number of previous TRA procedures (including prior angiography, intra-arterial lines or arterial blood sampling) and current left ventricular systolic function. The patients past medical history will also be collected including presence of hypertension or features suggestive of hypertension on ECG or TTE, dyslipidaemia, chronic kidney disease, diabetes mellitus, past or present smoking, peripheral vascular disease and stroke.

Patients undergoing coronary angiography via a transradial approach will be randomised to receive either subcutaneous GTN or subcutaneous placebo (Normal Saline 0.9%) in the usual local anaesthetic subcutaneous injection prior to radial artery puncture. A target total of 300 participants will be enrolled in the study with 150 participants in each arm. Randomisation will be computer-generated and the participants will by randomised equally into each arm of the study. A radial artery assessment will be performed by the operator to mark where on the right wrist that the arterial puncture will be performed. Ideally two centimetres proximal to the radial head.

Prior to sterile preparation, the patient will have an ultrasound scan of their left radial artery and then following sterile preparation a scan of their right radial artery.
Patients will then be administered a subcutaneous injection to the right wrist with either one millilitre GTN (500 micrograms / millilitre) with one millilitre lidocaine 2% or one millilitre Normal Saline 0.9% with one millilitre lidocaine 2%.

One minute after injection, repeat ultrasound measurements will be taken of the right and left radial arteries. The operator will then proceed to arterial puncture and will record the number of forward advances of the needle required before successful puncture. The time from first puncture to sheath insertion will be recorded.

The operator level of experience will also be recorded and divided into the following categories: <100 coronary angiograms, 100-500 coronary angiograms or >500 coronary angiograms.

Patients will be asked immediately after the procedure to provide a pain score using a visual analogue scale (0-10). Each participant will be asked 'how would you score the discomfort of the procedure with 0 being no pain and 10 being the most severe pain?'. The VAS has been validated for people suffering acute pain[6].

The other variables recorded will include whether the procedure was completed via a TRA or if cross-over to TFA was required and if so, what the reason was. Potential vascular issues including haematoma formation, arterial dissection, radial artery spasm and compartment syndrome will also be recorded.

End-points summary:

In summary we aim to analyse the effects of subcutaneous GTN in radial artery coronary angiography versus placebo. The key endpoints will be:

- Radial artery diameter as measured by ultrasound
- Radial artery puncture success as measured by number of forward needle advances and time to sheath insertion
- Patient experience and satisfaction as measured by VAS of acute pain

Data Collection:

Prospective data collection during the time of inpatient and outpatient coronary angiography.

Follow-up:

Patients involved in the trial will have follow-up as per usual practice. Immediately post coronary angiography, patients will receive routine care with close monitoring including telemetry. Enrolment in the trial will not affect their overall length of stay in hospital.

Risks and Benefits:

Risks:

The risk associated with the use of glyceryl trinitrate include:

- Headache: >2% incidence, suspected dose related and seem more commonly with transdermal preparation and typically subside with prolonged use.
- Flushing: >2% incidence, seen with initiation of dose and typically subsides.
- Hypotension: 4% incidence, more common when in an upright position (patients will be supine when dose administered). Dose related and more prevalent if already hypotensive.
- Syncope: 4% incidence, more commonly seen when in an upright position and associated with hypotension.
- Presyncope: 2-4% incidence, typically short lasting and related to hypotension.
- Paradoxical angina: 0.1-2% incidence, typically short lasting and related to hypotension.
- Contact dermatitis: 0.1-1% incidence, typically seen in transdermal preparations and usually self-limiting. Significant allergic contact or angioedema is rare.

The use of intra-arterial GTN is used routinely in coronary angiography and is associated with the same adverse effects. The commonest adverse effects involve hypotension which can be managed effectively in the procedural setting using intravenous fluids and or vasopressors.
The systemic absorption of subcutaneous GTN is likely to be less compared to intra-arterial GTN and as such the frequency of adverse effects is also likely to be less.

Patients will have consented separately for a coronary angiogram with the potential for percutaneous coronary intervention including stenting. Patients will have continuous monitoring throughout the procedure and any potential significant adverse effects will be managed as required.

There is the potential that a significant adverse effect could delay the planned coronary angiogram, however management can be provided immediately and the majority of adverse events are short lasting.

There is risk of physical harm due to the potential exposure to subcutaneous GTN however as these adverse effects are short lasting and can be effectively managed this risk is minimised.

Benefits:

Enrolment in this study will provide more information on the effects of GTN on the peripheral vasculature as well as to clarify if local application has a systemic effect. There is no guarantee that participants will have a direct benefit from enrolment in the study. However, as GTN will potentially increase the diameter of the radial artery, this is hypothesised to also improve the success rate of TRA puncture. Subsequently fewer puncture attempts will be needed which should be associated with less pain and less risk of vascular injury.

Arterial vasodilation should also reduce the risk of peripheral arterial spasm during coronary angiography and passing of coronary catheters which will potentially reduce rates of pain, vascular injury and need to cross-over to a TFA procedure.

Results from this study will potentially change future management during TRA coronary angiography and could be incorporated into guideline directed therapy. Overall, it is felt that the benefits of this study outweigh the risks of physical harm.

Data Management

All data will be kept on a password protected Queensland Health computer server. A procedure report will be generated and stored on the IMPAX system but this will not be kept as part of the trial data. Patients will be de-identified and recorded on the data sheet by a research number to protect patient anonymity. This data will be securely stored and later deleted as per Queensland Health guidelines.

Statistical analysis will be completed using Excel and SPSS 23 software. Experimental precision has been estimated based on previous research projects[4,5]. As the study progresses, retrospective experimental precision analyses will be performed to guide estimated sample sizes. There will be a paired analysis on the data to assess for statistical significance. Student's t test will be used to compare continuous data. Univariate and multivariate regression analysis will be used to examine potential correlations between radial artery diameter and variables such as sex, age, height, body mass index (BMI), hypertension, diabetes, stroke, chronic kidney disease and peripheral vascular disease. All statistical analyses will be carried out for 5% level of significance and a two-tailed p value of <0.05 will be considered significant.

This study will aim to be for the trial to be published in a peer-reviewed journal and presented at a national or international meeting once complete. Participants will be able to access this information once published.

References

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