

Side Effects and Possible Drug Interactions of Study Drugs:-
PISCES Study

EPHEDRINE	ETILEFRINE
Tachycardia	Tachycardia
Anxiety	Anxiety
Nausea	Nausea
Restlessness	Restlessness
Tremors	Tremors
Hypertension	Hypertension
Cardiac Arrhythmias	Cardiac Arrhythmias & angina
Dry mouth	cannot be excluded
Circulatory disturbances	Circulatory disturbances
Headache	Headaches or pressure in the head

These side effects are rare and the elderly are more susceptible. These adverse effects can be abolished with dose reduction.

Possible Drug Interactions:-

Ephedrine should be avoided in patients on monoamine oxidase inhibitors such as moclobemide, tranylcypromine and phenelzine, which are antidepressants.

It should be avoided in patients on other catecholamines such as Norepinephrine.

It may also increase the effects of Dexamethasone.

Increased risk of arrhythmias with volatile liquid anaesthetics and tricyclic antidepressants. Alcohol may antagonize the effects of Ephedrine but causes no adverse reactions.

Etilefrine may have an increased effect with guanethidine (blood pressure tablets), steroids and other tricyclic antidepressants and monoamine oxidase inhibitors. Beta blockers abolish its effects partially or completely.

APPENDIX E

SERIOUS ADVERSE EVENT REPORT FORM

In this trial it is important that unexpected serious adverse events are reported immediately to the principal investigators.

A serious adverse event (SAE) is defined as any undesirable experience occurring to a patient, whether or not considered related to the investigational drug, which results in:

- f) death
- g) immediate risk of death at the time the observation was made
- h) hospitalisation or prolongation of hospital stay
- i) persistent or significant disability or incapacity
- j) a congenital anomaly or birth defect

Serious adverse effects should be reported within 24 hours of the first full working day or after the weekend to the trials office by filling in the appropriate documentation and faxing it to Julie Morris and Dr Ade Olujohungbe.

DESCRIPTION OF ADVERSE EVENT

Signature Date

Name Position

Please fax to:-

Please fax to:-

Mrs Julie Morris fax: 0161-291-5815
e-mail: Julie_M@FS1.with.man.ac.uk

Or

Dr Ade Olujohungbe fax: 0151-529-3310 e-mail:
ade.Olujohungbe@aht.nwest.nhs.uk

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Suggested care pathway for the management of an acute attack of Priapism during PISCES study period

Acute Priapism is an intractable painful erection lasting more than 4hours, which fails to resolve despite optimal medical management.

In order to standardise its treatment in all PISCES study centres, the following is recommended. Treatment should be by a multidisciplinary team with a Urological Surgeon skilled in intracorporeal aspiration and instillation of intracavernous pharmacotherapy. **This treatment algorithm can however be overruled at the discretion of the primary physician of the patient.**

TIME OF STUDY	TREATMENT OPTION
<u>PHASE A</u>	If a patient gets stuttering Priapism during phase A, they should be taught “ <i>self- help</i> ” “measures which can abort or ameliorate an attack such as moderate exercise, rigorous oral hydration with fluids, warm baths. It is important to try to establish a “ true event rate ” before randomisation into phase B. A minimum observation period of 3 months is recommended. If however the frequency and/ or severity of attacks increases, the individual can be randomised earlier to phase B by discussing with the clinical coordinators or withdrawn from the study. It must be emphasised that this is at the discretion of the patient and local doctors and in the best interest of the patient. We would still collect data on the chosen treatment thereafter and its outcome in relation to the frequency of attacks for all recruited patients in the study. If the attacks become prolonged (more than 4 hrs) they should present to the hospital where penile aspiration of blood within the corpora should be carried out with instillation of diluted solution of Phenylephrine. A 19-gauge needle is inserted into one corpus cavernosum. Blood is aspirated and sent for blood gas analysis to document the degree of ischaemia. Blood is then aspirated from the corpora (10-15ml), discarded and replaced with an equal amount of normal saline. This process is repeated until the aspirate is bright red. A solution of phenylephrine is prepared by taking 1ml containing 10 mg and diluting it to 100nl with normal saline. 3-5ml of this dilute solution is then injected into the corpora and this process is repeated at 10-minute intervals until the erection subsides. The patients pulse and blood pressure should be monitored during this procedure. A competent Urological surgeon in collaboration with the study physician should only undertake this manoeuvre.. The date of the attack should be noted and the patient should then be randomised between the four arms of the study drugs and continue as in phase B.
<u>PHASE B</u>	If a patient gets an acute attack during phase B while receiving one of the study drugs, the patient should have intracorporeal aspiration and instillation of a diluted solution. A competent Urological surgeon in collaboration with the study physician should only undertake this manoeuvre. The date of the attack should be recorded in the diary and notified to the study statistician or chief investigator through the local investigator. This event will be classed as a “ <i>treatment failure</i> ”. The code of the randomised treatment arm will be “broken” and the patient should receive subsequent care as determined appropriate by their local physicians/surgeons. We will still be interested in following up the patient long term by filling in the diary with notification of chosen second line treatment option and its outcome.

References

(1)Virag R et al (1996)

Preventive treatment of priapism in sickle cell disease with oral and self-administered intracavernous injection of etilefrine.

Urology: 47(5): 777-781.

(2)Elpis Mantadakis, David H Ewalt, Joe Don Cavender, Zora R Rogers, and George R Buchanan (2000)

Outpatient penile aspiration and Epinephrine Irrigation for Young Patients with Sickle Cell Anemia and Prolonged Priapism

Blood, 1 January 2000. Volume 95, Number 1