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ADMINISTRATION OF FIBRINOLYTIC THERAPY IN THE RURAL PREHOSPITAL SETTING

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TRIAL STUDY APPROPRIATENESS

The use of fibrinolytic therapy in the hospital setting to manage acute myocardial infarctions has become a widely accepted treatment. With the recent addition of single-bolus fibrinolytic agents, it now appears feasible to consider reperfusion therapy for those patients suffering ST segment elevation myocardial infarctions (STEMI) in the prehospital setting. To date, there have been a number of large randomized studies which have shown that fibrinolysis within the first two (2) hours following STEMI has proven more beneficial than delayed PCI and has provided a significant reduction in post-infarction complications and 30 day mortality. Because of these positive findings, the Advanced Cardiac Life Support (ACLS) standards of the American Heart Association now advocate the consideration of fibrinolytic therapy in the prehospital settings where transport times are sixty (60) minutes or greater¹.

The latest *ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction-Executive Summary*² recommend that the following components exist before implementing prehospital fibrinolysis.

1. Transport times are more than 60 minutes in high-volume (more than 25,000 runs per year) EMS system.
2. Ability to transmit ECG's.

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3. Paramedic initial and on-going training in ECG interpretation and myocardial infarction (MI) treatment.
 4. Online medical command.
 5. A medical director with training/experience in management of STEMI.
 6. Full-time paramedics.

We have evaluated each of these components and found that our proposed trial study clearly meets these standards. We have outlined a response to each of the five criteria listed above.

1. The selected provider agency for this trial study has lengthy ground ambulance transport times which average 103 minutes. The Sonoma County component of the Coast Valleys EMS Region averages approximately 40,000 EMS calls annually.
2. The selected provider agency has the ability to fax both the ECG's and the Fibrinolytic Checklist from either the patient's home or the ambulance during transport.
3. The selected provider agency's personnel have already received formal training on acquiring and interpreting 12 lead ECG's. In addition, the above mentioned cardiologists have been performing monthly QI sessions with the provider agency to review and critique all calls where 12 lead ECG's were performed.
4. On-line medical control will be provided by the on-call cardiologist for the Northern California Medical Associates. This cardiology group currently provides 24 hour referral and consultative services to all of the outlying hospitals and clinics in the Coastal Valley EMS Region. These cardiologists have already been briefed about the trial study protocol and have agreed to actively participate in this study. *If at any time the on-call cardiologist is unavailable, medical direction will be supplied by the Emergency Department physician of the intended receiving facility. If neither the cardiologist nor the ED physician is available, treatment will revert to standard CVEMSA ACS protocol*
5. The Lead Investigator of this proposed trial study will be functioning as the overall medical director for this project. He is a Board Certified Cardiologist with extensive experience managing STEMI in both the urban and rural environments. He currently works closely with the medical director of the selected provider agency on cardiac related QI review and training issues.
6. The selected provider agency utilized full-time paid professional paramedics with extensive prehospital experience.

7. Every incident of fibrinolytic use will be evaluated by the investigators and the CVEMSA Medical Director.

BACKGROUND

The Coastal Valleys EMS Region is comprised of Napa, Sonoma and Mendocino Counties. A large portion of these counties are rural in nature which cause extended ground ambulance transport times to the nearest acute care facility. In addition, the majority of the tertiary care facilities for the region are located within the urban areas of Santa Rosa and Napa. This additionally requires lengthy ground ambulance transports for patient requiring interfacility transfers from the outlying hospitals. Transports by EMS Aircraft from the field or interfacility are frequently inhibited by inclement weather or lack of aircraft availability thus requiring lengthy emergent ground transports.

OBJECTIVE

To determine whether early identification of STEMI patients in the field (transport times greater than 60 minutes) with subsequent medical control coordinated administration of prehospital fibrinolytic therapy and direct transport to a comprehensive cardiac facility would improve patient outcome over the traditional model of care.

STUDY DESIGN

A. Study Participants

This trial study participants would include a small number of specially trained professional paramedics and a 8 member cardiology group which would be available around the clock to review and coordinate the administration of these advanced therapies.

B. Inclusion Criteria

Patients who demonstrate ST segment elevation in two or more contiguous leads in the setting of cardiac ischemia related symptoms and who successfully pass the established inclusion/exclusion checklist².

C. Exclusion Criteria

Any patient who does not meet electrocardiographic findings, inclusion/exclusion checklist or in the judgment of the consulting cardiologist would be unacceptable for fibrinolytic reperfusion therapy.

D. Medication Selection

We selected Tenecteplase (TNK) as the fibrinolytic of choice due to its close relationship to Tissue Plasminogen Activator (t-PA) and its single-bolus method of administration. Because of the fibrin specific nature of TNK, concomitant administration of anticoagulation therapy is necessary to minimize the reocclusion potential during lengthy ground ambulance transports. It was felt that unfractionated heparin (UFH) was superior to low-molecular weight heparin because of its decreased

potential for intracranial hemorrhage and the ability to reverse its anticoagulant properties with Protamine.

E. Protocol

All of the advanced treatment provided in the field will be protocol driven. Any patient who is found to have a possible cardiac related presentation will have a 12 lead ECG performed in the field. If the 12 lead ECG is found to have ST segment elevation in two or more contiguous leads, then the paramedic will complete the Fibrinolytic Checklist and look for findings of absolute contraindications. Should an absolute contraindication be found, then treatment will revert back to the standard EMS treatment protocols. Absent any absolute contraindications, the paramedic will fax a copy of the 12 lead ECG and Fibrinolytic Checklist to the cardiologist on-call for the group. Each of these cardiologists have the ability to receive fax transmissions after hours at their homes. After reviewing the faxed 12 lead ECG and Fibrinolytic Checklist, the on-call cardiologist will consult with the treating paramedic by telephone or cell phone regarding the appropriateness of providing fibrinolytic therapy. If treatment is indicated, then administration of TNK and Heparin will be given per weight based dosing calculated by the cardiologist. No delay in patient transport will occur during the administration of these advanced medications.

F. Consent to Treatment

Patient consent is required before the administration of an agent with potentially harmful side-effects. Because of the unique dynamics which occur in the prehospital setting, the traditional informed/written consent method of treatment has been replaced with a simplified verbal assent to treatment. This approach was modeled from the United Kingdom's⁴ standardized method of administering prehospital fibrinolytics. The consent is attached to this document as an addendum, labeled "Consent To Treatment With Fibrinolytic Drugs."

G. Frequency of Utilization

A five (5) year review of the electronic PCR data specific to cardiac related calls with ground ambulance transport times over one (1) hours has demonstrated that approximately 20 to 25 patients annually would be considered for this new treatment modality. Depending on EMS Aircraft availability, actual prehospital reperfusion therapy could occur on 50% to 75% of these patient identified in the prehospital setting.

H. Training

All of the paramedics who will participate in this trial study have already received extensive training in obtaining and interpreting 12 lead ECG's for ST segment elevation in the field. In fact, the primary rural provider who will be participating in this study has been regularly performing 12 lead ECG's in the field for the past 5 years. Currently each of their 12 lead ECG's are reviewed by a cardiologist at a monthly QI session with the provider.

In addition, each paramedic participating in the study will receive five (5) hours of training specific to the presentation and management of acute myocardial infarctions with an emphasis on prehospital fibrinolytic administration. Audio-visual and skill based training material provided by Genentech, Inc. will be utilized to train the paramedics on reconstituting and determining the appropriate dosing of the medications. This special training session will conclude with both a practical and written exam to verify the participants knowledge of the subject material.

Because the frequency of actual fibrinolytic administration in the field is anticipated to be one to two times each month, participating paramedics will be required to attend monthly hospital rotations to maintain skill proficiency. These rotations will be focused on cardiac related care and administration of fibrinolytic and anticoagulant therapy. In addition, the mentoring cardiologists have agreed to also allow the paramedics to observe interventional cardiology related procedures to further their knowledge base.

I. QA/QI Program

All calls where STEMI was identified in the field, regardless of fibrinolytic administration, will be reviewed by the Lead Cardiologist Investigator for prehospital decision making and appropriateness of treatment. Each instance of prehospital fibrinolytic administration will be initially reviewed by the Lead Cardiologist Investigator and the CVEMS Medical Director for adherence to study protocol and difficulties encountered during the administration of the medication and/or transport of the patient. During monthly cardiology QI meetings with the participating provider agency paramedics, each call involving STEMI identified patients in the prehospital setting will be critiqued by the participating cardiologist with information provided by the Lead Investigator.

I. Outcome Review

Outcome review will focus on comparing the group receiving prehospital administered fibrinolytics and direct transport to a comprehensive cardiac facility to a cohort group managed with standard prehospital MONA treatment and transport to the closest emergency department for reperfusion therapy. Comparison of mortality, stroke, serious bleeding, infarct size and if available, ejection fractions will be used to scientifically evaluate outcome differences between the two groups.

References:

1. 2001 ACLS Provider Manual reflecting the 2000 ECC Guidelines. P. 126
2. Journal of the American College of Cardiology Vol. 44, No. 3, 2004 August 4:p. 675-677
3. Journal of the American College of Cardiology Vol. 44, No. 3, 2004 August 4:p. 683

4. **Prehospital Thrombolytic Therapy: Joint Royal Colleges Ambulance Liaison Committee: www.nelh-ec.warwick.ac.uk/JRCALC_Guidelines_v3_2004.pdf**

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TRIAL STUDY CHEST PAIN PROTOCOL UTILIZING PREHOSPITAL FIBRINOLYTIC ADMINISTRATION

Revision Date July 2007

BLS TREATMENT

- Assessment and History
- Oxygen administration
- Obtain base line vitals signs

ALS TREATMENT

- Obtain 12 lead ECG
- I.V. Normal Saline TKO
- Treat significant arrhythmia's
- Nitroglycerin 0.4 mg SL. Repeat every 5 minutes if pain persists and SBP > 100 (use with caution in Inferior Wall MI).

If Cardiac Ischemia Suspected

- Aspirin 325 mg (or 4 X 81mg) PO/chew if no contraindications
- Consider Morphine Sulfate 2-5 mg IVP. Repeat in 2 mg doses as needed for pain control (use with caution in Inferior Wall MI).

If Acute STEMI Detected On 12 Lead ECG

- Completes Prehospital Fibrinolytic Checklist
- Consider establishing 2nd IV

EXTENDED ALS TRANSPORT (Greater than 60 minutes from STEMI identification to arrival at comprehensive cardiac care facility)

- Cardiology consult at earliest convenience.
 - If cardiologist unavailable, consult with anticipated receiving facility ED physician
- Fax or transmit 12 Lead ECG to on-call Cardiologist (or receiving ED physician)
- Fax completed Prehospital Fibrinolytic Checklist to on-call Cardiologist (or receiving ED physician)
- Verbally review 12 lead ECG and Fibrinolytic Checklist results with on-call Cardiologist (or receiving ED physician)
- Alert Receiving Facility ASAP

If Medical Direction is unavailable, or unable to transmit ECG, revert to standard CVEMSA ACS protocol

Treatment

- Apply 1/2 inch of 2% Nitroglycerin paste. May apply an additional 1/2 inch Nitroglycerin paste if chest pain reoccurs. Do not let SBP drop below 100 and use with caution in Inferior Wall MI. Wipe paste off if SBP less than 100mmHg.

Physician Order Only

If evolving STEMI and no contraindications concurred by consulting Cardiologist (or receiving ED physician)

- Single intravenous bolus of TNK (Tenecteplase) over 5 seconds.

Patient Weight (kg)	TNK Dose (mg)	Reconstituted TNK (ml)
less than 60	30 mg	6 ml
60 to 69	35 mg	7 ml
70 to 79	40 mg	8 ml
80 to 89	45 mg	9 ml
90 or greater	50 mg	10ml

Treatment (continued)**Physician Order Only**

Heparin intravenous bolus of 70 IU/kg (maximum bolus of 4000 IU).

Patient Weight (kg)	Heparin Dose (IU)						
20	1400	30	2100	40	2800	50	3500
21	1470	31	2170	41	2870	51	3570
22	1540	32	2240	42	2940	52	3640
23	1610	33	2310	43	3010	53	3710
24	1680	34	2380	44	3080	54	3780
25	1750	35	2450	45	3150	55	3850
26	1820	36	2520	46	3220	56	3920
27	1890	37	2590	47	3290	57	3990
28	1960	38	2660	48	3360	58	4000
29	2030	39	3730	49	3430	59	4000

Treatment Of Reperfusion Arrhythmias

In general, reperfusion arrhythmias tend to be self-limiting. Should a prolonged life-threatening arrhythmia develop, it should be treated as follows-

Lidocaine- 1.0 mg/Kg slow IV push

If the life-threatening arrhythmia does not respond to a single dose of lidocaine, repeat at 1/2 initial dose.

If further arrhythmia intervention is required, treat as per CVEMSA protocol.

Treatment of bleeding

Apply direct pressure to bleeding site if possible

If direct pressure will not control bleeding, contact medical direction and expedite transport

CONSENT TO TREATMENT WITH FIBRINOLYTIC DRUGS

Considering your symptoms and your ECG tracing, we have contacted doctors and believe you are having a heart attack. This is a serious and potentially fatal condition. This is caused by a blood clot blocking a blood vessel supplying blood to your heart. The sooner we clear this blockage, the less damage will be done to your heart. Studies have shown that patients have a higher chance of survival and less long term complications the sooner we begin treatment. We have a long transport time to the nearest hospital and it would be better to begin some type of treatment now. The best treatment available right now is a 'clot dissolving' drug called Tenecteplase. This might be the same treatment as you would receive in a hospital emergency department. The only difference being that it is given earlier by the ambulance crew, under the supervision of a physician. This allows us to start treatment now rather than waiting to arrive at the hospital. Once the blood clot starts to dissolve your symptoms should start to ease. This occurs in about 80% of patients. The options now are to wait to start treatment until we arrive at the hospital or to start treatment now.

Because the drug dissolves blood clots it can cause unwanted bleeding in a small percentage of patients. This bleeding is usually minor and does not result in harm. In rare instances it can be serious or fatal. The risk of having a fatal bleeding problem is 1-4% percent. In other words, 96-99% of treated patients do NOT have life threatening problems. Considering all patients, the risk of the heart attack outweighs the risk of receiving the medicine. Your answers to the questions I have just asked suggest you are in a low risk group and the benefits of the drug should far outweigh any risks. The risk of not starting treatment is a lower chance of survival and a greater chance of long term complications such as heart failure. The largest study has shown that the chances of dying drop from 5.7% to 2.2% when these drugs are started before arriving at the hospital.

The ambulance service guidelines are very strict, and the questions I have asked you would put you in a low risk group. The benefits of this drug far outweigh the risks, which is why this treatment is so important.

Are you comfortable with me giving you the medication?

Yes, I understand that there is a small risk of serious or fatal side effects (bleeding) with this treatment. I am willing to take the medication (Tenecteplase).

X _____