ORIGINAL RESEARCH PAPER

Medical Science

TO STUDY THE EFFECT OF GLUCOSE-INSULIN-POTASSIUM TREATMENT IN ACUTE MYOCARDIAL INFARCTION PATIENTS

KEY WORDS: acute myocardial infarction (AMI), Glucose- Insulin- Potassium infusion (GIK), Cardiogenic shock,

Reena Gandhi Assistant Professor, Department of Pharmacology, Maharaja Agrasen Medical College, Agroha, Hisar

Suman Rana* Associate Professor, Department of Pediatrics, Maharaja Agrasen Medical College, Agroha, Hisar *Corresponding Author

Harender Simar Assistant Professor, Department of Microbiology, Maharaja Agrasen Medical College, Agroha, Hisar

ABSTRACT

Acute myocardial infarction(AMI) is a one of the commonest diagnosis in patient reporting in emergency department with high mortality rate if delay in early treatment initiation. The pathophysiological mechanism of AMI is the rupture of an artherosclerotic plaque in an epicardial coronary artery, exposing sub endotheial tissue to a subsequent thrombogenic response and leading to a complete obstruction of the vessel. Strategies directed towards achieving early and sustained re-perfusion of the infarct related artery have reduced mortality. Thrombolytic agents, aspirin, anti-platelet agent, beta-blockers & ACE inhibitors have been used as routine treatment during the early hours of AMI. Glucose- Insulin- Potassium have multiple metabolic effects which changes the metabolic / physiological function in infarction patients. According to inclusion & exclusion criteria, 50 patients were enrolled in the study. Patients were randomly divided into two equal groups, control group received routine usual treatment and GIK group received Glucose- Insulin- Potassium infusion. Various parameters like blood glucose level, serum electrolyte, ECG, Heart rate, Blood pressure, fluid input and output etc. were monitored at pre determined time interval and recorded for analysis. Glucose-Insulin-Potassium (GIK) infusion in acute myocardial infarction patients reduces the mortality rate as compared to the usual care. In comparison to the usual care the GIK infusion has less incidence of cardiogenic shock and heart failure.

INTRODUCTION

Acute myocardial infarction (AMI) is one of the most common cause of mortality in both developed & developing nations. In 1990, Ischaemic heart disease was the leading cause of death world wide, accounting for about 6.3 million deaths.[1] In recent past, several treatments including aspirin, thrombolytic therapy, beta- blockers & ACE inhibitors have been shown to improve prognosis in patients with AMI.[2,3] However despite the development of these effective treatments, mortality &/or re-infarction remain susbstantial in patients with AMI. The concept of metabolic modulation in patients with AMI with Glucose- Insulin- Potassium infusion was initially proposed by Sodi Pallaers in 1962.[4] This renewed interest in GIK was largely prompted by a wealth of new evidence regarding the importance of diabetes and glucose control in patient with ischaemic heart disease.[5] The use of GIK infusion in medical & surgical ischaemia is safe & cheap technique with proven benefits.[6] Several mechanisms by which GIK acts include suppression of circulating levels and myocardial uptake of free fatty acids (FFA'S) which are toxic to infarct myocardium, Insulin stimulate Na+ k+ ATPASE, stabilization of cell membrane along with decrease incidence of arrhythmias, restoration of myocardial intracellular potassium, increase in in glycolytic flux, increase in serum osmolarity, decrease in lysosomal activity, acceleration of wound healing.[5, 7, 8, 9, 10, 11] Insulin has anti FFA's effect, which may be particularly important when toxic effects of FFA's are accentuated by catecholamines.[12] GIK infusion has a potential in reducing the arrhythmic complication of AMI as well as reducing the myocardial infarct size.

MATERIAL AND METHODS:

The study was conducted on 50 cases of Acute myocardial infarction who were admitted in the department of cardiology, PBM hospital & associated group of hospital, S.P. Medical college, Bikaner after permission from the Institutional Ethical Committee.

Inclusion criteria:

1. Suspected AMI with persistent ST- elevation (>1mm) or LBBB
2. Within 12 hours since symptoms onset
3. Informed consent signed and obtained

Exlusion criteria:

1. Type-I Diabetes mellitus (diagnosed before age 30 yrs)
2. Hemorrhagic stroke within the last 12 months
3. Known renal impairment e.g. serum creatinine >2.0 mg/dl or 175 umol/L
4. Pregnancy
5. Advanced neoplastic or concomitant life threatening disease, which might life expectancy to < 1 month.
6. Known hyperkalemia at the time of randomization (e.g. >5.5 mmol/L).
7. Anticipated poor compliance with randomized treatment & any other factor that may jeopardize 30 days follow up (e.g. no fixed address, long distance to hospital, etc.)

The patients were randomized at the time of enrollment & were accordingly put in Control group & GIK group.

Control group consisted of 25 patients were taken as control, in whom routine usual treatment was given

GIK group consisted of 25 patients, who received Glucose-Insulin- Potassium solution. 25 IU of insulin & 40 mmol of KCL was taken and both were injected into 500 ml bag of 25% glucose. The rate of infusion was 1.5 ml/kg/hr for 24 hours.

Various parameters were monitored at pre determined time interval and recorded for analysis.

Statistical Analysis:

RESULT AND DISCUSSION

Table 1: Glucose, sodium & Potassium levels (Means ± SE)at different hours in control & GIK Group & The 'P' value

Time (hours)	Glucose level (mmol/l)			Sodium Level (mmol/l)			Potassium Level (mmol/l)		
	Control	GIK	P value	Control	GIK	P value	Control	GIK	P value
Baseline	6.436 ± 0.66	7.548 ± 0.62	0.641	140.9 ± 0.86	141.3 ± 0.77	0.562	4.0 ± 7.6	4.0 ± 7.9	0.852

6±2	6.495 ± 0.67	7.624 ± 0.72	0.272	140.2 ± 0.8	141.7 ± 0.58	0.248	4.1 ± 7.7	4.2 ± 5.0	0.311
24 ±4	5.4678 ± 0.31	7.645 ± 0.49	0.004	136.6 ± 0.82	142.2 ± 0.7	0.358	4.1 ± 5.8	4.3 ± 6.2	0.020

In GIK group patients the glucose and potassium values was significantly increased during infusion period. The glucose and potassium values observed at 24 ±4 hrs for GIK treated group were significant ($p < 0.05$) compared to that of control group. Ours results were consistent with earlier findings reviewed by Rogers et al 1977, Rackley et al. 1981.[13, 14] No significant change in sodium levels were detected.

The fluid volume input & output was measured in 24 hrs in both the groups. In the control group, Mean ± SE of fluid input for 23 patients was 1954± 102 ml, in 2 patients it was not measured due to death. The urine output for the same number of patients was 1163±77ml. in GIK group, fluid input was 3581±167 ml for 24 patients since 1 patient death occurred. The urine output (Mean ± SE) for the these 24 patients was 1931±78ml. the 'p' value of fluid intake and urine output was <0.001, which is highly significant. Ours results were consistent with earlier findings reviewed by Rogers et al 1977.[13]

5 (20%), 2 (8%), 4 (16%) patients in Control group, and 4 (16%), 1 (4%) & 6 (24%) patients in GIK group had a prior history of DM, 2 previous MI & hypertensive respectively.

ECG was recorded at the time of randomization in patients of both groups. In both the control & GIK group 18 (72%) patients had anterior MI. Inferior MI was 6 (24%) & 4(16%) in control and GIK group respectively. Lateral MI, posterior MI & Right side infarct was seen only in 1(4%) patient in GIK group. (Table 2)

Table 2: Showing baseline ECG at the time of randomization

	Control Group No. (%)	GIK Group No. (%)
Anterior V1-V6	18 (72)	18 (72)
Inferior II, III, AVF	6 (24)	4 (16)
Lateral I, AVL	0 (0)	1 (4)
V_3R- V_6R	1 (4)	1 (4)
$V_{7,8,9}$	0 (0)	1 (4)

Table 3: Showing Events observed within first 7 days of treatment in both groups

Event	Control Group No. (%)	GIK Group No. (%)
Cardiogenic shock	2 (8)	0 (0)
Heart failure	2 (8)	1 (4)
Death	3 (12)	1 (4)

Cardiogenic shock and heart failure were reported in the 2 patients (8%) in control group only. However heart failure was a complication seen in 1 patient (4%) in GIK treated group only. The mortality rate during our randomized study was 12% in the control group & 4% in GIK group. The four deaths in control group occurred due to cardiogenic shock in two patients and heart failure in two patients. The only single death in GIK group was due to pump failure. In the previous study of Rogers et al 1979, mortality was 15% in control and 13% in GIK group.

During the 30 days follow up period various outcomes and procedures were noted. In the control group 2 patients had undergone angiography, and re-infarction in 1 patient. While in the GIK group only 3 patients had undergone angiography, and no incidence of re- infarction in any patient.

CONCLUSION:

We conclude from this study that Glucose-Insulin-Potassium (GIK) infusion in acute myocardial infarction patients reduces the mortality rate as compared to the usual care. In comparison to the usual care the GIK infusion has less incidence of cardiogenic shock and heart failure.

REFERENCES:

1. Murray CJL, Lopez AD: Mortality by cause for eight regions of the world. Global burden of disease study. Lancet 1997; 349: 1269-76
2. Machanisms for the early mortality reduction produced by- blockade started early in acute myocardial infarction: ISIS-1 (First International Study of Infarct Survival) Collaborative Group. Lancet. 1988 Apr 23; 1(8591): 921–923
3. Pfeffer JM et al. Angiotensin converting enzyme inhibition and ventricular remodeling after myocardial infarction. Ann Rev Physiol 1995; 57: 805.
4. Sodi-Pallares D, Testelli MR, Fishleder BL, et al. Effects of an intravenous infusion of potassium-glucose-insulin solution on electrocardiographic signs of myocardial infarction: A preliminary clinical report. Am J Cardiol. 1962; 9: 166–81.
5. Malmberg K, Ryden L, Hamsten A, Herlitz J, Welden strom A, Wiedel H. Effects of insulin treatment on cause specific one year mortality and morbity in diabetic patients with AMI. DIGAMI study group. Eur. Heart J 1996; 17: 1337-1344.
6. Broomhead CJ and Colvin MP. Editorial. Glucose, insulin, and thye cardiovascular system. Heart 2001; 85: 495-496
7. Regon TJ, Harman MA, Lehan PH, et al. Ventricular arrhythmias and K+ tranfer during myocardial ischemia and intervention with procaine amide, insulin or glucose solution. J Clin Invest 1967; 46: 1657-1668.
8. Wildenthal K, Skelton CL, Caleman HN. Cardiac muscle mechanics in hyperosmotic solutions. Am J Physiol 1969; 217: 302-306.
9. Opie LH, Tausey M, Kennelly BM. Proposed metabolic vicious circle in patients with large myocardial infarcts and high plasma free fatty acid concentration. Lancet 1977; 2: 890-2
10. Oliver, Opie LH. Effects of glucose and fatty acids on myocardial ischaemia and arrhythmia. Lancet 1994; 343: 155-8
11. Gudbjarnason S, Fenton JC, Wolf PL, et. Al. Stimulation of reparative processes following experimental myocardial infarction. Arch Intern med 1966; 118: 33-40.
12. Gal J , Smith A, Riedel B, et. Al. Preservation and protection of myocardial function. J Cardiothor Vasc Anesth 2000; 14 (Suppl. I): 22-36.
13. Roger J, Rusell O, McDaniel G, Rackley E. Acute effects of Glucose- Insulni-Potassium infusion on myocardial substrates, coronary blood flow and oxygen consumption in man. The Am J of Cardio 1977; 40: 421-428
14. Rackley E. Rogeus J, Russell O, Mantle A, McDaniel G, et. al. Cliinical experience with glucose- insulin-potassium therapy in acute myocardial infarction. Am Heart J 1981; 102: 1038- 1049.