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"Association of Prolonged QTc dispersion with left ventricular Diastolic Dysfunction in patients with acute anterior myocardial infarction: A study in National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh"

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Abstract:
Aims: *Diastolic operate typically declines before heartbeat operate, and this precedes clinical signs in patients with acute coronary syndrome. Therefore, diagnosing of beat disfunction is extremely necessary for early diagnosing, follow-up, treatment, and prognostic analysis in cardiopathy with preserved ejection fraction (HFpEF) patients. The most objective of the study was to seek out out association between prolonged QTc dispersion and left chamber beat disfunction in Non ST phase Elevation MI (NSTEMI) patients in HFpEF.* ***Objects:*** *This cross sectional analytical study was conducted within the Department of medicine and sixty patients were enclosed as study population from August 2016 to February 2017. Then the study population was divided into 2 teams, every cluster consisted of thirty patients.* ***Methods and Materials:*** *Fifty-nine consecutive patients with acute myocardial infarct were randomised to receive seventy mmol of metal (n=31) infused over twenty four h or pla-cebo (n=26) incidence of bodily cavity arrhythmias and vital sign variability (SD of 5-min mean sinus beat intervals over a twenty four h amount, SDANN; low frequency/high frequency amplitude quantitative relation, LF/HF ratio), and also the variety of ischae-mic episodes on vectorcardiography were measured from the ®rst day of treatment. QTc dispersion corrected for vital sign was measured from the 12-lead graph. {magnesium|Mg|atomic variety 12|metallic element|metal} attenuated the quantity of hourly bodily cavity premature beats (P<0´05).QTc dispersion corrected for heart rate was decreased in both measurements at 24 h and 1 week (P<0´001). SDANN and LF/HF ratio were unchanged. The number of ischaemic episodes on vectorcardiography were equal, and peak creatine kinase MB release did not diVer between the groups. In testing the pathophysiological mechanisms, serum magnesium levels after infusion corre-lated with hourly ventricular premature beats (r_s = "0´47; P<0´01), ventricular tachycardias (r_s="0´26; P<0´05), and QTc dispersion corrected for heart rate (r_s = "0´75; P<0´001), but not with SDANN, LF/HF ratio or peakcreatine kinase MB. QTc dispersion corrected for heart rate correlated with hourly ventricular premature beats (r_s =0´48; P<0´001) and ventricular tachycardias (r_s =0´27; P<0´05.* ***Conclusions*** *Magnesium suppresses early ventriculararrhythmias in acute myocardial infarction. The decreased arrhythmicity is related to enhancement of homogeneity in repolarization, but not to attenuation of prevailing is-chaemia, improvement of autonomic nervous derangements or myocardial salvage.*

Key Words: *Magnesium, acute myocardial infarction, QTdispersion.*

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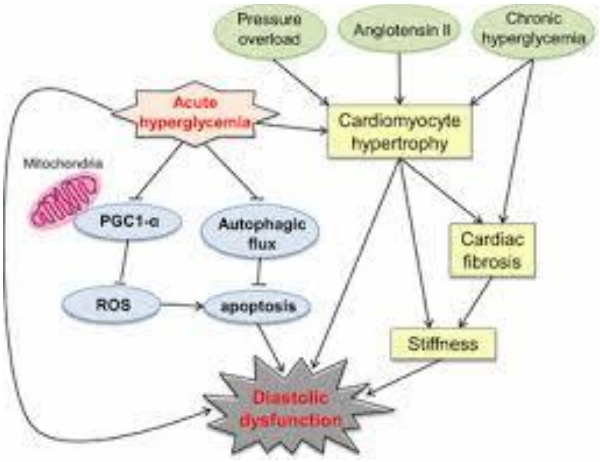
I. Introduction

Ventricular arrhythmias square measure a serious determinant of survival once acute heart muscle infarction [1, 2]. Their development is attributed to the pathophysiology of the broken myocardium [3], and changes within the nervous regulation of the guts and ischemia considerably modulate the generation. myocardial infarct begets nonuniformity in repolarization and involuntary imbal-ance, which may non-invasively be unconcealed as magnified spacialdiVerence between the longest and shortest QT interval on the cardiogram (QT dispersion)[4], associated depressed pulse variability on an mobile ECG[5]. Their degree is related to the looks of severe arrhythmias and magnified mortality [5, 6]. Metal administration has suppressed the emergence of arrhythmias [7, 8] and improved survival once acute heart muscle infarction [8, 9], though the

response has been questioned recently [10]. metal exerts a central role within the electrical stability and energy balance of the anemia myocyte[11], and it's the potential to aVect pulse either directly or by modi-fying the involuntary nervous management of the sinus node[12,13]. These properties may account for the bene®cialeVect. This study investigates whether or not blood vessel metal, administered within the early part of myocar-dial infarct, will suppress viscus arrhythmias. The in¯uence on involuntary regulation of the guts rate, unregularity in repolarization measured electro-cardiographically as QT dispersion, ischaemia, and also the extent of heart muscle injury were tested as pathophysiological determinants.



Dysfunction of the Left Ventricle
Source: Google

II. Methods

This study was patients aged <35 years admitted to the internal organ care units of the National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh. Ilx con-secutive subjects with acute infarction by cardiogram and/or creatin enzyme MB isoenzyme criteria and <12 h from onset of pain were randomised to receive metal or placebo once consent was received. Patients with sick sinus syndrome, chamber ®brillation, second- or third-degree chamber con-duction block, internal secretion dependent diabetes, uncontrolled blood vessel cardiovascular disease, or humor creatinine concentration >250 mmol . L"1 were excluded. Patients with signi®cant stenosed valve unwellness, for good paced rhythm or want for immediate ventilator treatment were additionally thought of ineligible.

Acute myocardial infarction

The criteria used for acute infarct con-sisted of wounding of >20 min length combined with ST section elevation of §0´1 mV in §1 of the limb leads or §0´2 mV in §2 of the chest leads, or a rise in liquid matter organic compound accelerator MB isoenzyme unit of measure to >7 µg. l" 1. Organic compound accelerator MB was measured on admission and three times at twelve h intervals successively. The localization was thought of as anterior, if the changes occurred in chest leads V2±V6, and inferior in leads II, III, and aVF. The acute infarct was de®ned as a alphabetic character wave acute infarct, if an innovative alphabetic character wave of §40 ms emerged. The patients received pharmaceutical treatment as clinically acceptable and it's begin preceded the study infusion.vessel beta-blocker, nitrate, oral anodyne and drugs medi-cation got per the judgement of the attending professional.

Magnesium administration

In a trial manner, the patients received eight mmol of 100% Mg salt in ten min followed immedi-ately by sixty two mmol in five hundred milliliter of physiological binary compound infused over twenty four h. The corresponding volumes of binary compound resolution served as placebo. Blood samples for determination of body fluid Mg and metal concentrations were taken before the study treatment started and at the tip of it.

Holter recording

A 24 h Holter recording was started prior to the magnesium/placebo administration. The second record-ing was performed prior to discharge from hospital on the 7th to 14th day, after the patient's condition had stabilized. A two-channel recorder (Marquette 8500, Marquette Electronics Inc., and Milwaukee, WI, U.S.A.) was used and the tapes were analysed by the same observer with a Marquette 8000 Holter Analysis System utilizing 5.8 software. The automatic QRS classi®cation was edited when necessary. The number of supraven-tricular and ventricular premature beats were calculated. Three or more consecutive supraventricular

premature beats or ventricular premature beats >120 beats.min**"**[1] were classi®ed as supraventricular or ventricular tachy-cardias. Ventricular tachycardias<120 beats. Min"[1] were de®ned as slow ventricular tachycardias.Heart rate variability was assessed by time domain and frequency domain methods from the entire 24 h recording. To calculate heart rate variability, the software uses only normal sinus beat intervals. Ectopic or artifact periods are excluded and replaced by holding the previous coupling interval level through to the next valid coupling interval. Fast Fourier Transformation was used to separate the R-R ¯uctuations to frequencies. The spectral bands used were 0´15±0´40 Hz (high fre-quency; HF) and 0´04±0´15 Hz (low frequency; LF). The spectral measures are computed as amplitudes, which are square roots of areas under power spectrum, and are presented in ms. The areas represent signal variance within frequency bands while the square root represents the standard deviation. The HF and LF components were determined from the entire 24 h recording. LF/HF amplitude ratio was calculated and used as an indicator of sympatho-vagal balance [14]. During the ®rst recording the patients were resting but during the second they were allowed normal activity.The standard deviation of the averaged normal-to-normal R-R intervals for all 5 min periods of the 24 h recording (SDANN) was used as the time domain method.

Electrocardiographic measurements

A standard 12-lead ECG was recorded at a paper speed of 50 mm. s**"**[1] immediately on arrival at hospital (base-line), 24 h after the start of the study treatment and prior to discharge. Of these, sinus cycle length, PQ interval and QRS durations were analysed by standard criteria from lead II or V_2. QT interval was measured from the beginning of the Q or R wave to the point where a tangent drawn along the maximal slope of the decending limb of the T wave (or ascending when the T wave was inverted) crossed the isoelectric TP baseline. If a bipha-sic T wave was present, the latter part was used for drawing. A separate U wave was disregarded [15]. In cases where the T wave was isoelectric or the termination of the T wave could not be reliably calculated, the lead was excluded from the analysis. QT interval measurements were calculated from three consecutive sinus beats and averaged. QT dispersion was de®ned as the diVerence between the maximal minus the minimal QT duration appearing in any of the 12 leads and corrected for heartrate according to the formula by Bazett, $QTc=QT/ RR^{1/2}$[16]. At least nine analysable leads in each record-ing was expected. All the measurements were done blindly by the same observer.

Ischaemia detection

Continuous on-line vectorcardiography (MIDA 1000; Ortivus Medical AB, TaÈby, Sweden) was started fifteen min before the study infusion. In MIDA, the orthogonal Frank lead system is employed to reckon vectorcardiogra-phy signals, that area unit averaged over 2-min periods. The ®rst 2-min average amount shaped the reference and every one changes were compared with it. The vectorcardiography parameters used were QRS vector diVerence, ST vector magnitude and ST amendment vector magnitude [17]. Associate in Nursing anemia episode was de®ned as a reversible increase of >15 ìVs in QRS vector diVerence from the present base level lasting >2 min, or a reversible increase of >0´1 mV in ST vector magnitude or ST amendment vector magnitude [17]. Associate in Nursing anemia event on Holter was de®ned as ST depression of §1 metric linear unit measured eighty ms once the J purpose, lasting for §1 min and a minimum of one min apart. A symptom-limited bicycle exercise take a look at victimisation 3-min steps and twenty five W employment increments was per-formed before discharge. ST depression of §1 metric linear unit measured eighty ms once the J purpose was de®ned as anaemia.

Table 1: Demographic data. The values are median (range), or numbers (percentage). The groups were statistically equal (n=57).

	Magnesium		**Control**	
	(n=31)		(n=26)	
Age (years)	60 (30±73)		59 (36±74)	
Male sex	26	(84)	22	(85)
Prior AMI	3	(10)	3	(12)
Prior beta-blocker	6	(20)	6	(23)
Prior aspirin	1	(3)	1	(4)
Diabetes	2	(6)	2	(8)
Hypertension	7	(23)	6	(23)

AMI=acute myocardial infarction.

Other measurements

Prior to discharge, echocardiographic left chamber end-diastolic diameter and ejection fraction, high reso-lution signal averaged electrocardiograms and blood vessel barore¯ex sensitivity were recorded. In signal average graphical record measure-ments, the overall ®ltered QRS period, the root-mean-square voltage within

the terminal forty ms and also the period of high frequency low amplitude signals below forty ìV were calculated (Marquette natural philosophy MAC-12/15, Milwaukee, WI, U.S.A.). Criteria for a positive late potential enclosed QRS period >110 ms, root-mean-square voltage 35 ms. The mean&SD noise voltage was 0´6&0´3 ìV. Baroreex sensitivity was assessed by plotting every beat-to-beat R-R interval against the preceding beat blood pressure obtained by invasive recording, victimisation AN endovenous 0´1 mg adrenergic drug bolus inflated in steps of 0´05 mg till AN anticipated 15± forty mmHg rise in blood pressure was observed [18]. The mean of 3 slopes of statistical regression lines with a correlation coeYcient §0´8 was de®ned because the baro-re¯ex sensitivity index (ms. mmHg" 1). Knowledge recording and analysis was performed with a speci®ed software package package (Cafts, MedikroOy, Finland) body fluid creatinine concentration was measured on admission and knowledge regarding numerous patient characteristics were recorded. The investigational protocol was approved by the moral Committee of Human analysis of the Department of drugs in capital of Finland University.

Statistics

Group diVerences between continuous variables were analysed with the Mann±Whitney U check. Serial changes inside the teams were analysed with the Wilcoxon signed-rank check or economic expert statistics. Bonferronicor-rection was applied in multiple comparisons. The information area unit expressed as median and vary. The chi sq. or the Fisher's actual check was wont to compare unconditional vari-ables. Correlation between variables was checked with the Spearman rank correlation test. All comparisons area unit two-tailed and also the signi®cance level was set at*P* value <0´05.

III. Results

The baseline characteristics were well balanced in the study groups (Table 1).The infusion caused the plasma magnesium concentration to rise to 1´30 mmol. L"1 (1´11±1´74 mmol. l"1) in the magnesium patients but it fell to 0´74 mmol. L"1 (0´61±0´92 mmol. l"1) in the controls (P<0´001 between the groups).

Table 2: Clinical pro®le and treatment of the acute myocardial infarction during the ®rst 24 h. Values are median (range) or numbers percentage (n=57).

	Magnesium		**Control**	
	(n=31)		(n=26)	
Anterior Q wave AMI	16	(52)	6	(23)*
Inferior Q wave AMI	9	(29)	14	(54)*
Thrombolytic treatment	28	(90)	23	(88)
Time to thrombolytic treatment (h)	2´0 (1±9)		3´5 (0´5±9)	
Time to study medication (h)	8 (5´5±12)		9 (5±12)	
Intravenous beta-blocker	16	(52)	12	(46)
Aspirin	25	(81)	22	(85)
Serum Mg baseline (mmol . l"^{1})	0´78 (0´61±0´93)		0´78 (0´66±0´99)	
Serum Mg 24 h (mmol . l"^{1})	1´30 (1´11±1´74)		0´74 (0´61±0´92)***	
Serum K baseline (mmol . l"^{1})	3´90 (3´50±4´50)		4´00 (2´80±5´10)	
Serum K 24 h (mmol . l"^{1})	4´10 (3´50±4´70)		4´00 (3´50±5´00)	
Peak CK-MB (µg . l"^{1})	113 (7±1106)		181 (12±639)	

AMI=acute myocardial infarction; CK-MB=creatine kinase MB.
**P*<0´05; ****P*<0´001.

Table 3: Ventricular arrhythmias. Values are median range (n=57).

	First 24 h				**At discharge**			
	Magnesium (n=30)		Control (n=24)		Magnesium (n=26)		Control (n=18)	
Mean sinus rate (beats . min"^{1})	72	(57±97)	70	(50±97)	66	(58±87)	68	(49±79)
VPB. h"^{1}	6	(0±115)	29	(1±469)***	0	(0±6)	1	(0±130)*
Number of couplets VPBs	3	(0±163)	13	(0±528)*	0	(0±2)	0	(0±16)
Number of R-on-T VPBs	0	(0±4)	1	(0±89)**	0	(0±15)	0	(0±7)
Number of slow VTs	0	(0±86)	4	(0±664)*	0	(0±0)	0	(0±1)
Number of VTs	1	(0±38)	5	(0±248)*	0	(0±1)	0	(0±0)

VPB=ventricular premature beats; R-on-T=ventricular premature beat appearing on the T wave; VT=ventricular tachycardia.
**P*<0´05; ***P*<0´01; ****P*<0´001 between the groups.

Electrocardiographic data

Table 5 summarizes the electrocardiographic data. Sinus cycle length, QTc duration, QTc corrected for heart rate.The acute myocardial infarction data are summarized in Table 2. Non-Q wave acute myocardial infarction was equally distributed between the groups but anterior Q wave acute myocardial infarction was more prevalent in the magnesium patients than the controls. Time from onset of thrombolytic treatment to onset of the study treatment was 5´3 h (1±10´5 h) in the magnesium group and 5´0 h (2±10 h) in the control group (ns). Radiologi-cal left ventricular failure developed in seven (23%) and in six (23%) of the patients in the magnesium and control groups, respectively (ns). During the study period, diuretics and angiotensin converting enzyme inhibitors were given comparably. Three patients, all in the control group, experienced conduction disturbances: one persistent grade I atrioventricular block, one persistent left anterior hemiblock and one temporary grade II atrioventricular block of Wenckebach type. An episode of atrial ®brillation developed in ®ve (16%) of the magnesium patients and in two (8%) of the controls. Sustained ventricular tachycardia was not observed.

Table 4: Heart rate variability. Data are median range (n=57).

	First 24 h				At discharge			
	Magnesium (n=30)		Control (n=24)		Magnesium (n=26)		Control (n=18)	
Mean RR interval (ms)	829	(615±1059)	864	(614±1191)	908	(682±1035)	865	(755±1229)
SDANN (ms)	66	(30±148)	67	(38±135)	96	(35±183)	86	(54±159)
HF (ms)	7	(2±22)	13	(4±59)**	8	(4±179)	11	(4±33)
LF/HF ratio	1´9	(0´9±3´3)	1´8	(1´0±2´4)	2´2	(0´9±3´0)	1´8	(0´8±3´0)

SDANN=standard deviation of averaged normal-to-normal R-R intervals; HF/LF=high/low frequency.
***P*<0´01 between the treatment groups.

Duration, PQ interval (®gures not shown) and QRS duration (®gures not shown) did not diVer at any measurement point between the groups. QTc dispersion corrected for heart rate was signi®cantly lower in the magnesium patients throughout the study period. Al-though QTc dispersion corrected for heart rate seemed to increase (though not statistically) during evolving acute myocardial infarction in the controls, it decreased in the magnesium patients (*P*<0´05). Patients who had QTc dispersion corrected for heart rate ≤100 ms at 24 h (n=12) were detected in the control group only (*P*<0´001).

Infarction characteristics

Arrhythmias

During the ®rst twenty four h on Holter, atomic number 12 treatment reduced the incidence of hourly cavity premature beats, cavity premature beat showing on the T wave, cavity couplets, and cavity arrhythmia episodes (Table 3). At discharge, the incidence of hourly cavity premature beats were reduced. There was no diVerence in supraventricular arrhythmias, and none of the patients had sustained cavity arrhythmia or cavity ®brillation.

Heart rate variability

SDANN or LF/HF ratio did not diVer in either record-ing. HF amplitude was lower in the magnesium group (Table 4).

Ischaemia features

In vectorcardiography, 18 (58%) of the magnesium patients and 10/23 (43%) of the controls had at least one episode of ischaemia (ns). The number of episodes in these patients was two (1±13) and three (1±12), respectively (ns).During the ®rst 24 h on Holter, six (19%) of the magnesium patients and two (8%) of the controls had 17 (2±32) and seven (3±11) episodes of ischaemia, respect-ively (ns). At discharge, the corresponding incidences were 3/18 (17%) and 2/12 (17%) and the number of episodes 24 (4±37) and 18 (9±27), respectively (ns).Peak creatine kinase MB release or ischaemia on an exercise test did not diver between the groups. An emergency coronary angiography was performed in seven (23%) of the magnesium patients and in two (8%) of the controls (ns). Of these, six in the former and all in the latter led to PTCA or CABG later during hospitalization.

Other measurements

On echocardiography, the left ventricular end-diastolic diameter was 52 mm (39±59 mm) in the magnesium patients and 54 mm (44±71 mm) in the controls (ns). The left ventricular ejection fraction did not diver between the groups: 57% (23±76%) in the magnesium patients and 53% (27±76%) in the controls (ns).The signal averaged electrocardiograms were registered in 48 patients. A positive late potential was detected in 7/28 (25%) of the magnesium patients and in 6/20 (30%) of the controls (ns). The barore¯ex sensitivity index could be determined in 34 patients (20 magnesium patients and 14 controls). The groups did not diVer: 6´6 ms. MmHg"[1] (1´0±14´6 ms. mmHg"[1]) in the magnesium patients and 4´0 ms. MmHg"[1] (2´0± 22´0 ms. mmHg"[1]) in the controls (ns).

Relationship to acute myocardial infarction site

Ventricular arrhythmias were equally distributed whether the acute myocardial infarction was anterior or inferior. Furthermore, acute myocardial infarction location did not aVectQTc dispersion corrected for heart

Table 5: Electrocardiographic data. The values are median range (n=57).

	Baseline		24 h		At discharge	
	Magnesium (n=31)	Control (n=26)	Magnesium (n=30)	Control (n=26)	Magnesium (n=28)	Control (n=25)
Sinus cycle length (ms)	770 (560±1420)	805 (585±1150)	860 (580±1080)	850 (570±1290)	920 (600±1350)	975 (710±1230)
QTc mean (ms)	409 (344±464)	419 (373±481)	445 (285±546)	429 (390±494)	404 (352±442)	397 (352±481)
QTcD (ms)	76 (11±108)	78 (31±141)	50 (14±88)	97 (49±166)***	41 (19±75)	67 (24±107)***

QTc=QT duration corrected for heart rate; QTcD=QT dispersion corrected for heart rate.
****P*<0´001 between the groups.

Table 6: In¯uence of infarct site on the eVect of Mg during the ®rst 24 h. Values are median (range) or numbers percentage (n=57).

	Anterior AMI				**Inferior AMI**			
	Magnesium (n=16)		Control (n=6)		Magnesium (n=9)		Control (n=14)	
VPB. h"[1]	12	(0±115)	149	(8±264)*	6	(0±59)	29	(1±125)*
Number of VTs	3	(0±21)	9	(0±65)	2	(0±38)	5	(0±66)
QTcD (ms)	53	(32±69)	107	(75±166)***	42	(14±52)	97	(61±142)***
SDANN (ms)	58	(30±110)	60	(38±91)	83	(59±148)	73	(40±135)
LF/HF ratio	1´9	(0´9±2´8)	1´6	(1´3±2´1)	2´0	(1´4±3´3)	1´9	(1´2±2´4)
Number of patients with ischaemia on VCG	6	(38)	4	(67)	8	(89)	6	(50)
Peak CK-MB (µg . l"[1])	187	(7±1106)	144	(44±639)	44	(20±538)	186	(25±357)*

VCG=vectorcardiography; for other abbreviations, see earlier tables.
**P*<0´05; ***P*<0´01; ****P*<0´001.

dispersion corrected for heart rate §100 ms at 24 h had more ventricular tachycardias (*P*<0´05) and hourly ven-tricular premature beats (*P*<0´01) during the ®rst 24 h than the patients with QTc dispersion corrected for heart rate <100 ms. No correlation was found between the appearance of ventricular arrhythmias and any of the heart rate variability parameters, transient ischaemia on vectorcardiography, or the early use of intravenous beta-blockers.

Other relationships

QTc dispersion corrected for heart rate at 24 h was strongly inversely correlated with serum magnesium concentration after the infusion (r_s = "0´75 respectively; *P*<0´001) (Fig. 1). There was also a negative correlationbetween serum magnesium concentration and HF (r_s = "0´45; *P*<0´01), but not between magnesium and the LF/HF ratio or SDANN during the ®rst 24 h. In patients with transient ischaemia on vectorcardiography (n=28) or Holter (n=8) during the ®rst 24 h, QTcdisper-sion corrected for heart rate did not diVer from the patients free of ischaemia. QTc dispersion corrected for heart rate measurement did not necessarily coincide with the appearance of the ischaemiaindeces.

Associates of ventricular arrhythmias

There was an association between the appearance of ventricular arrhythmias during the ®rst 24 h, serum magnesium concentration, and QTc dispersion corrected for heart rate: serum magnesium concentration after the infusion correlated negatively with hourly ventricular premature beats (r_s = "0´47; *P*<0´01), the number of couplet ventricular premature beats (r_s = "0´29; *P*<0´05), and the number of ventricular tachycardia (r_s = " 0´26; *P*<0´05). QTc dispersion corrected for heart rate at 24 h correlated with hourly ventricular premature beats (r_s =0´48; *P*<0´001) and the number of ventricular tachycardias (r_s =0´27; *P*<0´05). The patients with QTcrate, LF/HF ratio, ischaemia on the two Holter record-ings, vectorcardiography or exercise test. The patients who had an anterior Q wave acute myocardial infarction had greater peak creatine kinase MB levels (175 IU (7±1106 IU) vs 97 IU (9±538 IU); *P*<0´05), and a lower SDANN (*P*<0´05) and HF amplitude (*P*<0´01) on the ®rst 24 h Holter recording but not at discharge, than the patients with an inferior acute myocardial infarction. Among the patients with an anterior Q wave acute myocardial infarction, QTc dispersion corrected for heart rate throughout the study period, the incidences of hourly ventricular premature beats, and ventricular pre-mature beats appearing on the T-wave (*P*<0´05) during the ®rst 24 h were reduced in the magnesium patients compared to the controls. Heart rate variability, is-chaemia or peak creatine kinase MB did not diver between the study groups (Table 6). Among the patients with an inferior Q wave acute myocardial infarction, QTc dispersion corrected for heart rate throughout the study period, and hourly ventricular premature beats during the ®rst 24 h were lower in the magnesium patients compared to the controls. Heart rate variability and ischaemia did not diver, but peak creatine kinase MB release was lower in the magnesium patients (Table 6).

IV. Discussion

The main ®ndings in the present study are suppression of ventricular arrhythmias and a decrease in QTc dispersion in patients treated with magnesium in the early phase of acute myocardial infarction. Evicts on auto-nomic nervous balance, ischaemia, or extent of myocardial damage were not found. A pathophysiological link between magnesium treatment, decreased QTc dispersion and decreased incidence of ventricular arrhythmias may be suggested on the basis of the interrelationship between these factors.

Magnesium and ventricular arrhythmias in acute myocardial infarction

The ventricular arrhythmia reduction in the present study was substantial during the magnesium infusion, suggesting a true treatment evict. In other studies evaluating the ®rst 24 h evict, Abraham *et al*. showed a reduction in ventricular arrhythmias from 34´8% to 14´6% [19]. The LIMIT-2 study noticed no suppression in clinically documented peri-infarct arrhythmias.Similar result was evident in a Holtersubstudy of 48 patients [9, 20]. ThoÈgersen*et al*. found only a tendencytowards a reduction in episodes of repetitive ventricular premature complexes [21]. Applying longer detection periods, Rasmussen *et al*. reported a decrease from 47% to 21% in the incidence of arrhythmias requiring treatment during the initial week of hospitalization [7]. In ISIS-4, the largest trial assessing magnesium's evict in acute myocardial infarction, fewer patients with magnesium treatment experienced ventricular ®brillation during hospitalization, without consequent implications on overall mortality [10].

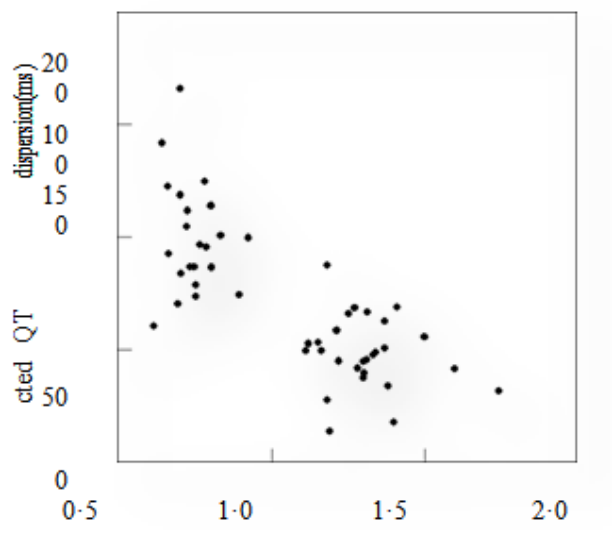


Figure 1: The association between serum Mg level and corrected QT dispersion at 24 h, assessed by the Spearman rank correlation test. r_s = "0´75; P<0´001.

Combining the heterogenous arrhythmia de®nitions, registration periods, and administration protocols, the meta-analysis of small-scale trials by Horner revealed a 49% reduction in the incidence of ventricular tachycardia and ®brillation by magnesium treatment [8]. Although magnesium dosing in our study corresponds with that in LIMIT-2, the responses diver. A higher pro-portion of our patients treated with thrombolytics (*2*90% vs*2*36%) and later onset of magnesium administration might contribute to the diverence.

Magnesium and QTc dispersion in acute myocardial infarction

Our data demonstrate that the early increase in QTcdispersion, known to follow acute myocardial infarc-tion[4,22], is abolished by magnesium treatment and theVect is maintained for up to one week. The response is not attributed to alterations in QTc or QTc corrected for heart rate durations, which remained comparable between the treatment groups. This is in agreement with previous ®ndings that QT dispersion is not related directly to QTc duration, and interventions that prolong QTc duration do not implicitly increase QT dispersion [23]. Furthermore, magnesium has not been found toalter the electrocardiographic QTc interval in healthy subjects [12].Spatial QTc dispersion is recognized as a marker of regional inhomogeneity in ventricular refractoriness, prominent in the border zone between non-ischaemic and ischaemicmyocardium [24], and thus, a substrate for re-entrant ventricular tachyarrhythmia's[25±27]. Repolarization can be modi®ed by the ischaemic process itself [28], changes in the nervous regulation of the heart [29], and some pharmacochemicalinterventions [23, 30]. While transientischaemia, peak creatine kinase MB release, and heart rate variability measures were not associated with the degree of QTc dispersion, serum magnesium levels were, suggesting that magnesium was a major determinant of homogenous repolarization.The bene®t following magnesium treatment was still recognizable at one week, implying that magnesium might induce long-term modi®cations in the evolving arrhythmia substrate. Among patients with acute myo-cardial infarction, excessive dispersion in repolarization detected at discharge has predicted increased susceptibility to later life-threatening ventricular arrhythmias or sudden death[6,27], but not within the ®rst 3 days[31].

Magnesium and autonomic control of heart in acute myocardial infarction

Magnesium exerted no in¯uence on the sympathovagal balance either in the early phase or at discharge, as demonstrated by the unchanged SDANN or LF/HF ratio. The early decrease in HF amplitude in the mag-nesium patients probably re¯ects the anterior acute myocardial infarction dominance in these patients, since anterior acute myocardial infarctions were associated with lower HF amplitude, as also shown in other groups [29, 32]. Furthermore, barore¯ex sensitivity was not in¯uenced by magnesium treatment. It has been shown that impairment of cardiac neural function occurs within minutes after cessation of coronary blood ¯ow and reversibility is only achieved with rapid interventions [33]. Relatively late administration of magnesium after onset of symptoms and thrombolytic treatment may have failed to save the function of autonomic innervation within myocardium. As blunted heart rate variabilityand barore¯ex sensitivity after acute myocardial infarction are powerful, independent estimators of survival and malignant ventricular arrhythmias[6,34,35], theobserved neutral eVect lessens the probability of magnesium's modifying the prognosis via changes in autonomic control of the heart.

Magnesium, ischaemia and acute myocardial infarction size

Dynamic vectorcardiographic monitoring is a sensitive non-invasive method of identifying recurrent myocardial ischaemia and vessel patency in association with acute myocardial infarction [17, 36] and of estimating prognosis after acute myocardial infarction [37]. Althoughexperimental data promotes magnesium's anti-ischaemic[11,38,39] and reperfusion injury reducing[40±42]properties, early ischaemia suppression could not be veri®ed in our study. It is concluded, that despite the reduction in ischaemia in patients with unstable angina following magnesium [43], it cannot restrict early residual ischaemia once infarction has emerged (ISIS-4; our data). Furthermore, the extent of myocardial damage, assessed by cardiac enzyme release, left ventricular dimensions and function, or appearance of late poten-tials, was not diminished. This is consistent with in vivo studies that show infarct size limitation only if magnesium administration is initiated before or at the time of reperfusion [40, 41].

Determinants behind arrhythmia suppression

The diminished arrhythmicity was closely ascribed to magnesium's ability to decrease QTc dispersion. This association has not been noticed earlier. In general, while QTc dispersion has identi®ed patients at increased risk for arrhythmic death, the connection between decreased QTc dispersion and suppression of ventricular arrhythmias has not been con®rmed in acute myocardial infarction patients previously [44].Under experimental ischaemia, magnesium has the potential to modify repolarization. Magnesium is a co-factor of several membrane-bound ion pumps and a regulator of some ion channels operating during repolarization of the myocyte[11]. Apart from anti-ischaemicaction [11, 38, 42, 43], restoration of the electrochemical gra-dient across the sarcolemma, induced mainly by potass-ium and calcium ¯uxes secondary to ischemia [11,45±48],has been shown. Accordingly, the ischaemia-induced early prolongation of the epicardial monophasic action potential duration is shortened by magnesium [49]. Based on the present clinical data, it may be assumed that the primary magnesium action is to modify the unstable electrical environment, not to alleviate ischaemia. This gains support from the observation that magnesium acted electrically, i.e. reduced arrhythmias, and not by diminishing infarction. Secondly, dispersion in repolarizationre¯ects conditions in the electrophysiological substrate for ventricular arrhythmias [24, 26, 50]. Thirdly,regarding the dependence of QTc dispersion on the location (present study) and the extent of infarct [28], magnesium's in¯uence was independent of these (Table 6).The reduction in QTc dispersion, a marker of a re-entrant arrhythmia mechanism, explains inaccurately the decrease in the incidence of ventricular ectopic beats, that are considered an expression of increased excitability due to acute ischaemia[51]. Whether true re-entrant ventricular arrhythmias, sustained ventricular tachycardias, are also prevented by magnesium could not be judged.

V. Clinical implications

The arrhythmia reduction was obvious during the early hospitalization. While arrhythmia reduction has improved in-hospital [52] and long-term prognosis [8, 53]in small studies, LIMIT-2 did not raise this mechanism to explain the reduced mortality [9, 20]. In the absence of robust end-points (sustained ventricular tachycardia, ventricular ®brillation, and death), and regarding the mechanistic, not prognostic nature of the present study, caution is warranted in estimating the clinical signi®-cance of the observed arrhythmia suppression on morbidity or mortality. However, increased frequency of hourly ventricular premature beats at discharge after acute myocardial infarction has also predicted adverse outcome under thrombolysis [2, 54]. Increased homogen-eity in repolarization, demonstrated to last through the recovery phase, would be assumed to protect against generation of life-threatening ventricular arrhythmias or sudden death. The deviating in¯uence of magnesium treatment on the prognostic markers may partly explain the discrepant outcomes in the studies evaluating magnesium's eVect on survival after acute myocardial infarction.

VI. Conclusions

The present study demonstrates that intravenous magnesium administered in the early phase of acute myocardial infarction attenuates the incidence of ventricular arrhythmias. The reduced AR rhythmicity by magnesium is closely linked to enhancement in homogeneity of repolarization, but not to improvement of autonomic regulation of heart, alleviation of ischemia, or myocardial salvage.

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