

LETTER TO THE EDITOR

STUDY OF SERUM LIPID PROFILE CHANGES IN MET-ENKEPHALIN TREATED RATS

Sir,

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The enkephalins are found in tissues other than the brain and pituitary. Endocrine cells in the gastrointestinal mucosa enkephalin in man, mouse, chicken, rat, guinepig, rabbit, cat, monkey and pig. The enkephalins are present in substantia gelatinosa of nerve terminals. (1,2). Thus they are distributed in sites involved in glucose homeostasis, central and peripheral divisions of the autonomic nervous system, pancreas, the gut and the hypothalamapituitary tract (3,4,5). First suggestion that opioids might be involved inhuman diabetics came from the work of Pyke and Leslie, (6). Endogenous opiates may be factor in the development of hyperglycaemia and defective insulin secretion in human type-2 (Non insulin dependent) diabetes mellitus).

Atherosclerotic Heart disease of coronary arteries is the most important single cause of death in the diabetes mellitus. Morphine pellet implantation showed rise in total plasma cholesterol, raised low-density lipoprotein plus very low-density lipoprotein. The resultant increase in artherogenic index was accompanied by enhanced aortic cholesterol deposition. These alterations were prevented by daily administration of Naltrexone (7,8,9). This study was undertaken to stress the role of opioid on serum lipid level in experimental animal.

The present study was conducted on

adult male Albino rats (Charles Foster stain) weighing 150-250 gms maintained on L: D 12:12 with light phase from 0700-1900 hrs. and at temperature $22 \pm 1^\circ \text{C}$. Animals were fed with soaked gram and water ad libitum.

Blood was collected after standard technique, after all aseptic measures were taken. Blood samples were collected at 0,20,30,60,90 minutes. Serum was separated and blood chemistry was done with the help of spectrophotometer (Systronics spectrophotometer 106, Made in India).

Serum Triglyceride and cholesterol were estimated by enzymatic method and routine method (Wybanga method) (10). HDL was determined by phosphotunstate/magnesium method followed by Wybanga method. (Serum is free from LDL, VLDL and Chlomicron). Low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) were found out by formula utilizing the values of cholesterol, Triglycerides, HDL and LDL. *Statistical analyses were carried out by unpaired student "t" test.

Grouping :

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|----------|--|
| Group I | Saline treated group (i.p.)
(S) $n = 6 \times 6 = 36$ animals |
| Group II | Metenkephelin group (i.p.)
(M) $n = 6 \times 6 = 36$ animals |

Group III Naloxone+Metenkephalin
(i.p.) (N+M) n=6×6=36animals
Total Animals = 108 Rats

Actual value of HDL was calculated bearing in mind the dilution factor of 1.125

LDL estimation: Low density lipoprotein was estimated according to the formula

$$\text{LDL} = \text{Total Cholesterol} - \text{TG}/5 + \text{HDL}$$

VLDL estimation:

$$\text{VLDL} = \text{Total Cholesterol} - (\text{HDL} + \text{LDL})$$

Serum Cholesterol: In group II Met-enkephalin increases cholesterol (77.7 mg to 91.01 mg% mean value (P<0.05) Naloxone blocked the effect of met-enkephalin significantly 91.01 mg% to 77.96 mg% (P<0.05) in group III Met-enkephalin effect on serum cholesterol was statistically significant at 20, 60, 90 minutes. Saline

group (Group I) controlled values were achieved after Naloxone blocked the Met-enkephalin effect. It is concluded that Met-enkephalin raised serum cholesterol in this experimental study.

Serum Triglyceride :

Fluctuations of serum Triglyceride values from control values were seen. Metenkephalin caused significant rise in serum Triglyceride from 65.5 to 71.33 mg%, (mean value P<0.05). Naloxone blocked significantly (P<0.001), the effect of met-enkephalin on serum Triglyceride value. Rising trends were observed at 0,20,30,60 minutes.

H.D.L. Cholesterol: Met-enkephalin did not cause any significant fluctuations in serum HDL.

Serum cholesterol level (mg%).

	0 Min	10 Min	20 Min	30 Min	60 Min	90 Min
I	86.4±3.2	71.2±8.64	80.8±8.2	88.2±3.96	72.5±5.7	74.8±8.4
II	80.25±7.27	69.15±2.44	95.00±3.36	91.4±7.5	100.5±4.2	99.0±4.58
III	75.8±10.5	76.75±3.5	74.0±3.65	86.33±3.78	72.00±5.86	73.0±2.94

Serum Triglyceride Level (mg%).

	0 Min	10 Min	20 Min	30 Min	60 Min	90 Min
I	56.5±3.44	61.4±2.88	63.25±3.86	61.0±4.16	68.25±3.86	65.5±5.32
II	63.0±3.16	64.4±4.03	71.25±2.98	74.80±5.16	75.75±4.42	71.33±2.51
III	63.2±3.27	57.25±3.77	59.0±6.21	66.0±3.91	65.50±4.65	62.0±2.94

Effect of Met-enkephalin on Serum Lipid Fraction (mg%).

	0 Min	10 Min	20 Min	30 Min	60 Min	90 Min
HDL	12.00±2.9	17.90±1.62	18.44±1.86	17.42±2.32	16.96±4.26	15.06±0.81
LDL	57.47±9.68	37.90±2.75	62.17±4.03*	57.40±4.24*	69.37±4.76*	69.66±3.74
VLDL	12.60±0.63*	12.88±0.80*	14.25±0.59*	14.96±1.03*	15.15±0.00	14.26±0.50

(*P<0.05, Significant)

L.D.L. Cholesterol: Met-enkephalin caused significant rise in serum LDL at 20, 30, 60 min ($P < 0.05$).

Very low density lipoprotein (V.L.D.L.)

Rise in VLDL after met-enkephalin injection from 12.73 mg% to 14.21 mg% were observed ($P < 0.05$) Naloxone blocked the Met-enkephalin effect from 14.21 mg% to 12.53 mg% ($P < 0.05$) in this study.

In present study significant changes in blood lipid levels were found in Met-enkephalin treated animal. Elevation of Cholesterol level ($P < 0.05$) was noted at 20, 60, 90, min. Triglycerides level ($P < 0.05$) was observed at 0, 20, 60 min. Serum LDL cholesterol was raised at 20,60,90 min and serum VLDL cholesterol showed increased level at 0, 20, 30, 60 minutes. Met-enkephalin did not alter serum HDL levels significantly. It is concluded that serum lipid profiles were altered by intra peritoneal (i.p) injection of Met-enkephalin.

It is well known that families of lipoproteins cholesterol, triglyceride and phospholipid are transported in the blood in the form of Lipo-protein complexes. VLDL cholesterol is primarily formed in liver. They in turn are converted to intermediate density lipo-protein (IDL) and LDL. LDL is attached to the receptor on the surface of many cells in the body and is ingested into cells by endocytosis.

The present results are similar to the findings of Bryant et al (7) that implantation of Morphic pallet elevated total plasma cholesterol, raised LDL plus VLDL and lowered the level of HDL and increased aortic cholesterol deposition as the resultant increase in atherogenic index. Also endogenous opioid peptides have assigned lipolytic properties under several experimental condition, Beta endorphins have been reported to stimulate lipolysis in the rabbit both in vivo and vitro. The reason being lipolytic activity in exercise is indicated by Neuro and hormonal changes involving catecholamine, decrease insulin, increase glucagons, growth hormone and cortisol level. In vivo, in rats, Naloxone showed anti lipolytic activity. On contrary, beta-endorphin induced lipolysis in rabbit adipocytes in vitro experiment cyclic AMP mediated the lipolytic activity of endorphins, enkephalins and naloxone (11, 12, 13, 14).

This study confirmed the important effect of Met-enkephalin on serum lipid profile. It is concluded that the cause of this is due to Met-enkephalin which may have effect on increased lipolysis, by direct effect on Hepatocyte via Catecholamine and serum cortisol level, as it has been reported earlier that opioid peptide modulate, circulatory and endocrine response to mental stress in human (15) and in cerebrospinal fluid and peripheral plasma of anaesthetized ponies (16).

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