Pathophysiology of Stress Hyperglycaemia following Surgery

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INTRODUCTION

Surgical and non-surgical injury triggers the release of stress hormones which stimulate a cascade of metabolic changes leading to substrate mobilisation (hyperglycaemia) with the breakdown of protein, fat and carbohydrate stores [1]. The metabolic changes appear to be proportional to the severity of the operation with plasma cortisol and blood glucose concentration rising slightly during minor surgical procedures but significantly during major intra-abdominal operations [2].

The pathophysiology concerned with stress hyperglycaemia of major abdominal surgery has not been viewed in detail so far. The present study was undertaken in adult males to evaluate the effect of major abdominal surgery (cholecystectomy) on glucose tolerance and on three major 'stress hyperglycaemia' related hormones viz; insulin, growth hormone and cortisol.

MATERIAL AND METHODS

50 male patients admitted in the General Surgery Dept of Institute of Medical Sciences, Srinagar, Kashmir undergoing elective cholecystectomy were taken for this study. The age of the patients ranged from 30-45 year and the weight ranged from 52-64 kgs (Table 1).

Table 1
Effect of surgery on glucose (mg%)

Time	Pre-operative blood glucose (mg/dl)	Post operative blood glucose (mg/dl)	P
	Mean ± SD	Mean ± SD	
Fasting	76.27 ± 7.6	107.95 ± 9.93	P < 0.01
30 min	114.82 ± 6.54	145.73 ± 13.05	P < 0.01
60 min	104.09 ± 5.25	125.05 ± 7.49	P < 0.01
120 min	87.09 ± 7.55	111.50 ± 7.61	P < 0.01

Criteria for patient selection

a. Patients with diabetes, renal failure and hypertension were not included in this study. Patients previously diagnosed to have diabetes mellitus or those with abnormal 'glucose tolerance test' were also excluded from the study; this was aided by HbA_{1c} estimation done prior to surgery.

b. All patients underwent elective cholecystectomy.

Sample Collection

On study days all feeding, except for intravenous electrolyte infusion, was omitted for 8-12 hours prior to blood sampling in order to avoid interference with metabolic response to surgery.

i. **Pre-operative sample** (24 hours before surgery) - sample "A" was taken at 9 a.m. in the fasting state and under circumstances as mentioned above, for a fasting blood glucose, HbA_{1c} and fasting immunoreactive insulin (IRI); human growth hormone (HGH) and cortisol. Sample "A" also consisted of three more samples taken at the intervals of 30 minutes, 60 minutes and 120 minutes as I.V. glucose tolerance test for blood glucose.

ii. **Post-operative sample** (24 hours after surgery) - Sample "B" was taken at 9 a.m. in the fasting and included a basal sample for blood sugar and hormone estimation and three more samples at 30 minutes, 60 minutes and 160 minutes interval for blood glucose during I.V.G.T.T. The blood sugar estimation was done on Hitachi 704 from Boehringer Mannheim. HbA_{1c} was analysed on automatic HbA_{1c} analyser from Kyota Japan. After HbA_{1c} values were obtained, all those patients with abnormal HbA_{1c} were excluded from the study.

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The GTT performed by an intravenous injection of 50% glucose over a 3-minute period in an amount corresponding to 0.5 gm/kg body weight [3]. Intravenous method was used since post-operatively oral feeds were started on the evenings of the first post-operative day.

HGH and IRI were estimated by radio-immunoassay method based on the competition of unlabelled hormone in the standards (or samples) and radio-iodinated hormone for the limited binding sites for the specific antibody. Cortisol estimation was done by the WHO reagent programme assay for cortisol. The assay is conventional radio-immunoassay that utilises dextran charcoal for separation of free form antibody bound hormone.

Statistical Evaluation

The data was subjected to "Students t test" for paired data.

RESULTS

22 male patients aged between 30-35 years (Mean ± SD : 37.55 ± 4.03) and weighing between 52-64 kgs (Mean ± SD : 58.77 ± 2.89) were studied.

Comparison of post-operative GTT with preoperative GTT showed a highly significant elevation of blood glucose levels post-operatively in the basal state and following I.V. glucose challenge (Table 1).

The pre-operative and post-operative levels of IRI, HGH and cortisol (Table 2) showed a statistically significant elevation in the individual hormone levels post-operatively. This was particularly pronounced in case of cortisol.

Table 2
Effect of surgery on hormones

Hormones	Pre-operative	Post-operative	t	P Remarks
	Mean ± SR (Range)			
IRD	10.37 + 7.84	19.94 ± 12.81	3.05	P<0.05
μv/ml	(1.83 - 26.21)	(4.4 - 54.50)		
HGH	1.90 ± 2.06	4.72 ± 4.28	2.79	P<0.05
(ng/ml)	(0.17 - 7.76)	(0.83 – 15.89)		
Cortisol	10.01 ± 5.15	18.64 ± 8.67	4.05	P<0.01
(nmol/l)	(1.3 – 19.04)	(4.98 – 38.45)		

DISCUSSION

The endocrine, metabolic and inflammatory responses to injury and infection are composed of a variety of physiological changes often grouped together and called the surgical stress response.

Surgical injuries trigger the release "Stress hormones" like catecholamines, cortisol, growth hormone and glucagon, all well known glucogenic factors. The metabolic changes appear to be proportional to the severity of the operation, with plasma cortisol and blood glucose concentration rising slightly during minor surgical procedures but, significantly during major intra-abdominal operation [2].

The present study was undertaken to evaluate the effect of surgical stress on the glucose tolerance of these patients on the first post-operative day and to study the hormonal responses related to the hyperglycaemia. It was observed that the pre-operative fasting blood glucose values were in the normal range (76.27 ± 7.6 mgs%) while the post-operative one's changed to 107.95 ± 9.93 mgs%, the elevation being statistically highly significant. However, post -operative blood glucose values were not in the diabetic range. These findings are in agreement with those of H. Ross et al [4] who studied the effect of abdominal operation on GTT in patients undergoing partial gastrectomy, colonic resection and cholecystectomy and concluded that elective surgery was followed by a period of impaired GTT which reached a peak in the first 24 hours. Markku Aarimaa et al [3] also observed that GTT of all patients undergoing elective femoral osteotomy showed a diabetic pattern.

There was a significant elevation in the cortisol levels with mean cortisol levels changing from a per-operative value of 10.01 ± 5.15 nmol/l to 18.64 ± 8.63 nmol/l post-operatively which is statistically highly significant. Cortisol rise due to surgery has been observed by Nistrup [5], Kehlet et al [6], Clan Hagen [7], Virtue et al [8] and R.H. Goschke et al [9].

Growth hormone levels changed from a preoperative value of 1.90 ± 2.06 ng/ml to 4.72 ± 4.28 ng/ml postoperative, which is statistically a significant change. H. Ross et al [4] also observed a rise in GH in patients undergoing abdominal surgery. GH increasing during various major surgeries also has been confirmed by Clan Hagen et al [7] during cholecystecomy, Cheryl P. Salter et al

[10] during open heart surgery, and H. Goschke et al [9] during cholecystectomy and colonic surgery.

Immuno-reactive insulin (IRI) changed from a pre-operative value of 10.34 ± 7.84 μU/ml to 19.94 ± 12.8 μU/ml post-operatively. HH New some & James have also reported a similar increase in insulin levels following surgery [11].

From this study it is clear that abdominal surgery of moderate severity altered the blood glucose levels significantly in the immediate post-operative period. This was associated with significant elevation of cortisol, GH and IRI in the post-operative period. It remains to be seen whether such a response is helpful or harmful in maintaining the constancy of internal melieu and whether there is a cut-off point separating the physiological from a pathological response.

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