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Full Length Research Paper

A comparative study of serum ferritin and other "acute phase reactants" (APR) in minor and major surgery

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This study was carried out on serum ferritin, acute phase reactants (APR), iron (Fe) and total iron binding capacity (TIBC) in healthy women in Ado Ekiti, Nigeria and in female patients undergoing suture (minor operation) and ceaserean operations at the Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Nigeria between February and March, 2009. The results revealed post-operative serum ferritin and APR concentrations to be significantly higher (p > 0.01) while iron and TIBC were significantly lower in patients undergoing caesarean operation compared to both patients with minor operation and healthy women. The pre-operative results of serum ferritin were however significantly lower in patient undergoing major operation than in patients with minor operation. The present study was carried out to examine the changes in serum ferritin and other acute phase reactants in response to the magnitude of tissue damage. It can be concluded that the concentrations of serum ferritin and acute phase reactant increases as the magnitude of tissue damages increases. There is an acute phase response of serum ferritin levels following major surgery.

Key words: Suture, surgery, ceaserean, acute phase reactants

INTRODUCTION

Ferritin is the soluble form in which iron is stored within cells. Ferritin is found in all tissues and in high concentration in liver, spleen and bone marrow. It is accepted that plasma ferritin is normally derived from cells of the reticulo endothelia system (RES) and any movement of iron from red cells to the storage compartment is reflected by a corresponding change in plasma ferritin concentration (Wormwood, 2001).

Serum ferritins have been found to be significantly correlated with body iron stores in normal subjects and patients with iron deficiency or overload (Jacobs et al., 2002). The level of serum ferritin can be raised in acute and chronic inflammatory disorders, which may be due to inflammatory bowel disease (Bartels et al., 1998), viral or bacterial infection (Birgegard et al., 2008) and endotoxic without iron overload and this hyperferritinaemia may reflect the severity of hepatocellular damage and rheumatic fever (Bentley and Williams, 2002). Elevated serum ferritins have been linked with malignancy (Jacobs et al., 2002).

Acute phase reactants play a part in the very complex defensive process of inflammation. Their concentrations rise significantly during acute inflammation due to causes such as surgery, myocardial infarction, infections and tumors. This rise, caused by increased synthesis in the liver, do not aid in the diagnosis of the cause of inflammation, but measurement of those proteins with the largest and earliest rises can be useful in monitoring the progress of the inflammation or its response to treatment (Pepys, 2007).

The limited information available makes serum ferritin, as an index of iron stores unreliable when there is tissue damage. Therefore, the magnitude of the changes in serum ferritin, iron concentration and total iron binding capacity (TIBC) in pregnant women undergoing suture and caesarean surgery was studied. These were choosing as examples of minor and major surgery respectively. For comparison, the plasma levels of C reactive protein (CRP) which is an established 'acute phase

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Table 1. Pre and post-operative ferritin, acute phase reactant, iron and total iron binding capacity in pregnant women with minor surgery.

Parameter	Pre-operative	Day 1-2	Day 3-4	Day 5-6	Day 7-8	Day 9-10	Day 11-13	Day 14-17	Day 18-20	Day 21+	5 weeks
Ferritin (µg/ml)											
Mean ± SD n = 30	13 ±1.14	50* ± 3.50	78* ± 5.20	60 ± 3.45	52 ± 3.50	-	-	-	-	-	17 ± 0.92
Range	14 – 119	45 – 700	70 – 800	59 – 6.94	48 – 400	-	-	-	-	-	19 – 200
APR (mg/l)											
Mean ± SD n = 30	72 ±3.40	100* ±10.11	73* ±5.12	26* ± 4.80	20±5.33	-	-	-	-	-	75 ±4.45
Range	68 – 100	35 – 340	22 – 260	30 – 190	20 – 150	-	-	-	-	-	70 – 95
Iron (µmol/l)											
Mean ± SD n = 30	8.95±1.80	4.00* ± 0.11	5.40* ± 0.30	6.30*±1.80	7.32 ± 1.91	-	-	-	-	-	12.30 ±2.33
Range	2.25 – 40.5	1.01– 13.00	1.80 – 16.00	2.70 – 12.50	2.90 – 1.40	-	-	-	-	-	3.50 – 35.50
TIBC (µmol/l)											
Mean ± SD n = 30	60 ± 5.00	53* ±3.60	43*±3.11	47* ±4.18	45 ±1.22	-	-	-	-	-	61±5.23
Range	41 – 80	38 - 67	36 – 62	27 – 59	25 - 58	-	-	-	-	-	43 - 79

SD = Standard Deviation * $p < 0.01$

reactant' was also measured for comparison.

MATERIALS AND METHODS

Subjects

All the subjects used for the present study were admitted to the Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria except the normal women.

The subjects were divided into three groups with thirty (30) patients in each group. Group 1 was made up of thirty (30) normal women with aged range of 30 - 65 years. These women were not suffering from any dis-ease or taking any medication. Group 2 were thirty (30) women involved in motor accidents who were admitted to the Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Nigeria for various suture ope-rations and they represent groups with minor surgery. Their age ranged from 30 - 65 years with the mean age of 45.5 years. The average blood loss was estimated as 200 ml, there was no post-operative transfusion and no patient had any post-operative complications. Group 3 comprises of thirty (30) patients all pregnant women in their third trimesters that were also admitted to the Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife, Nigeria for ceaserean operation. The mean age of the group was 40.8 years with the range of 20 - 45 years.

Blood samples were obtained pre-operatively, on the first post-operative day and thereafter at two-day intervals for twenty one (21) days and at fifth week.

Methods

Serum ferritin was measured by an ELISA method (Anderson and Kelly, 1981). Iron and TIBC were deter-mined by the method approved by theInternationa0l Committee on Standardization in Haematology (ICSH as described by (Tietz, 1986) while APR was estimated using radioimmuno assay (Claus et al., 1996).

Statistical analysis

All experiments were carried out in triplicate. Results were expressed as mean ± standard deviation and the data were analysed by Students' t-test to verify the statistical significance at $p < 0.01$.

RESULTS

There were increases in the serum ferritin and CRP with sharp increase in days 3 - 4 (average-ly I0-fold increase) and days 1 - 2 (averagely 18 fold increases) respectively in group 1 patients (Table 1). There after concentration of both ferritin and CRP decreased and returned to pre-operative levels at 5 weeks follow-up. So also, iron and TIBC levels were found to be lowest on days 1 - and days 3 - 4 respectively.

Group 2 patients showed peaks of serum ferritin and CRP concentrations at 3 - 4 days post operative (average 8 fold increase and average twenty fold increase) respectively.

Thereafter, levels of serum ferritin and CRP remained elevated. Serum ferritin concentrations

Table 2. Pre and post-operative ferritin, acute phase reactant, iron and total iron binding capacity in pregnant women with major surgery.

Parameter	Pre-operative	Day 1-2	Day 3-4	Day 5-6	Day 7-8	Day 9-10	Day 11-13	Day 14-17	Day 18-20	Day 21+	5 weeks
Ferritin (µg/ml)											
Mean ± SD n = 30	105±10.55	408 ± 20.40	430* ±35.11	382* ± 20.48	450* ± 30.12	470 ± 20.22	500 ±30.80	520 ±38.00	530 ±30.22	460±20.48	-
Range	60 – 1890	53 – 3552	56 – 3000	59 – 2400	120 – 1700	140 – 1837	250 – 1162	234 – 1511	210 – 1110	190 – 850	-
APR (mg/l)											
Mean ± SD n = 30	80 ± 10.33	165*±15.80	155* ±20.22	120* ±11.00	100 ± 20.22	59* ± 15.00	49 ±10.28	630 ± 30.18	20 ±1.23	15 ± 0.99	-
Range	2 – 170	15 – 2197	35 – 700	8 –1934	1 – 2300	2 – 1450	1 –3227	1 - 3660	1 – 2290	2 – 1800	-
Iron (µmol/l)											
Mean ± SD n = 30	8.90 ±2.44	5.01* ± 1.85	5.00* ± 1.22	6.70* ± 2.55	7.00* ±0.80	6.80* ±2.11	7.80 ± 1.80	7.70 ± 1.99	6.80 ± 1.45	6.30 ±1.80	-
Range	4.00-25.00	2.0012.50	1.90 – 12.60	2.50 – 14.20	1.90 – 20.00	3.80 – 9.80	2.50 – 22.00	2.40 – 19.00	3.91 – 9.6	2.25 – 20.8	-
TIBC (µmol/l)											
Mean ± SD n = 30	57±1.11	44* ± 2.11	43* ± 3.00	40* ±5.22	46* ± 6.11	42* ± 5.88	38* ± 4.57	45 ± 3.00	44±3.09	-	-
Range	36 - 75	30 - 55	15 - 70	20 - 60	25 - 70	25 - 58	25 - 56	20 - 58	20 - 58	-	-

SD = Standard Deviation * p<0.01

were significantly higher in 51 - 65year old group than in younger subjects. There were highly significant differences (p > 0.001) in the levels of all the parameters studied in pre and post operative states

DISCUSSION

The results obtained from this study have shown that patients undergoing minor surgery had a significant low level of pre-operative serum ferritin relative to their age matched healthy women. This implies that, there is depletion of body iron stores in these patients as majority of them had menorrhagia. The serum CRP levels in patients undergoing caesarean operation (Table 2) which is a major operation (group 2) were found to be significantly (p < 0.01) higher than what is obtained for patients with minor operation, although both showed a decrease level of iron and TIBC.

There was a continued marked increase in serum ferritin and CRP in group 2 patients (Table 2). This might be a reflection of high incidence of post-operative complications that may occur in these patients. This observation was in agreement with the reports of Bartels et al., (1998) and Elin et al., (2007) that major surgical procedures and inflammatory diseases result in large increases in serum ferritin and CRP concentration.

A two fold rise in serum ferritin levels which peaked on the third post- operative day and not significantly elevated by day 7 in minor surgical procedure of arthroscopy has been reported (Mohammed et al., 2005). Results obtained from the present study show much higher rises following more extensive surgical procedures. This shows that the magnitude of the elevation in serum ferritin levels depends on the degree of associated stress. This may be due to length of post-operative stay, length of anesthesia and likelihood of complications.

It can be concluded that there is an acute phase response of serum ferritin levels following major surgery.

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