



Analysis of Drain Fluid for the Presence of Procalcitonin and C-Reactive Protein as Early Markers of Intestinal Anastomotic Leakage

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Abstract

Introduction

Resection and anastomosis is a key procedure employed in the surgical management of various intestinal diseases. Though a complicated procedure with a steep learning curve, it can be a lifesaving procedure for many and can negate the need for a stoma which can cause considerable decrease in the quality of life as well as considerable morbidity and mortality.

Resection and anastomosis can be defined as the restoration of two previously distant segments of intestinal after the removal of the intervening pathological segment.

Despite being a commonplace procedure, intestinal anastomotic leak is one of the most dreaded postoperative complications of intestinal anastomosis.

Incidence of anastomotic leak in literature is found to be about 2-5% with the mortality rate being as high as 10-15%. Anastomotic leak is seen most commonly on the third to sixth postoperative day.

C-reactive protein is an acute phase reactant produced by the liver hepatocytes in response to IL-6 which is in turn produced by macrophages in response to bacteria and other inflammatory markers. CRP shows a rapid and pronounced rise of serum concentration in response to infection and inflammation.

Procalcitonin (PCT) is produced from two sources in the body. The first is the well-known production of thyroid

procalcitonin which acts on the Endocrine cells which is converted into calcitonin, which is released into the blood stream from which it has its various effects. The second source and that which is important to this study is the inflammatory procalcitonin which is produced from the adipocytes and is present in the fluid around the anastomosis. The measurement of this biomarker can be a rapid and objective diagnosis of anastomotic leak.

Objectives

To evaluate procalcitonin and C-Reactive protein as reliable and sensitive indicators of intestinal anastomotic leak in abdominal drain fluid.

Materials and Methods

All eligible patients admitted in a tertiary care hospital in Karnataka during the study period from December 2023 to May 2024.

This study was conducted from December 2023 to May 2024 as a prospective observational study with a sample size of 48 patients who underwent intestinal resection and anastomosis without the creation of a proximal stoma. The various surgeries were performed by different surgeons for a variety of pathologies. Both elective and emergency procedures were included in the study.

Serial estimations of C-Reactive Protein and Procalcitonin were done on POD - 3, POD - 5 and POD - 7 for each patient and the results were carefully recorded. All the investigations were sent to the same laboratory and the procedure of the tests was maintained to be the same in every way possible.

Sample Size

As per the records of a tertiary care hospital in Ballari, with 95% confidence level, anticipated prevalence of AL among all laparotomy patients as 20% and desired

precision as +/- 10%. The minimum sample size is 48 with finite population correction.

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean +/- standard deviation were used. Chi-square test was used for association between the two variables.

Sensitivity and specificity were calculated to check relative efficiency.

If the p-value was <0.05, then the results were considered to be statistically significant. Otherwise, it was considered to not be statistically significant. Data was analyzed using SPSS software v.23.0. and Microsoft office 2007.

Inclusion Criteria

All patients who underwent elective and emergency intestinal resection and anastomosis.

Exclusion Criteria

Patients who underwent exclusively ileostomies or colostomies were excluded.

Patients who underwent resection and anastomosis with the protection of a proximal stoma.

History of patients were noted and detailed examination of the patient was done.

Patients who underwent small intestinal anastomosis, colonic anastomosis, sigmoid resection, high anterior resection, low anterior resection and subtotal colectomy with ileorectal anastomosis were included.

All patients received proper active antibiotic prophylaxis and intra abdominal drain postoperatively and antibiotic therapy as per need. To obtain the drain fluid, a drain was kept at the anastomotic site and was left in place during the first 7 postoperative days.

Drain fluid reservoirs were emptied 2 times a day within a 12 hours interval, respecting the rules of sterility. The evening collection was disposed off, the morning

collection was sent for the analysis of CRP and PCT on the 3, 5 and 7 postoperative days.

Instrument used was mini VIDAS BLU for testing the samples. Technique - CLIA (Chemiluminescence Immunofluorescent Assay)

Table 1: The mean C- Reactive protein according to anastomotic leak is tabulated as follows:

| C - Reactive Protein | Anastomotic Leak | | | | P value |
|----------------------|------------------|------|------|------|---------|
| | YES | | NO | | |
| | Mean | SD | Mean | SD | |
| POD - 3 | 2.66 | 2.77 | 1.08 | 0.40 | 0.001 |
| POD - 5 | 2.84 | 2.77 | 0.84 | 0.48 | <0.001 |
| POD - 7 | 2.83 | 3.06 | 0.59 | 0.31 | <0.001 |

Cases with no anastomotic leak, mean CRP levels at POD 3,5,7 were 1.08, 0.84 and 0.59 whereas mean value of CRP in anastomotic leak cases were higher i.e 2.66, 2.84 and 2.83 on POD - 3,5 and 7 respectively.

Table 2: The diagnostic efficacy of C-Reactive Protein was tabulated as follows:

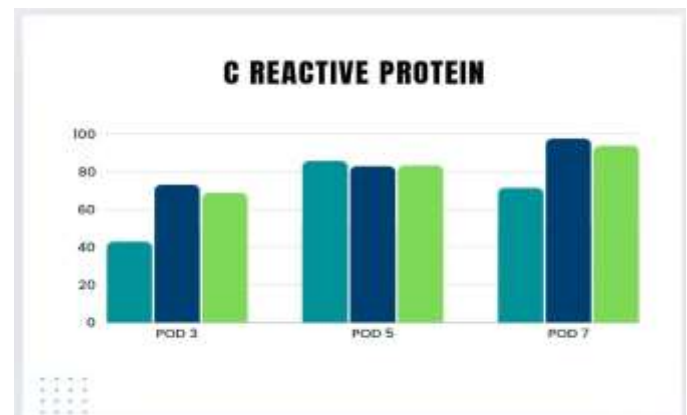
| C-Reactive Protein | POD - 3 | POD - 5 | POD - 7 |
|--------------------|---------|---------|---------|
| Sensitivity | 42.86% | 85.71% | 71.43% |
| Specificity | 73.17% | 82.93% | 97.56% |
| PPV | 21.43% | 46.15% | 83.33% |
| NPV | 88.24% | 97.14% | 95.24% |
| Accuracy | 68.75% | 83.33% | 93.75% |

Diagnostic efficacy of C-reactive protein is represented in a graphical form as follows:

Results

48 patients with intestinal anastomosis were observed with the estimation of procalcitonin and C-reactive Protein in drain fluid on POD - 3, POD - 5 and POD - 7.

Graph 1:



SENSITIVITY SPECIFICITY ACCURACY

Sensitivity is the maximum on POD - 5 (85.71%)
 Specificity is maximum on POD - 7 (97.56%)
 Accuracy is maximum on POD - 7 (93.75%)
 Sensitivity and specificity of C-Reactive Protein increases with time with sensitivity on POD - 5 being 85.71% and 97.56% on POD 7.

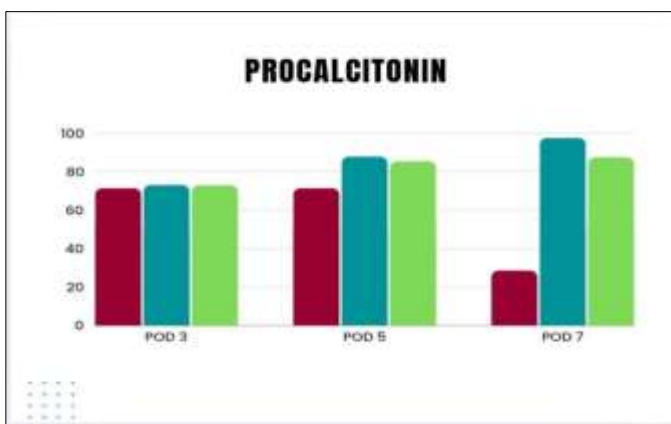
Table 3: Mean Procalcitonin according to anastomotic leak is tabulated as following:

| Procalcitonin | Anastomotic Leak | | | | P-value |
|---------------|------------------|------|------|------|---------|
| | YES | | NO | | |
| | Mean | SD | Mean | SD | |
| POD - 3 | 3.19 | 2.95 | 1.17 | 0.61 | <0.001 |
| POD - 5 | 1.62 | 0.65 | 0.98 | 0.61 | 0.015 |
| POD - 7 | 1.07 | 0.79 | 0.67 | 0.41 | 0.046 |

In the cases with no anastomotic leak mean Procalcitonin levels at POD - 3,5 and 7 were found to be 1.17, 0.98 and 0.67 respectively whereas mean value of procalcitonin in patients with anastomotic leak were higher i.e 3.19, 1.62 and 1.07 respectively on POD - 3,5 and 7 with significant p-value.

Diagnostic efficacy of Procalcitonin is represented in a graphical form:

Graph 2:



SENSITIVITY SPECIFICITY ACCURACY
 It was found that, sensitivity of procalcitonin is highest and equal to on POD - 3 and POD - 5 i.e 71.43% and low on POD - 7 i.e 28.57% and specificity of

procalcitonin is increases with time and is maximum on POD - 7 i.e 97.56%.

Conclusion

Evaluation of C-Reactive Protein and Procalcitonin in drain fluid on POD 3,5 and 7 were found to be associated with higher than normal values in patients suffering from anastomotic leak.

Sensitivity and specificity of C-Reactive Protein increases with time with sensitivity on POD - 5 being 85.71% and 97.56% on POD 7.

Positive predictive value of CRP is 83.33% on POD - 7. Negative predictive value of CRP is 95.24% on POD - 7. Accuracy of CRP is 93.75% on POD - 7.

Sensitivity of Procalcitonin is highest on both POD 3 and POD 5 i.e 71.43% and low on POD 7 i.e 28.57% and specificity of Procalcitonin increases with time and is the maximum on POD - 7 of 97.56%.

Positive predictive value of Procalcitonin is 66.67% on POD - 7. Negative predictive value of Procalcitonin is 94.74% on POD - 5. Accuracy of Procalcitonin is 87.50% on POD - 7.

CRP and Procalcitonin were found to be reproducible and reliable indicators for the early detection of anastomotic leak as compared to conventional methods of diagnosis.

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