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EFFECT OF BARIUM SULPHATE AND GASTROGRAFIN DYE ON WOUND HEALING IN THE GASTRO-INTESTINAL TRACT OF ALBINO RAT - AN EXPERIMENTAL STUDY

Medical Science

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ABSTRACT

Surgeons concern for complications and outcomes of gastrointestinal tract surgery, especially in patients who has received intraluminal contrast media before surgery. As of now in most of the diagnostic radiology, non ionic contrast agents have replaced barium sulphate as contrast medium of choice but still barium sulphate is being used as contrast medium at primary and secondary care centers. Therefore we conducted this experimental study to compare the effect of barium sulphate and gastrografin dye on intraluminal wound healing in the gastrointestinal tract of albino rats particularly in context of macroscopic and histological findings.

Materials and Methods: This experimental study with prior approval of animal ethics committee was conducted in the department of general surgery at NSCB Medical College, Jabalpur, India. 45 Albino Rats were divided into 3 study groups (n= 15) and as per fixed protocol, linear incision was made on the anti mesenteric border of colon. O.5 ml of NS, Barium sulphate and gastrografin was instilled intraluminaly in Group A, B and C subsequently. Post instillation, colon was repaired transeversally with full thickness vicryl 6-0 sutures. Half of the rats from each group were sacrificed on POD 7 and rest on POD 21. After macroscopic examination, repaired area of bowel was taken out for histological assessment and the HPR were graded as per 'tissue morphological score' Shackleton KL et al [1].

Results: 50 % of survived rats in each group were sacrificed and analyzed as per tissue morphology score on POD 7. The tissue morphological score is based on neutrophillic infiltration, lymphocytic infiltration, collagen formation, granuloma formation and mucosal continuity. Mucosal continuity is a major determinant of wound healing and the best mucosal continuity was noted in-group C. About 90% cases of gastrografin dye group showed good mucosal continuity in comparison to 60 % cases of barium group. On POD 21, the findings of all the three groups were similar.

Conclusion: Gastrografin (Non Ionic contrast) group showed good tissue healing in early phases with less complications. It is a better contrast medium as compared to barium sulphate. On the other hand, Barium sulphate resulted in more complications like adhesion and pus pocket formation.

KEYWORDS

Surgeons often express their concern regarding complications and outcomes of gastrointestinal tract surgery, especially in patients who have received intraluminal contrast media before surgery. As of now in most of the diagnostic radiology, non ionic contrast agents have replaced barium sulphate as contrast medium of choice but still barium sulphate is being used as contrast medium at primary and secondary care centers. Barium sulphate is in use because of its low cost and less expertise requirement but some of its properties create concerns to the surgeons who are planning a immediate surgical procedure. Barium sulphate causes deleterious effect on peritoneal cavity because of its non-absorbable nature and residual particulate. Barium sulphate is commonly used for conditions like swallowing dysfunction, dysphagia, hiatal hernia etc. There are well documented deleterious effects due to contrast leakage in the peritoneal cavity in association with fecal contamination as well [1,2,3,] The available data on any untoward effect of barium sulphate or gastrografin on intraluminal wound healing is still not sufficient for us to arrive at a concrete and level I conclusion [4]. Considering these concerns we conducted this experimental study to compare the effect of barium sulphate and gastrografin dye on intraluminal wound healing in the gastrointestinal tract of albino rats particularly in context of macroscopic and histological findings.

MATERIALS AND METHODS:

This experimental study was conducted in the experimental surgery unit of the department of surgery at NSCB Medical College, Jabalpur (M. P.) India. Approval of animal ethics committee was taken before commencement of this study. 45 Albino Rats with mean weight of 320 g were enrolled and divided into 3 study groups A, B and C. Each group was having 15 Albino rats. Each rat had gone under exploratory laparotomy with all aseptic precautions. As per the fixed protocol, a linear incision (5mm) was made on anti-mesenteric border of colon, 2 cm distal to the caecum. All incisions were transmural exposing the lumen of the colon. In group A rats, 0.5 ml of normal saline was instilled in colonic lumen. Similarly barium sulfate in group B and Gastrografin dye in group C was instilled ensuring no peritoneal spillage [Fig-1]. After instillation, Colonic incision was repaired transversely with full thickness vicryl 6-0; round body needle and thereafter abdominal closure was done. Post operatively rats were kept nil orally for 36 hours and subcutaneous injections of saline and antibiotics were given. Half of the animals from each group were sacrificed on 7th POD. Autopsies with thorough macroscopic examination were performed and repaired area of colon was dissected out for histopathological assessment. Later rests of the rats from each group were sacrificed on POD 21. Similar protocol was followed for assessment of delayed healing. Rats who died before the stipulated time were excluded from study and assessed for the early cause of death. All sacrificed animals were evaluated macroscopically on autopsy and anastomotic segment was harvested for histological assessment of healing.

Macroscopic examination:

All sacrificed animals were examined macroscopically for evidence of peritonitis, adhesion formation, anastomotic leaks (if any), and pus pockets.

Histological evaluation:

All sacrificed animals were evaluated histologically for (a) Neutrophillic infiltration, (b) Lymphocytic infiltration (c) Collagen deposition (d) Granuloma formation (e) Mucosal continuity. On the basis of these histopathological findings the rats were graded into various groups according to the grading of ***'Tissue morphological score'*** Shackleton KL etal [4].Table-1

Results were compared and statistical analysis was done.

OBSERVATION AND RESULTS:

The experimental design of our study was tailored to evaluatethe acute and delayed influence of barium sulfate and gastrografin dye on wound healing in the gastro intestinal tract of albino rats. All animals had weight gain and stayed healthy throughout the duration of study. In post op period, 6,4 & 5 rats in groups A, B, & C were died respectively.

Rats who died before stipulated time (n=15) were excluded from the study.

Macroscopic evaluation

Intra peritoneal adhesions and pus pockets formations were noticed after autopsy. The adhesion rate was higher in barium group than gastrografin and control group, which was 60% with barium, 33.3% with gastrografin and 20.0% in control group. Above findings were suggestive of fewer adhesions with gastrografin although this data is not statistically significant. Pus pockets were noted in barium sulphate group only. This complication was found in 13.3% rats of group B (barium). Data was not statistically significant when compared with each other.

Microscopic assessment of colonic incision healing was done and as per ***tissue morphology score,*** they were divided into multiple grades. This score is based on neutrophillic infiltration, lymphocytic infiltration, collagen formation, granuloma formation and mucosal continuity [4]. Tissue morphology score assessment was done in all rats sacrificed on POD 7 and POD 21.

POD 7 Histopathological analysis

50 % of survived rats in each group were sacrificed and analyzed on POD 7. Microscopic examination of their anastomotic/repaired colonic site was done and which showed significant neutrophilic infiltration at anastomotic sites in all three groups. Lymphocytic infiltration was seen mostly in group C (gastrografin), a few lymphocytes were also seen in group B and A. Deposition of fibro-collagenous fibers at the site of anastomosis was also seen which showed the presence of healing but maximum collagen deposition was noted in group C & A. In group B, few free barium particles and some in phagocytic cells were also noted at the site of anastomosis. One or two giant cells were also noted in group C.

Mucosal continuity is a major determinant of wound healing and the best mucosal continuity was noted in group C. About 90% cases of gastrografin dye group showed good mucosal continuity. Similarly mucosal continuity was noted in about 75% cases of control (group A) and 60 % cases of barium group.[fig-2]

In control group the histopathological score was grade 1(very good) in maximum rats while in Group B (barium) maximum rats (n=4) had Grade 3(fair) histological score. Similarly most of the rats (50%) in group C (Gastrograffin) showed the histology score of Grade 1(very good) (Fig-3)

POD 21 Histopathological analyses

On POD 21, the findings in all three groups were almost similar. There was good mucosal continuity in all the three groups (Grade 1). There was no neutrophilic infiltration in any group. Few lymphocytes were present in all the three groups. Collagen fiber deposition was similar in all the three groups. We noticed the deposition of barium particles in group B. Overall we found good anastomotic healing in all the three groups at 3 weeks.

Non parametric test Kruskal-Wallis Test was applied for comparison of these grades in studied groups and it was observed that the group C had significantly lower mean rank of grades (11.00) while the group A and group B showed 14.50 and 20.41 respectively ($P<0.05$). The finding of the median test suggests that Group C had a very high proportion of cases in grades lower than the median (median=2). Only 1 case was seen with upper median class while in group B and C these proportions were at higher side of median and the findings were considerably significant.

Histopathological grading of Group A, B, C showed better early healing (on 7th day) in group C as compared to group B and this difference was found statistically significant. On comparing our data of 21st day with the grading score of reference on 4 weeks i.e. grade 2.2 (fair), in our study all the three groups showed the histological score of Grade 1(very good).

DISCUSSION

Emphasis on peritonitis related to free spillage of barium sulfate in the peritoneal cavity in the medical literature caused surgeons to become apprehensive and concerned about the effect of barium on wound healing. The debate between surgeons and radiologists frequently revolves around the use of barium sulfate as a positive-contrast agent in patients examined for possible small-bowel obstruction, stricture, any small suspicious leak who might undergo surgery. This debate is fostered by surgeons' concerns about potential toxic reactions if intraluminal barium sulfate spills into the peritoneal cavity and by the implied effect on wound healing after incisions are made in the tubular viscera. We try to find out the effect of barium sulphate and gastrografin on intraluminal wound healing in the gastrointestinal tract of albino rats in context of macroscopic and histological assessment.

Overall mortality was similar in all three groups. Although barium had more deleterious effect on mortality as compared to water contrast media when instilled intraperitonealy as stated by Hernanz – schulman M et al [5] the overall mortality is much higher in our study as compared to no mortality in the study of Shackleton KL etal [4]

The adhesion rates were higher in group B i.e. 60% with barium as compared to 33.3% with gastrografin and 20.0% with control group although there was minimal peritoneal contamination. In the study by Shackleton KL etal[4], adhesions were found as a macroscopic finding and were more in barium used group as compared to control although the data was not statistically significant. Our study showed the comparable data although it is insignificant. Pus pockets were present only in barium group of our study. This complication was found in 13.3% rats of group B (barium) as compared to other study [4], which had similar results. No pus pocket was seen with gastrografin group and control group rats.

In most of the rats of control group the histopathological score was grade 1(very good) while in Group B maximum rats (n=4) had Grade 3(fair) histological score. These data are comparable with Shackleton KL et al [4] as it showed 3.5 score with barium instillation. Similarly most of the rats (50%) in group C showed the histology score of Grade 1(very good). These data showed differences on comparison [4] as it showed 3.5 score with barium instillation. On comparing the histological scores of the gastrografin instilled rats of our study with the barium instilled rats of Shackleton et al[4], we found that there was a significant difference. This data showed that there was better and early healing in gastrografin instilled rats.(Fig-4)

Najjar et al [6] documented the minimal deleterious effect of barium sulfate by using the dog as an experimental animal. They describe an inflammatory response, especially by neutrophilic granulocytes, when tissue was exposed to barium sulfate. After the barium sulfate was phagocytosed by macrophages, the inflammatory response decreased dramatically as in our study also after initial response inflammation subsided on 21st day.

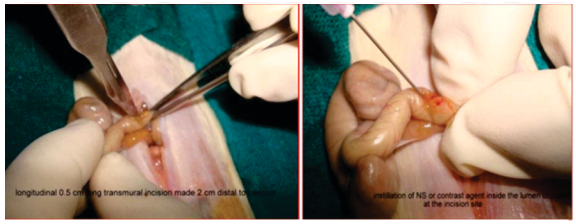
To our knowledge, the effects of barium sulfate on wound healing have been documented in only one article in the literature; we could find no clinical documentation on literature search in PubMed and Google search engine about trans-mural wound healing is compromised by the presence of barium sulfate.

CONCLUSION:

Gastrografin showed good tissue healing in early phases with fewer complications. It is a better contrast medium as compared to barium sulphate and can be used for assessment of site of perforation, anastomosis patency etc. On the other hand, Barium sulphate resulted in more complications like adhesions and pus pocket formation although there was no difference in delayed phase of wound healing with both the contrast media.

We can conclude that gastrografin is owing to good tissue healing in early phase and is a good contrast media as compared to barium sulphate. It can be used for assessment of site of perforation, anastomosis patency, assessment of anastomosis of tracheo-oesophageal fistula etc.

Fig - 1



Operative Picture

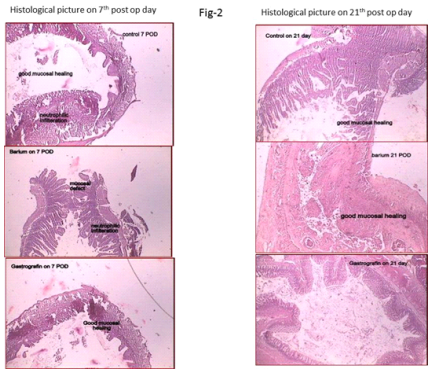


Fig-2

Figure-3

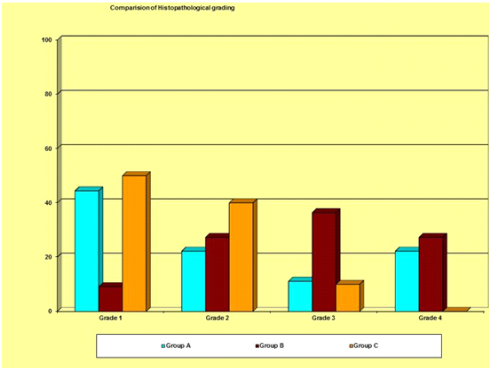
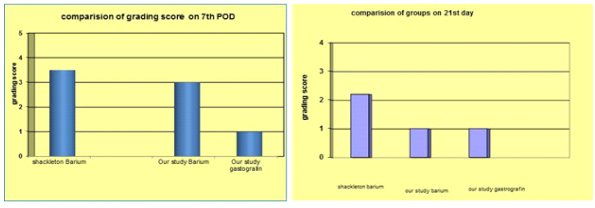


Table 1:-Tissue Morphology Score [4]

Grade	Criteria
1	Normal tissue, good mucosal continuity, no cellular infiltration and no abscess formation.
2	Good mucosal continuity, No neutrophil and/or 0-50 lymphocyte per high power field on the serosal surface or within incision and/ or vascularized fibroblastic proliferation around barium sulfate crystals and/or focal aggregation of giant cells in reaction to a foreign body and/or complete granuloma formation
3	Good mucosal continuity, 0-50 neutrophils and 0-50 lymphocytes per high-power field on the serosal surface or within the incision and/or fibroblastic proliferation and/or cellular infiltration into the submucosa and focal necrosis, and/or incomplete granuloma formation
4	Poor mucosal continuity , 100-200 neutrophils and /or few lymphocytes per high-power field on the serosal surface or within the incision and/or fibroblastic proliferation , no granuloma formation
5	No mucosal continuity ,>200 neutrophils and /or few lymphocytes per high-power field on the serosal surface or within the incision and/or fibroblastic proliferation , no granuloma formation

Fig-4



Comparison of average grading scores

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