International Journal of Biomedical And Advance Research

ISSN: 2229-3809 (Online)
Journal DOI:10.7439/ijbar
CODEN:IJBABN

Review Article

Non operative management of perforated peptic ulcer an algorithm approach

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Abstract

Ulcer disease remains the most common cause of gastroduodenal perforation, with an incidence between 2% and 10% in patients with ulcers. With the advent of proton pump inhibitors(PPI) the surgery for perforated peptic ulcer has changed from perforation closure with definitive acid reduction surgeries to simple omental patch. The trend of minimal is better holds good. With advances in laparoscopic surgery and its application in emergency abdominal conditions it has been shown feasible for management of perforated peptic ulcer. Though there have been various studies showing successful nonoperative management of perforated peptic ulcer, Conservative treatment has not gained widespread acceptance as an alternative approach to surgery. The reason being lack of uniform selection criteria and management guidelines for conservative management. This review article aims at introducing an algorithm approach towards successful non operative management of perforated peptic ulcer.

Keywords: Perforated peptic ulcer, non operative management, conservative management, contrast gastroduodenogram, PULP score

1. Introduction

Ulcer disease remains the most common cause of gastroduodenal perforation, with an incidence between 2% and 10% in patients with ulcers.[1] Despite dramatic improvements in peptic ulcer management in the last two decades (new potent anti-secretory drugs as well as Helicobacter pylori eradication)[2], the frequency of perforated gastroduodenal ulcer has remained stable or even increased[3]. This may be due to an increase in prescription of aspirin and/or non-steroidal anti-inflammatory drugs, especially in older subjects.[4]

With the advent of proton pump inhibitors (PPI) the surgery for perforated peptic ulcer has changed from perforation closure with definitive acid reduction surgeries to simple omental patch. The trend of minimal is better holds good. With advances in laparoscopic surgery and its application in emergency abdominal conditions it has been shown feasible for management of perforated peptic ulcer. Though there have been various studies showing successful non-operative management of perforated peptic ulcer, Conservative treatment has not gained widespread acceptance as an alternative approach to surgery. The reason being lack of uniform selection criteria and management guidelines for conservative management. This review article aims at introducing an algorithm approach towards successful non operative management of perforated peptic ulcer.

The earliest report of the recovery of a perforated peptic ulcer without a surgical treatment was recorded in I870 by Redwood[5]. Study of the natural history of gastroduodenal ulcer perforation during the first half of the 20th century[6], has shown that, after perforation occurs, it is promptly sealed by adjacent organs. A fibrin clot appears quickly on and around

the perforation. This is the start of a definitive closure which associates adhesion between perforated and adjacent organs and healing of the digestive tract wall. According to Donovan, this phenomenon of self-healing is efficient in at least 50% of patients[7] .Indeed, it is a common experience for surgeons who operate for perforated ulcer to observe that they first have to mobilize the perforation from adjacent organs before being able to suture it. Moreover, in the event of gastroduodenal perforation the peritoneal cavity usually remains sterile for 12 hours, the bacterial load being low in the upper gastrointestinal tract. However, some patients experience peritonitis as well as septic complications. This can be due to continuous fluid extravasation, stronger bacterial load of the proximal digestive tract and/or poor healing ability impairing spontaneous sealing of the perforation. In 1935, Wangensteen noted that ulcers were able to self seal and he reported on seven cases which were treated without surgery**.**[8] In 1946 Taylor presented the first series of successfully outcome of conservatively treated patients with PPU with a mortality rate of 5.2%**.** [9]

Conservative treatment has not gained widespread acceptance as an alternative approach to surgery for perforated gastroduodenal ulcer. It was developed at a time when surgical closure was associated with high mortality[10]. As surgical and anaesthetic patient care have improved, the morbidity and mortality of emergency surgical ulcer closure have markedly decreased, so that mortality figures are currently in the range of 3–9%[11]**.** Though studies have shown similar mortality with conservative management and open surgery of around 5-8%[12] there has been a wide variation in failure rates (13–46%[13]. Failure of conservative treatment is generally defined as development of septic shock, multiple organ failure or intra-abdominal abscess . Conservative treatment failure exposes patients to the risk of delayed surgical closure with mortality rates between 3 and 50%.[14]

Nevertheless, none of these studies on conservative treatment was performed exclusively in patients treated with PPI and/or benefiting from Helicobacter pylori (HP) eradication. Also there were no uniform selection criteria and management guidelines which led to varied results of conservative management with high failure rates.

2. Need for Risk stratification

Boey *et al*[15] in 1987 formed a risk assessment score for perforated peptic ulcer based on major medical illness, preoperative shock and long standing perforation. The mortality rate increased progressively with increasing numbers of risk factors: 0%, 10%, 45.5%, and 100% in patients with none, one, two, and all three risk factors, respectively**.** Irvin[16] attempted to validate the Boey Score on acohort of 265 consecutive patients who had operations for perforated peptic ulcer. 176 of these were 70 years or above, of which two-thirds were female. All 5 patients with three Boey Score risk factors died. At a cut-off of two risk factors the accuracy was less good, with 13 patients surviving from 29 (false positive rate 45%). With improvement in surgical and anesthetic technique the mortality rates have have reduced to about 3-8%. High false positivity rates of Boey's score is no longer acceptable. In a study by David *et al*[17] it was shown that Boey score, the ASA score, the APACHE II score, and the sepsis score predict mortality poorly in patients with Perforated peptic ulcer. Recently peptic ulcer perforation score(PULP)[18] has been evaluated for accurate predictor of mortality. Though these scoring systems can accurately predict outcome of surgical treatment there is no scoring system for predictor of outcome of conservative management. There is a need to develop a selection criteria for nonoperative management of perforated peptic ulcer.

Study by Smita[19] multivariate analysis of factors affecting morbidity following perforated peptic ulcer showed that preoperative shock, concomitant medical illness and abdominal distension showed statistical significance. Similarly in a study by Myung Kim *et al*[20] high ASA score and preoperative shock showed statistical significance. It is interesting to note neither age nor duration of perforation were significantly associated with postoperative morbidity.

3. Selection criteria

The initial clinical examination is unreliable in predicting which patients with perforations and peritonitis have sealed perforations. Water soluble contrast medium gastroduodenogram has been utilized to identify the presence or absence of active leakage of perforated ulcers. Approximately 40% of perforated duodenal ulcers examined using this method were found to be sealed at the time of examination. Ulcer releaking occurred in only two of 109 patients treated nonoperatively[21]. A study by Berne and Donovan[22] reported 35 patients had perforated duodenal ulcers with gatroduodenogram documented sealed perforations. The mortality rate of these 35 patients treated nonoperatively was 3%; while the mortality rate for 259 patients treated operatively during the same period was 6.2%. Berne and Donovan concluded that perforated duodenal ulcers can be safely treated nonoperat ively when the gastroduodenogram documents show the ulcer is self-sealing. Occasionally, the extraluminal contrast may be localized to the area adjacent to the perforation—a collar-button leak. The process of self-sealing is a dynamic one and is believed that a collar-button leak represents a late stage in this process. A

second gastroduodenogram shortly after demonstration of such a restricted spillage may reveal a complete seal[23].

Nonoperative treatment of peptic ulcer has been shown in a randomized trial[24] to be safe and effective in selected patients: those under 70 years old who were hemodynamically stable, been perforated for less than 24 hours, and could be carefully monitored for any evidence of deterioration. The overall mortality rates in the two groups (surgery versus non-surgery) were similar (approximately 5%), and did not differ significantly in the morbidity rates (40% vs 50%). Songne *et al*[25] in 2004 reported his prospective study in 82 patients on non-operative treatment for perforated peptic ulcer and concluded that more than 50% of patients with perforated peptic ulcer responded to conservative treatment without surgery and that the association of few criteria (size of pneumoperitoneum greater than size of the first lumbar vertebra, heart beat over 94, pain at digital rectal exam and age over 59) required emergency surgery.

Pascal *et al*[26] found that only preoperative shock was predictor for failure of conservative treatment and found no association with age of patient but this was a small study in patient unfit for surgery.In a study by Hanumanthappa *et al*[27] Showed 82 % success rate of conservative treatment and neither age or duration of perforation was significantly associated with failure rate. Selection criteria for conservative management are age <70 yrs, hemodynamic stability, and demonstration of a sealed off perforation on contrast gastroduodenogram.

4. Conservative management

Elements involved in the nonsurgical treatment of a patient with a self-sealed perforation include gastric drainage, antibiotics, and early administration of an proton-pump inhibitor. Absolutely nothing is given by mouth[28],Careful positioning of the nasogastric tube in the distal part of the greater curvature and nasogastric suction are the most important elements in the conservative treatment which keeps the stomach empty, allowing the sealing of the perforation to take place ,. Strict input and output charts should be maintained. Intravenous antibiotics (cefazoline 1g QID and metronidazole 400mg TID) and proton pump inhibitors should also be given. Following the initial correction of hypovolemia, fluid requirements should barely exceed that needed for maintenance. Fluid sequestration into the peritoneal cavity (third spacing) will cease. It is crucial to monitor the pulse rate, the BP and the temperature. The abdomen should be examined frequently for tenderness, rigidity and bowel sounds. The rigidity regresses rapidly, disappearing from below upwards, and it is usually gone within 24 to 48 hours .

With widespread use of antimicrobials for conservative treatment there has been reports of increased incidence of fungal peritonitis. Antimicrobial therapy causes alteration of faecal flora and transmigration of organisms into the peritoneal cavity. Most commonly candida species, fungal peritonitis is associated with high mortality rate between 14-25% [29] so it is advisable to add antifungal agents to patients who are being managed conservatively with long periods of antibiotic therapy. There have been many reports of CRP levels being a strong of predictor of mortality [30] for peritonitis and as a general marker of an unfavorable course in conservative management[31]. Also there have been reports of serial CRP level estimation to monitor response to antibiotic therapy. [32]

In a study by Pascal *et al*[26] conservative management comparing H2- blockers and PPI showed that Morbidity was 73% versus 16% (p = 0.023) for H2-blocker and PPI groups respectively, of the patients presenting general complications in the H2-blocker group, all were classified grade IV, while in the PPI group one was grade II and two were grade IV. Hospital mortality rates were 64% vs 11% (p = 0.008) for the H2-blocker and PPI groups. Therefore PPI are better at acid suppression and enhanced healing.

Misoprostol has been used in treatment of NSAID ulcer it has been shown that 800 ug/day was superior to 400 ug/day for the prevention of endoscopic gastric ulcers [33]. Misoprostol caused diarrhoea at all doses, although significantly more at 800 ug/day than 400 ug/day . Misoprostol also reduced the risk of clinical ulcer complications. Thus routine use of Misoprostol 800ug/day in three divided doses can be used in faster healing of ulcer during conservative management of perforated peptic ulcer.

It has recently been shown that NSAID use is associated with a poor prognosis after hospitalization for perforated peptic ulcer [34]. Thus, use of alternative analgesics by high-risk patients is warranted. Tramadol consumption has increased substantially during the last decade. Pain management guidelines currently propose tramadol as a treatment option for mild-to-moderate pain in patients at high risk of GI side-effects, including peptic ulcer disease[35]**.** In patients with peptic ulcer perforation, it is possible that tramadol use could worsen prognosis. The analgesic effect may mask symptoms of perforation, increasing time to surgical treatment that is one of the most important prognostic factors[36].Also, the immune suppression caused by opioids may increase the risk of severe infections and sepsis after perforation[37]. In a study by M. L.

Tørring *et al*[38] it was shown that mortality rates of perforated peptic ulcer were increased by two fold in tramadol users as compared to none. Thus use of tramadol during conservative management of perforated peptic ulcer can mask the clinical symptoms and make regular assessment of patient condition difficult. Thus serial measurement of CRP levels can be a better alternative to clinical examination for patients who are on tramadol or epidural opioids for pain management.

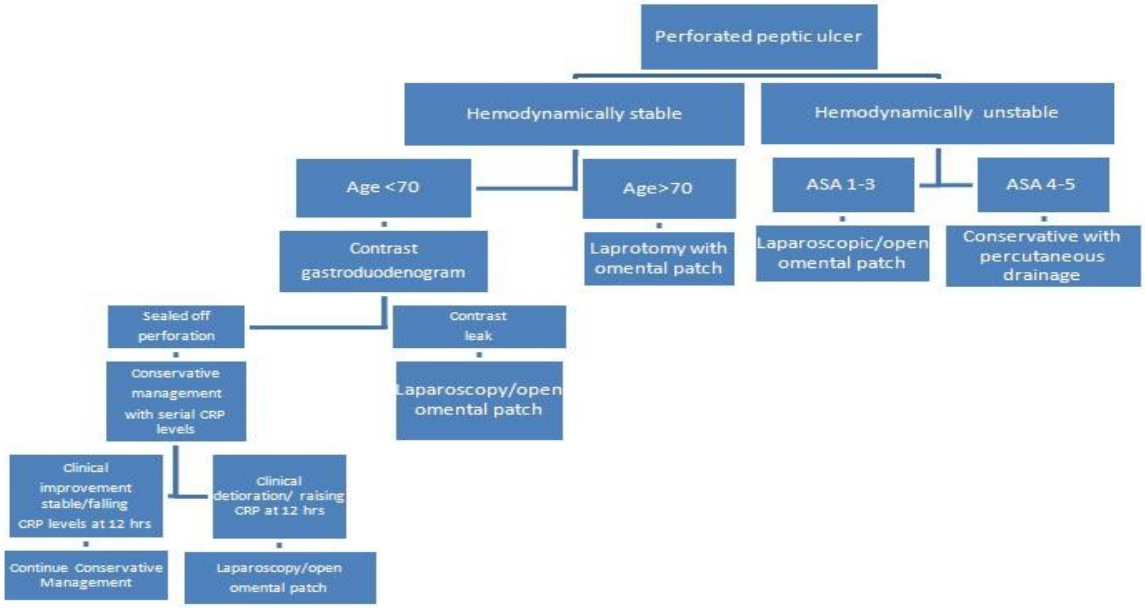
In critically ill patients being managed conservatively percutaneous drain placed in right iliac fossa under local anesthesia. The procedure has been performed at the bedside and by using a technique similar to open diagnostic peritoneal lavage. These should be of the sump suction type. An external fistula is established. Surgery can be deferred briefly pending completion of essential medical therapy. Tension pneumoperitoneum, if present, can have severe deleterious effects on cardiorespiratory function during the period of preoperative preparation. A needle paracentesis can provide dramatic relief.

The most common complication of a non-operative management is peritoneal abscess formation. Fortunately, most of the abscesses can be treated with antibiotics and/or percutaneous drainage without any sequelae[39]. In a study by Takatsugu *et al*[40] it was shown that routine percutaneous drainage of moderate to large peritoneal collection during conservative therapy decreased the conversion rate from 43.3% to14.3% also there were no intraabdominal abscess formation in the percutaneous drainage group. Thus routine drainage of peritoneal collection using ultrasound guided pigtail catheter or percutaneous drain placement is advocated. A high percentage of *H pylori* infection has been reported in patients with perforated duodenal ulcer. Ng *et al*[41] reported that 51 (70%) of 73 cases of perforated duodenal ulcer were infected with *H pylori*. If NSAID users were excluded, the number rose to 58 (80%).Tokunaga *et al*[42] reported *H pylori* in 92% of cases of perforated ulcer. The tissue density of infection was greater with perforation than with hemorrhage or obstruction.

Results of conservative management have shown the spontaneous seal of a perforated duodenal ulcer is remarkably secure. Among 152 cases of self-sealing documented by gastroduodenogram treated nonsurgically and reported from the institutions with which we have been associated, there were 2 instances of repeat leak. The rate of intra-abdominal abscess following nonsurgical treatment was 3% [43]. These results in patients with nonsurgical treatment are equal or better than the record in patients with surgical closure of the perforation.In a study by Thomas *et al*[22] an intra-abdominal abscess developed in 1 of the 35 patients. Reperforation did not occur. The mortality rate for the 259 cases treated operatively during this period was 6.2%; the mortality rate of the 35 cases treated nonoperatively was 3%.

Finally one always has to bear in mind that PPU can be a symptom of gastric cancer, so if conservative treatment has been chosen after a few weeks endoscopy should be performed . And all patient managed conservatively should be evaluated for *H.Pylori* infection and anti *H.pylori* eradication done and should be put on lifelong acid suppression therapy with PPI to prevent recurrence of ulcer.

Fig 1: Algorithm for management of perforated peptic ulcer.



5. Conclusion

Perforated peptic ulcer is one of the serious complications of peptic ulcer disease. With over 50 % presenting as a sealed off perforation selected patients can be managed conservatively. The patients who present with hemodynamic stability with sealed of perforation on contrast gastroduodenogram can be considered for non-operative management. Use of PPI, antibiotics, misoprostol, gastric aspiration combined with percutaneous drainage of peritoneal collection can treat most perforations with low mortality and morbidity.

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