

## Evaluate the Impact of Metronidazole on Pain Following Closed Haemorrhoidectomy

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### ABSTRACT:

**Background:** Haemorrhoidal disease is likely one of the earliest illnesses known to man, maybe dating back to the time when he first stood upright<sup>1</sup>. It causes considerable pain, suffering, and a decline in quality of life. Haemorrhoids are common vascular cushions within the canal. [1.2] The term haemorrhoids is derived from the Greek word haimorrhoids, which means bleeding, and the word pile is derived from the Latin word Pila, which means a pill or a ball, thus showing two cardinal symptoms: bleeding and prolapse of mass per rectum.

**Aim's & Objectives:** To evaluate the effectiveness of Metronidazole in giving relief from pain in all patients undergoing closed haemorrhoidectomy and to evaluate the requirement of analgesic use in relieving the pain, post closed haemorrhoidectomy .

**Methods & Materials:** The proposed study will be conducted on patients attending General Surgery OPD with chief complaint of Haemorrhoids from May 2012 to March 2014. There were 60 patients undergoing closed haemorrhoidectomy

**Results:** The mean VAS-Score of the pain in the group-A on the day 0 was 9.5 and in the group-B was 9.7 . On the day 7 the mean VAS-Score of the pain in the group-A on day 0 was 0.53 and in the group-B was 2.07 . The mean VAS-Score of the pain in the group-A on all the seven days was significantly lower than the VAS-Score of the group-B. The  $p < 0.05$  means significant; in all the days the p value is significant.

**Conclusion:** In the metronidazole group, there were no problems, whereas in the non-metronidazole group, three patients experienced fever and two had discharge from the surgical site. We observed that all patients with problems had haemorrhoids of grade . Thus, there is a higher rate of problems in the non-metronidazole group when the size of the wound is considerable. Metronidazole should be administered consistently to hemorrhoidectomy patients, according to the findings of the current study.

**Keywords:** effectiveness, Metronidazole, Haemorrhoids ,vascular cushions.

## **INTRODUCTION:**

Haemorrhoidal disease is probably one of the oldest ills known to man, perhaps since the time he assumed the upright position<sup>1</sup>. It leads to significant pain, discomfort and decreased quality of life. Haemorrhoids are vascular cushions within the canal and are ubiquitous [1.2] The term haemorrhoids is derived from the Greek word haimorrhoids, discharging blood while the word pile comes from Latin word Pila meaning a pill or a ball thus indicating two cardinal symptoms namely bleeding and prolapse of mass per rectum.

The incidence of haemorrhoids increases with age and it seems likely that at least 50% of the people over the age of 50 years have some degree of haemorrhoidal formation. Men seem to be significantly affected roughly twice as frequently as women. [3] Many theories abound as to the causation of this disease and probably even more methods to treat them. Every therapeutic modality has advantage and disadvantage. Haemorrhoidectomy by conventional techniques causes considerable postoperative pain because of wide external wound in the somatic-ally innervated perianal skin and this pain cause anxiety to patients and doctors and this operation has remained largely an inpatient procedure.

Reduction of pain after haemorrhoidectomy is an important goal, with the ultimate aim of reduction in length of inpatient stay and the possibility of day care or short stay surgery. In order for this to be effective patients must be selected appropriately and be well counseled before hand. A variety of preoperative and postoperative regimes have shown mixed benefits. In United Kingdom open haemorrhoidectomy is performed most often in contrast to United states where closed is more popular. Closed haemorrhoidectomy where the wound edges are sutured, facilitates more rapid healing and may cause less pain than open haemorrhoidectomy. However wound dehiscence secondary to infection may occur after the closed technique, which would reduce the proposed benefit of wound closure.

The art of proctology is based on the study of haemorrhoids and it seems appropriate to trace the history of development of our curent understanding of this rather incompletely understood subject. Haemorrhoidal disease has been referred to in the Edwin Sith papyrus (1700 BC), in the code of Hammurabi in Babylon(2250BC) and in the papyrus of Eber (1500BC). It is mentioned in Sushruta Samhita (2500BC) as Arsha Roga.

The Italians follow Galenic teaching referred to as profluvio de sanguie suggesting as overflow of blood. The ancient French referred to flux d'or flow of gold and the ancient Germans called it the golden ader golden veins implying that proctological symptoms may have been the prerogative of the rich. Polite society in the 17<sup>th</sup> century referred to haemorrhoidal disease as le mal de St.Phiacre. The medieval period was one of pile pondering & etiological thinking began. In 1295 Landfrank, one of the fathers of french proctology wrote chirurgie magna. In 1749 Morgagni attributed haemorrhoidal disease to erect posture of man. In 1855 Verneuil suggested occlusion of superior haemorrhoidal veins by fecal bolus caused anal varicosities.

In 1879 Daret said straining at stool was the main cause of rise in haemorrhoidal vein pressure.

In 1877 Hilton described the white line as the lowermost fibres of the internal anal sphincter as seen through the perianal skin when stretched tight. In 1896 Stroud described the pecten which was further described by Miles in 1919.

The surgical anal canal 3cms long, commences at the level where the rectum passes through the pelvic diaphragm, marked by the anorectal ring and ends at the anal verge. The dentate or pectinate line is an anatomic landmark, the true mucocutaneous junction and lies 1-1.5 cm above the anal verge & marks the cephaloid border of the anatomical anal canal. It represents the site of fusion of the proctodaeum and the postallantoic gut and the site of the anal membrane, remnants of which may frequently be seen as the anal papillae situated on the free margins of the anal valves. It separates above- the cubical epithelium, autonomic innervation (insensitive to pain), portal venous system from below squamous epithelium, spinal nerve supply (very sensitive) & systemic circulation [14].

The upper anal canal is lined by pink columnar epithelium of rectum, which extends into the surgical anal canal and is loosely attached to underlying structures & covers the internal rectal plexus. Passing downwards it clothes 8-12 longitudinal folds known as columns of Morgagni. Here the mucous membrane becomes cubical & red in colour called as the transition zone. Just above the anal valves the mucosa becomes plum coloured and just below the anal valves an abrupt but wavy transition (the dentate line) to squamous epithelium occurs and the mucosa appears parchment coloured. The loose epithelium above becomes firmly adherent to the internal sphincter at the anal valves via the mucosal suspensory ligament of Park.

The anoderm passes imperceptibly into the pigmented perianal skin but differs from it in that the anoderm is devoid of hair follicles, sebaceous gland or apocrine glands; important in distinguishing between cryptoglandular anal disease and hidradenitis suppurativa. The anal valves of Ball are a series of transversely placed semilunar folds linking the columns of Morgagni and constitute the waviness of the dentate line and are functionless remnants of the fusion of the post allantoic gut with the proctodaeum.

Crypts of Morgagni or anal crypts are small pockets between the inferior extremities of the columns of Morgagni. Into several of these mostly those situated posteriorly, opens one anal gland by a narrow duct (1st described by Chiari 1878). A few of them remain confined to the sub mucosa only, but majority of them, enter the internal sphincter, the intersphincteric plane and external sphincter as well to reach the ischiorectal fossa. They are implicated in the aetiology of anal fistulae.

Superiorly it is continuous with the circular muscle coat of the rectum and ends with well-defined rounded edge 6-8mm above the level of the anal orifice and 12-18mm below the

level of the anal valves. It is 2.5cms long and 2-5mm thick. Pearly white in colour, its spasm and contracture play a major part in anal fissures and other anal conditions.

Continuation of the longitudinal muscle coat of the rectum, intermingled with fibers of the puborectalis, the fibers fan out through the lowest part of the external sphincter to be inserted into the true anal and perianal skin. This extension constitutes the *currugator cutis* of Ellis (1878) and Milligan (1942). It creates tight compartments accounting for the intense pain seen in perianal infections. The main layer of longitudinal fibers in the anal canal lies between the internal and external sphincter & consists of smooth muscle with elastic tissues.

It constitutes part of the sphincter mechanism of the anal canal. It is a broad thin muscle attached peripherally to the inner surface of the side of the pelvis and united medially with its fellow of the opposite side to form the floor of the pelvic cavity. It consists of three parts- *pubococcygeus*, *iliococcygeus*, and the *ischiococcygeus*. The *puborectalis* is that part of the *pubococcygeus*, which arises from the posterior aspect of the symphysis pubis. It unites with the corresponding fibres of the opposite side to form a strong U shaped sling behind the rectum at the anorectal junction. It is important in maintenance of continence and in preventing rectal prolapse

In 1919, Miles described a circumferential flattened or rounded band of fibrous tissue between the skin of the lower part of the canal in the region of the pectinate line and true sphincter musculature. It is considered pathological and not existent in the healthy anal canal. It is due to passive congestion due to the loaded state of the rectum in the chronically constipated and varies in its thickness and density. It limits the expandability of the anal orifice and lead to incomplete emptying with decreased caliber of stools. Goligher says that it is really the inferior border of the internal sphincter when it is well developed because of its spasm in anal fissure.

It supplies the part of the anus derived from the cloaca. The inferior mesenteric artery continues as the superior haemorrhoidal artery in the root of the vertical limb of the sigmoid mesocolon to reach the upper end of rectum opposite the third piece of sacrum. Here it divides into two- the right and the left main branches, the level of bifurcation shows considerable variation. These branches descend on the rectal wall at first posteriorly, then inclining laterally each one breaking into smaller branches. They penetrate the muscle coat to reach the sub-mucosa on which they proceed as straight vessels, which run in the column of Morgagni. They terminate usually above the anal valves as capillary plexus.

The right branch divides into two major right and left whereas the left one continues undivided down the left lateral aspect (Miles 1939). This arrangement is said to account for the positions of the three primary piles but WHF Thompson (1975)<sup>16</sup> has disproved his hypothesis in an injection preparation of cadavers.

Derived from the internal pudendal artery in Alcock's canal, it traverses the ischiorectal fossa and breaks up into branches, which traverse the sphincter to supply the mucosa. The three hemorrhoidal vessels communicate with each other. It arises from the aorta about 1cm above its bifurcation and runs anterior to the last two lumbar vertebrae, sacrum and coccyx. Its terminal branches reach the anococcygeal raphe along which they reach the anal canal.

In the upper part of the anal canal and lower rectum from the submucosal internal hemorrhoidal plexus, begins the superior hemorrhoidal vein which drains into the inferior mesenteric vein and thus to the portal circulation. The anal orifice and lower anal canal are drained by subcutaneous external hemorrhoidal plexus of veins from which begins the inferior hemorrhoidal vein which enters the systemic circulation via internal iliac vein.

Lymphatics of the cloacal part pass upward with the arteries to the nodes along the middle hemorrhoidal and internal iliac arteries, along the superior hemorrhoidal and inferior mesenteric arteries to the preaortic group. The anal part drains with the rest of the perineum into the medial group of superficial inguinal nodes.

Sensory-the sensation from skin of the perianal region and of the wall of the anal canal below the level of the anal valves is carried by afferent fibers in the inferior hemorrhoidal nerve and is very sensitive while the mucosa of the anal canal above the level of the anal valves is sensed by afferent via parasympathetic nerves & is relatively insensitive.

Hemorrhoids (according to Peter A Hass)<sup>18</sup> have three parts- The lining- either mucosa above or anoderm below- Stroma with blood vessels smooth muscles and supporting connective tissue in the submucosa. The subepithelial vascular plexus called cushions by Thomson (1975) with serpiginous vessels connecting arteries to veins without intervening capillaries have been called the corpus cavernosi recti by Steltzner(1962) [19]

The vessels are supported by longitudinal smooth muscle fibers described by Treitz (1853). These fibers descend from the internal sphincter and coalesce beyond the dentate line under the anoderm forming a dense stroma around the venous saccules there. Contraction of the muscles thus both flattens the cushions as well as holds them up against the internal sphincter and the conjoint longitudinal coat.

The distribution of the three primary hemorrhoids at 3, 7, & 11 o'clock positions (at lithotomy position) has been attributed by Miles (1939) to the arterial branching pattern while another hypothesis suggests that it is due to lack of submucosal support between the three taeniae coli.

During the act of defecation as the internal sphincter relaxes there is an outward rotation of the vascular tissue and the pectin band producing parting of the anorectum. The cushions enlarge dramatically during defecation and decongest just as rapidly once they are returned to their normal position. At end of normal defecation voluntary sphincter contraction returns any residual fecal matter from anal canal to the rectum. Cushions then provide a spongy

variable volume washer on which the sphincter can contract thereby assisting its closure, loose textured above, tougher below, leading to a watertight seal . [17]

The anal sphincter tone normally ranges from 60-110 cm of water with episodes of spontaneous falls in resting anal pressures termed sampling reflexes. Higher sphincter pressures with higher than normal distribution of type 1 muscle fibers in the external sphincter suggest a state of tonic contraction of the muscle in some patients (Teramoto 1981). Birmingham manometer studies classified patients with hemorrhoidal disease into those with high anal pressures the so called hypertensive pile patients who are more often young males presenting with symptoms of bleeding; and those with low anal pressures often multiparous and older women presenting more often with prolapse.

Several theories have been proposed but no single theory has been found satisfactory;

1. Campbell and Cleave identified dietary factors resulting in constipation as a cause. Cleave termed it the “Saccharine disease”. They found a lower incidence in tribal Africa and it is possible to speculate that high fiber intake in rural societies may be the reason for the low incidence but there has been no positive or negative evidence that the incidence of hemorrhoidal disease has decreased since the advent of the bran mania of the 1970s. Other possible explanations could be that patients are more likely to complain in western societies because medical services and pharmaceutical preparations are more readily available.
2. Virchow and Allingham considered haemorrhoids to be hemangiomas and erectile in nature.
3. Steltzner called it the corpus cavemosum recti.
4. Graham Stewart<sup>20</sup> suggested that they are varicosities of the superior hemorrhoidal plexus of veins and could be divided into two types- vascular haemorrhoids which bleed, and mucosal haemorrhoids, which prolapse.
5. Theory of ageing- Jackson and Robertson<sup>21</sup> and the wear and tear theory of Adams and Gass [22] suggest that age related fragmentation and loss of elastic and anchoring tissue aggravated by daily trauma of straining leads to haemorrhoids.
6. Rangabhashyam and Manohar<sup>23</sup> attributed it to perineal descent syndrome especially in patients with constantly prolapsing and in recurrent haemorrhoids. He also found a high incidence of amoebiasis in patients with haemorrhoids. Squatting position tends to cause bearing down on pelvic floor and predisposes to prolapse of the pile masses.
7. Nesselrod considered anal infection as the principal factor and Mc.Givney described high incidence of round cell infiltration as an evidence of infectious process.



8. Haas[18] considered haemorrhoids as normal parts of human anatomy and that symptomatic haemorrhoids must be treated.
9. Role of heredity [13] - Leicester found a positive family history in 50% but there is no firm evidence of an inherited predisposition as diet and defecation habits are usually related to customs and environment.
10. Role of defecation habits- Though not backed by studies it is a frequent and reliable observation that many patients with hemorrhoidal disease are those who sit for 10-15minutes on a comfortable lavatory taking with them some reading material. Such patients are obsessed by the necessity to have a regular act of defecation and are determined to sit there till they do.
11. Venous obstruction by fecal bolus was suggested by Vemeuil
12. Morgagni attributed it to erect posture of man
13. Secondary haemorrhoids- the relation to definite organic disease is also controversial parturition when the supporting tissues of the anal cushions may be torn. [17]

Pressure of the fetus on the superior rectal veins causing obstruction has been postulated.

1. Communication between portal and systemic circulations- Jacobs in 1980<sup>27</sup> in his study showed that incidence of symptomatic haemorrhoids in portal hypertension is 28% whereas that in the general population is 50% (Buie *et al* 1937). The prevalence of Anorectal varices in cirrhotics without portal hypertension was 19% whereas it was 59% in cirrhotics with portal hypertension with history of bleed from esophageal varices. Hirschowitz<sup>18</sup> states that haemorrhoids do not necessarily occur in patients with esophageal varices. Swart<sup>18</sup> stated that because of the long distance between the portal and the haemorrhoids veins based on the Hagen-Pouisseuill equation. Venous pressure in the haemorrhoids does not increase appreciably and they are not an important site of collateral circulation between the vena cava and portal system. Macpherson<sup>3</sup> in a study of 128 consecutive cases of portal hypertension did not encounter a single case which he could attribute to cirrhosis.
2. Fecal mass in rectum may compress these veins- Parks ampullary pump theory.
3. Relation to carcinoma rectum- Causative relation has not been proved. Chronic straining due to obstruction or sensation of incomplete emptying and obstruction to middle rectal vein have been postulated. Other authors state that the relation is merely coincidental.

Bleeding is the most common and earliest symptom. The blood is bright red in colour, especially after passing a non-bloodstained hard stool, usually in absence of pain or pruritis. Later profuse bleeding, dripping into the pan like a tap or spattering the sides like a jet marks

the end of defecation, which is characteristic of haemorrhoidal disease. Still later continuous bright red bloody mucus discharge especially in elderly whose vascular cushions lie permanently outside the anus. The cause of bleeding<sup>16</sup> in the initial phases is due to trauma to the capillaries of the lamina propria which are protected only by a single layer of epithelial cells. Following prolapsed trauma due to wiping or contact with clothing often occurs.

Protrusion with spontaneous or self-digital reduction of the mass is highly characteristic and is the other cardinal manifestation. Patients may be quite unaware of these or on the other hand some may be plagued by a pile which prolapses and exudes mucus. Philips and Edwards gave the concept of a flutter valve mechanism of continence; the anterior rectal wall acting as a valve during rise in intra-abdominal pressure. In patients with weak pelvic floor it may be associated with the descending perineum syndrome.

The clinical assessment apart from detailed physical examination includes a digital per rectal examination and anoscopy. If facilities are available sigmoidoscopy should be done in all patients.

It has been traditional to grade haemorrhoidal disease into four degrees (three according to some) based on the extent of prolapse. Though far from satisfactory due to the fact that it assesses only one aspect of haemorrhoidal disease that is prolapsed and that it is variable from time to time it still remains one of the few clinical parameters for comparison of results. Haemorrhoids may also be classified as internal, external or combined based on the lining epithelium.

- a) In patients with principal complaints of loose stools, itching and smearing of blood on the toilet paper it is best to begin with a high fiber diet and thorough gentle lavage after defecation.
- b) Changing defecation habits- the three errors of bowel habit most prevalent in patients with hemorrhoidal disease .
- c) Diet manipulation- change to a high fiber diet, which is difficult; addition of a simple bulk forming agent- Bran, sterculia, ispaghula husk, psyllium seed extract and methyl cellulose.
- d) Vasotopic drugs- hydroxyl ethyl rutosides have been suggested and are supposed to decrease the edema and inflammatory swelling but studies have not proved their effectiveness (Birmingham a double blind prospective trial was abandoned due to the side effects of treatment and lack of any improvement in symptoms).
- e) Topical applications- anecdotal evidence suggests that they do produce some symptomatic relief. Most preparations contain several ingredients including topical anesthetics, steroids and antiseptics. Soft paraffin is frequently used by sufferers and probably works by lubricating the swollen cushions or skin tags. Astringents or



hygroscopic agents are often used. Superiority of one over the other remains unproved.

**Principles-** Three broad methods have developed in parallel with each one relating to a hypothesis; these are:

- Prevention of prolapse by mucosal fixation.
- Prevention of congestion or venous impedance by stretching or by sphincterotomy.
- Excision of the engorged vascular cushions.

The credit for the first operation is given to Salmon (1888) who showed that the main supply of the anal canal was derived from the superior hemorrhoidal artery and that piles could be dissected above the dentate line and the pedicle ligated without causing pain. Later Miles (1919) and Morgan (1937)<sup>28,29</sup> modified the technique by low ligation of the pedicle with excision technique. It is best suited for intero-external, prolapsed, thrombosed or secondary haemorrhoids and those with associated conditions of the anus like fissure or fistula. Contraindications include bleeding diathesis, inflammatory bowel disease especially Crohn's disease. The open technique is practiced most frequently as the Milligan-Morgan operation usually under spinal or general anesthesia in lithotomy position.

### Technique

The skin covered component of each of the main piles is seized with artery forceps and retracted outwards, the purple anal mucosal component is grasped and drawn down and out. With a V-shaped incision in the anal and perianal skin dissection is carried out to free the cushions off the internal sphincter for 1.5-2cms and the pedicle transfixed and ligated with either absorbable or non-absorbable suture. The isolated haemorrhoids is then excised a few mm below the apical ligature, the transfixation suture being left long. An adequate bridge of skin and mucosa should be left in between. The final wound, if it looks like a clover the trouble is over, if it looks like a dahlia, it is surely a failure. Conventionally a three quadrant haemorrhoidectomy is done but additional piles may be removed in a similar way. The anal canal is packed with paraffin wax impregnated gauze and dressings applied.

- 1) Pain: 71% the severity of pain experienced is patient dependent. Various suggestions as to the cause include
  - i. Ligation of sensitive epithelium below dentate line and thus submucosal technique was introduced but no benefit has been observed on comparative studies.
  - ii. Spasm of the sphincter- addition of four finger stretch or sphincterotomy was recommended but no benefit has been demonstrated.

iii. The most plausible cause is the exposed raw areas in the anal canal; thus the closed techniques by Parks and Ferguson-Heaton were introduced. With the former there is apparently no pain relief due to the open wound below the dentate line while the latter remains to be tested.

2) **Acute retention of urine:** 16.4%

The risk factors<sup>31</sup> identified include four quadrant excision/ three quadrant excision, morphine equivalents >33, male gender. Other risk factors are more than one operation, older age, intraoperative fluids and post operative fluids.

3) **Reactionary or secondary hemorrhage :** 7.6% those requiring re-operation-1 %

4) **Others;** rare and require specific treatment. These include- anal stenosis 2.9% anal fissure- 0.5%; abscess-0.6%, fistula in ano 1.2% long term incontinence<sup>32</sup> was noted in 2 patients (n=1 134). Other complications include anal skin tags. Pseudopolyps and epidermal cysts. Anal leakage and soiling is common (50%) during early postoperative period but settles in 6- 8 wks. Causes include anal dilation, loss of sensation and transient reduction in anal canal pressures. Return of anal canal pressure to normal has been described [23]

Described by Sir Alan Parks in 1956 [16] The technique involves use of an inverted racket shaped incision entirely within the anal canal with use of mucosal flaps. Disadvantages quoted include residual haemorrhoids requiring re-excision, more time and blood loss and no advantage with respect to pain relief.

In 1882 Whitehead [15,16] described excision of entire pile bearing area upto the muscle with primary closure. Similar techniques have been described for prolapsed circular grade IV haemorrhoids in the form of circular hemorrhoidectomy with anoplasty using the Hospital Leopold Bellan technique, also called radical hemorrhoidectomy [17]

More recently circular staplers have been used for the same purpose with advantages of reduction in time and blood loss. Other variants include clamp and suture methods by Mitchell (1903) and excision with clamp and cautery by Cusack (1846).

Due to disadvantages and complications including the very high incidence of pain and also a better understanding of the physiological role of haemorrhoids other methods have evolved with main advantages of being less painful and being out patient procedure.

Metronidazole is bactericidal against anaerobic bacteria; it exerts trichomonocidal activity and is also active against *Giardia lamblia* and *Entamoeba histolytica*. Its exact mechanism of action has not been entirely determined as yet. It has been proposed that an intermediate in the reduction of metronidazole, produced only in anaerobic bacteria and protozoa is bound to deoxyribonucleic acid and electron-transport proteins, inhibits subsequent nucleic acid synthesis.

In vitro and in vivo studies indicate that metronidazole has direct anti-inflammatory activity and affects neutrophil chemotaxis and cell-mediated immunity. An antioxidant action via inhibition of neutrophil-generated reactive oxygen species has also been demonstrated; this action is believed to underlie its anti-inflammatory effect.

The 1988 Canadian Guidelines for the Treatment of Sexually Transmitted Diseases in Neonates, Children, Adolescents and Adults recommends metronidazole for the treatment of this condition. Metronidazole is used widely to prevent post-surgical infections caused by susceptible anaerobic organisms. It is also often used to eradicate *Helicobacter pylori* along with other drugs.

Metronidazole is indicated in the treatment of serious anaerobic intra-abdominal infections due to susceptible anaerobic bacteria, such as *Bacteroides fragilis* (and other species of *Bacteroides*), *Clostridium*, *Fusobacterium*, *Peptococcus*, and *Peptostreptococcus* species. In the treatment of most serious anaerobic infections, intravenous metronidazole is usually administered initially. This may be followed by oral therapy with metronidazole capsules at the discretion of the physician.

A dose of metronidazole is commonly given after haemorrhoidectomy. Many have debated the role of regular metronidazole after haemorrhoidectomy. Carapeti et al. was the first study looking at the role of oral metronidazole on pain after day-case haemorrhoidectomy.<sup>5</sup> Patients were either given 400mg tablets or placebo thrice a day. They showed that pain was reduced every day in the first week but significantly between days 5-7. This also resulted in reduction in analgesia use, earlier return to normal activity and greater satisfaction in the metronidazole group. They went on to postulate that bacterial colonization and secondary infection to the post-operative anal wound leads to prolonged pain on days 3-7. This leads to sensitive friable anal mucosa due to inflammatory swelling and edema. Metronidazole is an effective antibiotic against anaerobic bacteria and most likely to be effective against organisms that colonize anal wound. They postulated that open wounds are more likely to benefit from antibiotic use although closed wounds will also benefit from prophylaxis in order to prevent dehiscence. Further study by Al-Mulhim et al. showed that pain was significantly reduced every day of the week in the metronidazole group compared to the placebo group. [18] They also showed earlier return to work but demonstrated no difference in complication rate. They agreed with Carapetti group that oral metronidazole should be routinely administered after haemorrhoidectomy. Conversely, study by Balfour et al showed no difference between the group taking oral metronidazole and placebo group in terms of post-operative pain, time to first bowel movement, return to normal activity, complication rates and overall satisfaction. [19] Two studies looked at the role of topical metronidazole on pain after haemorrhoidectomy. Nicholson and Armstrong showed that topical application of 2.5cc 10 percent metronidazole was associated with reduced pain after 7 and 14 days. [20] In addition, the metronidazole group was observed to have less postoperative edema and significantly better healing at 2 weeks compared to the placebo group. Ala et al. similarly did a

randomized controlled trial comparing topical 10% metronidazole with placebo treatment.<sup>41</sup>They showed that post-operative pain was less in the metronidazole group throughout the study period and also required less analgesia on days 2-7. They went onto conclude that metronidazole has 2 properties: an anti-inflammatory effect in the early phase and an antibacterial effect in the latter stages of treatment. Both phases will ultimately reduce post-operative pain.

They also demonstrated reduced pain on defecation and suggested that inflammation was important in interfering with defecation post-surgery. The emphasis is of preventing secondary infection in post-haemorrhoidectomy wounds. However, the incidence of perianal abscess, cellulitis and gangrene very rare after haemorrhoidectomy. Retrospective data report rates of 0-2% for abscess and fistula formation. [12] A bacteriological study of post-haemorrhoidectomy wounds for upto 4 weeks was conducted by De Paula et al.<sup>43</sup>They demonstrated that all 20 wounds healed without problems and all were colonized by aerobic organisms. On the other hand, Brook and Frazier demonstrated that 18 of the 19 infected wounds after haemorrhoidectomy were infested with anaerobic organisms. [24]The most common anaerobic organism isolated was *Bacillus Fragilis* and *peptostreptococcus*. It is based on findings like this that metronidazole either oral or topical is advocated as it is an effective antibiotic against anaerobic organisms.

Metronidazole has been shown to be carcinogenic in mice and rats . Unnecessary use of the drug should be avoided.It has no direct activity against aerobic or facultative anaerobic bacteria. In patients with mixed aerobic-anaerobic infections appropriate concomitant antibiotics active against the aerobic component should be considered. Known or previously unrecognized moniliasis may present more prominent symptoms after treatment.Severe neurological disturbances (i.e convulsive seizures and peripheral neuropathy) have been reported in patients . These have been observed very infrequently.

Patients should be warned about the potential for confusion, dizziness, hallucinations, convulsions or transient visual disorders, and advised not to drive or operate machinery if these symptoms occur. Metronidazole should be used with caution in patients with active or chronic severe peripheral and central nervous system diseases due to the risk of neurological aggravation.

Patients should be advised not to take alcohol or alcohol-containing medicines during the therapy and for at least one day afterwards because of the possibility of a disulfiram-like (Antabuse effect) reaction. The drug should be used with great caution in patients with a history of hepatic enzyme increase or liver injury associated with previous administration of metronidazole.

## MATERIALS AND METHODS:

The proposed study will be conducted on patients attending General Surgery OPD with chief complaint of Haemorrhoids from May 2012 to March 2014. There were 60 patients undergoing closed haemorrhoidectomy .

A written informed consent was obtained after its approval from the Local Ethics Committee. Thirty patients were randomly assigned to the metronidazole group (Group A) and 30 randomly assigned as non-metronidazole group (Group B). Symptoms and laboratory examinations of patients were documented and assessed in the outpatient clinic. They were admitted one day before the surgery. In the operating theatre, once the patient was anesthetized, in the lithotomy position the patient underwent closed hemorrhoidectomy.

In addition both the groups received tablet ofloxacin 200mg twice daily for 7 days. An analgesic, tablet diclofenac 50mg was given on demand with the maximum dosage of 150mg per day. The same team of surgeons conducted all the operations.

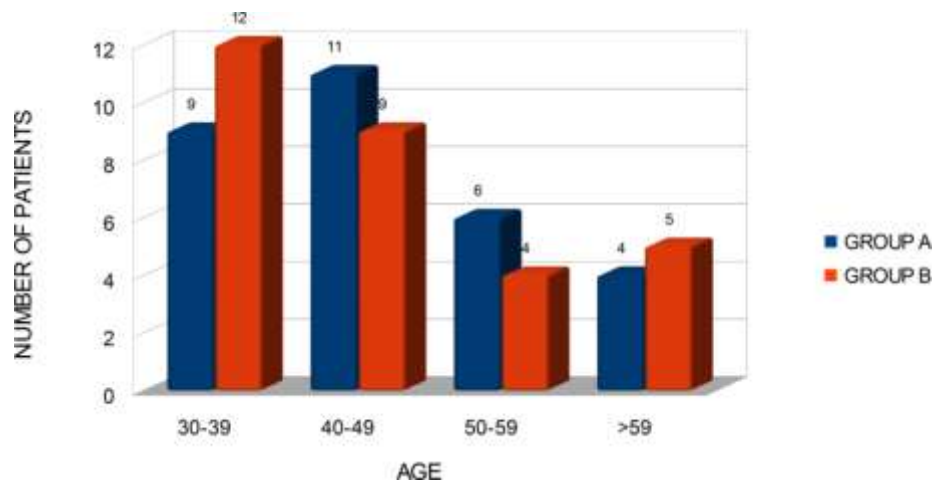
An outpatient appointment was arranged one week and 3 weeks post discharge and at 6 weeks postoperatively. Patients were assessed for postoperative pain on the day of surgery and every day for the first 7 days. We used 10 cm Linear Visual Analogue Scales (VAS) to record the worst pain experienced.

For the statistical analysis, Chi square ( $\chi^2$ ) test was used for comparison of frequencies and student's t test used for comparison of data presented as mean  $\pm$  SD of both groups. We took a value of  $\leq 0.05$  to be significant.

## OBSERVATIONS & RESULTS:

Table 1: Age distribution of the patients

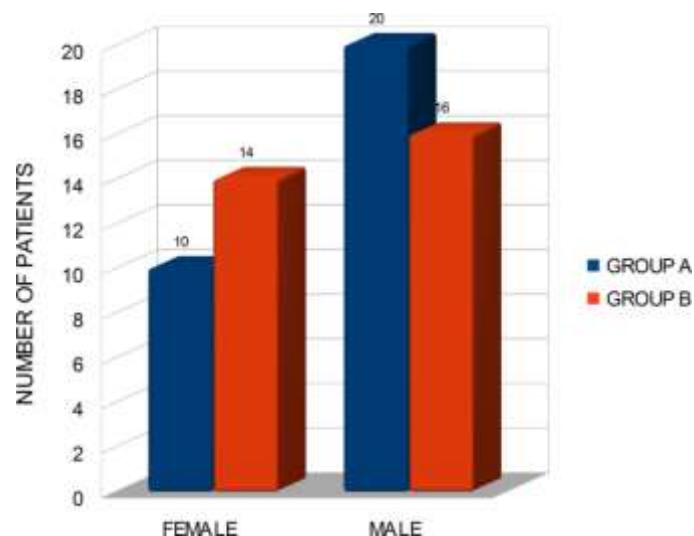
Age distribution in years		NUMBER OF PATIENTS	
		GROUP A	GROUP B
30-39		9	12
		30.0%	40.0%
40-49		11	9
		36.7%	30.0%
50-59		6	4
		20.0%	13.3%
>59		4	5
		13.3%	16.7%



There were total twenty one patients in between 30-39yrs of age group out of which nine patients were in Group-A and twelve patients in Group-B. Twenty number of patients were in between the 40-49yrs of age among these eleven patients were in Group-A and nine patients were in Group-B. Ten patients were in the range of 50-59yrs of age and six patients out of these ten patients were in group A and the rest were in the group B. The two groups comprised 60 patients: the metronidazole group(A), n=30 had a median age of 44(range 31-63)years, and the non-metronidazole group(B), n=30 had a median age of 43(range 31-63) years.

Table 2: Gender distribution of the patients

		GROUP A	GROUP B
GENDER	FEMALE	10 33.3%	14 46.7%
	MALE	20 66.7%	16 53.3%

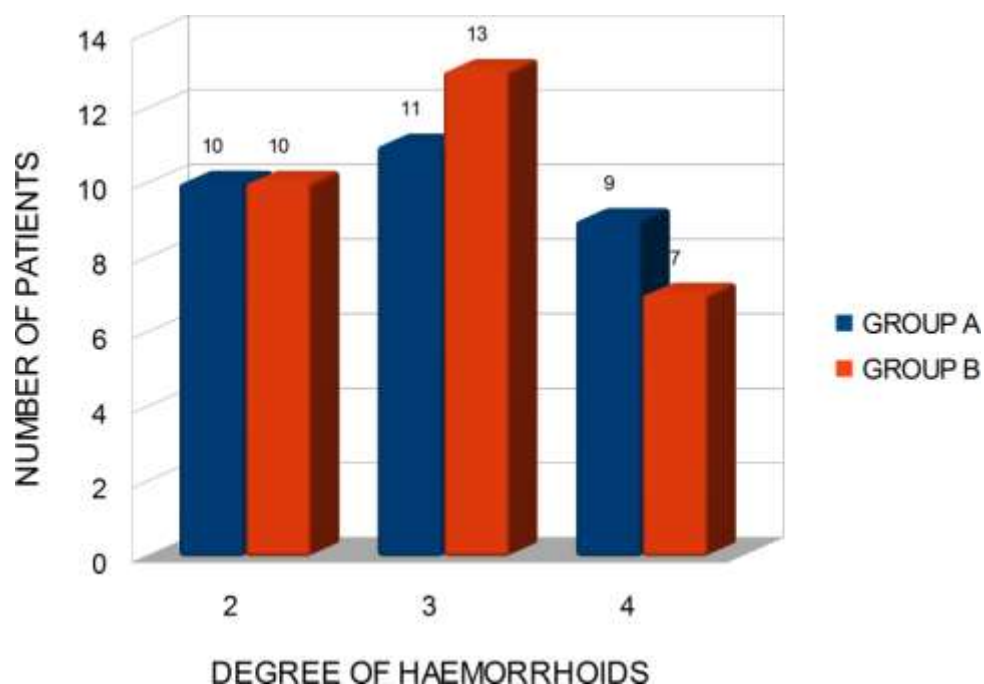




The number of female patients in the group A were 33.3% and in the group B are 46.7% where as the number of male patients in the group A were 66.7% and that in the group B were 53.3%. The ratio of males to females in group-A is 2:1 and the ratio of males to females in group-B is 1.1:1 .

Table 3: DEGREE OF HAEMORRHOIDS

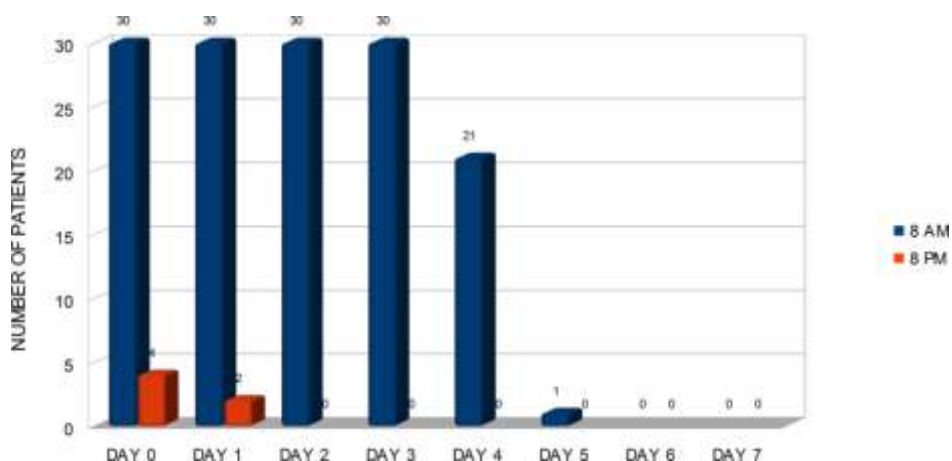
DEGREE	GROUP-A NUMBER OF PATIENTS	GROUP-B NUMBER OF PATIENTS
2nd	10 33.3%	10 33.3%
3rd	11 36.7%	13 43.3%
4th	9 30.0%	7 23.3%
RESULT	NOT-SIGNIFICANT	



This chart shows the distribution of the patients according to the degree of the haemorrhoids. In both the groups we had ten patients each with 2<sup>nd</sup> degree of haemorrhoids . Where as the patients with the 3<sup>rd</sup> degree haemorrhoids were twenty four in number . Out of these twenty four patients eleven patients with 3<sup>rd</sup> degree haemorrhoids were in group-A and thirteen patients were in group-B. Total sixteen patients were having 4<sup>th</sup> degree haemorrhoids out of which nine patients were in group-A and seven patients were in group-B.

Table 4: Post-operative analgesia group-A

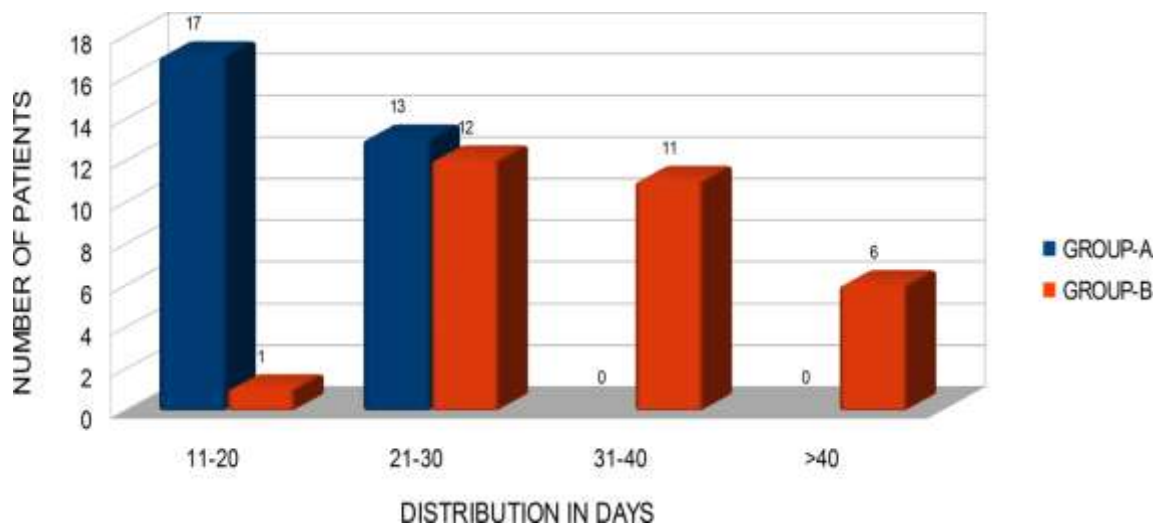
DAYS	8 am NUMBER OF PATIENTS	8pm NUMBER OF PATIENTS
DAY 0	30 (100%)	4 (13.3%)
DAY 1	30 (100%)	2 (6.7%)
DAY 2	30 (100%)	0
DAY 3	30 (100%)	0
DAY 4	21 (70%)	0
DAY 5	1 (3.3%)	0
DAY 6	0	0
DAY 7	0	0



All the patients (30) of group-A (metronidazole group) till day 3 were given analgesia in the morning(8 am) and on day 4- twenty one patients and on day 5 – one patient and day 6 and day 7 no analgesia was required. In the same group on day 0 and day 1 four patients and two patients required analgesia in the evening (8 pm) respectively where as on the rest of the days no evening dose was required.

Table 5 : Time to return to normal activity

DISRIBUTION IN DAYS	GROUP-A NUMBER OF PATIENTS	GROUP-B NUMBER OF PATIENTS
11-20	17 (56.7%)	1 (3.3%)
21-30	13 (43.3%)	12 (40.0%)
31-40	-	11 (36.7%)
>40	-	6 (20.0%)
p-Value	0.00	
RESULT	SIGNIFICANT	



This chart shows distribution of the time to return to normal activity in the two groups. Seventeen patients from the group-A and one patient from the group-B returned to routine work in between 11-20 days. The rest of the group-A patients i.e thirteen and twelve patients from the group-B returned to routine work in between 21-30 days. Eleven patients of group-B took 31-40 days to return to normal routine while six patients of group-B took more than 40 days to return to normal activity. The p-value is 0.00 which is significant. The median time to return to normal routine was 18.9 days (range 17-26 days) in metronidazole group(A) and 39 days (range 20-44 days) in non metronidazole group(B).

## DISCUSSION:

A great deal of emphasis has been applied to the management of pain after haemorrhoidectomy, not only because of the pain but also because of its role in urinary symptoms. The enthusiastic use of intravenous fluids during the procedure may contribute the high incidence of urinary retention, as will spinal anesthesia. Several studies have attempted to identify the various approaches to post-haemorrhoidectomy pain reduction. Although stapled haemorrhoidopexy is applicable for treating reducible haemorrhoidal prolapse and is associated with less postoperative pain but is also associated with number of reported complication the choice of surgical technique has also been a subject of considerable debate. The exposed area of the anal canal following open haemorrhoidectomy has been implicated as the cause of pain. For this reason, closed haemorrhoidectomy has been advocated, although the cost<sup>50</sup> per patient and morbidity does not show any statistically significant differences between the open and closed methods of haemorrhoidectomy. The Ferguson closed haemorrhoidectomy has reportedly been associated with less post-operative discomfort, faster healing, intact postoperative continence, and no need for subsequent anal dilation. Furthermore, the post-operative infection rate has been reported at 2% in the large series of 2038 patients. Similarly McConnell and Khubchandani reported a small incidence of postoperative pain, infection, and faster healing although initial results were favorable, the merits of this technique have not been supported by recent published series. In a randomized

trial, Arbman et al reported that although wound healing was considerably faster in patients operated on by the Ferguson technique there was no reduction in the postoperative pain. In another randomized trial, Carapeti showed that there was no significant difference in the mean pain score between the open and the closed haemorrhoidectomy techniques<sup>5</sup>. In yet another prospective, randomized trial, Gencomanoglu *et al* reports that the open technique is more advantageous in those patients who experience less discomfort during the early postoperative period, although the healing time was shorter with closed technique.

The metronidazole group (A), n=30 had a median age of 44 (range 31-63) years, and the non-metronidazole group (B), n=30 had a median age of 43 (range 31-63) years. The groups were statistically similar in terms of age and gender distribution. No significant difference was noted. The percentage of female patients in the group A were 33.3% and in the group B are 46.7% whereas the percentage of male patients in the group A were 66.7% and that in the group B were 53.3%. The ratio of males to females in group-A is 2:1 and the ratio of males to females in group-B is 1.1:1.

The distribution of the patients according to the degree of the haemorrhoids in the groups was noted. There were ten patients in each group with 2<sup>nd</sup> degree of haemorrhoids. Whereas the patients with 3<sup>rd</sup> degree of haemorrhoids were twenty four in number; eleven patients were in group-A and thirteen patients were in group-B. Sixteen patients were having 4<sup>th</sup> degree haemorrhoids; nine patients were in group-A and seven patients were in group-B. By Pearson Chi-Square we got p-value as 0.812 which is not significant.

We studied the postoperative analgesic requirement in both the groups. The requirement of analgesic was significantly at a lower side in the metronidazole group(A) starting at the day of the surgery and till the end of the 1<sup>st</sup> week post-operatively. The T-Value of the postoperative analgesic requirement between the two groups(A and B) at 8am was 0.858 and the p-value was

0.404 which was not significant. At 8 PM (*additional*) the T-Value was 3.29 between the two groups and the p-value was 0.0053 which was significant. A Randomized controlled trial comparing topical 10% metronidazole with placebo by Ala *et al*. [21] showed that post-operative.

We studied the mean hospital stay (numbers of nights) postoperatively. A significant number of nine patients from group-A only were discharged on the 4<sup>th</sup> postoperative day and rest of the group-A patients were discharged on the 5<sup>th</sup> postoperative day. The group-B patients started getting discharged from the 5<sup>th</sup> postoperative day. Nine patients on the 5<sup>th</sup> day, eleven patients on the 6<sup>th</sup> day and rest of the ten patients of the group-B were discharged on the 7<sup>th</sup> postoperative day. The p-value was 0.00 which is significant. This does not go in accordance with the study by Al-Mulhim *et al* in which the mean hospital stay postoperatively was not significant between the two groups.

In our study we noticed complications such as fever and discharge. None of the patients from the group-A showed any complications while in the group-B three patients had fever and two patients had discharge from the operated site. The p value was significant. The study by Al-Mulhim *et al.* showed complications of acute urinary retention in 4% in group-B but one patient in metronidazole group. Two patients in group -A and 16 patients in group-B showed unhealed perineal wound in 6 weeks OPD visit. To avoid urinary retention which is one of the commonest complication post haemorrhoidectomy we put a urinary foley's catheter in every patient till 3<sup>rd</sup> postoperative day. The emphasis is of preventing secondary infection in post- haemorrhoidectomy wounds. However, the incidence of perianal abscess, cellulitis and gangrene are very rare after haemorrhoidectomy. Retrospective data report rates of 0-2% for abscess and fistula formation. A bacteriological study of post-haemorrhoidectomy wounds for upto 4 weeks was conducted by De Paula et al. They demonstrated that all 20 wounds healed without problems and all were colonized by aerobic organisms. On the other hand, Brook and Frazier demonstrated that 18 of the 19 infected wounds after haemorrhoidectomy were infested with anaerobic organisms. The most common anaerobic organism isolated was *Bacillus Fragilis* and *peptostreptococcus*. It is based on findings like this that metronidazole – either oral or topical – is advocated as it is an effective antibiotic against anaerobic organisms.

## CONCLUSION:

Our study shows that demographic data (age distribution, gender distribution and degree of haemorrhoids) of 60 patients were similar for the 2 groups (metronidazole and non-metronidazole) of patients. As compared to the non-metronidazole group (B) the average pain experienced was statistically significant among the metronidazole group (A) patients from the day of the surgery till the end of the 1<sup>st</sup> week post-operatively.

The postoperative analgesic requirement was significantly at a lower side in the metronidazole group(A) starting at the day of the surgery and till the end of the 1<sup>st</sup> week post-operatively whereas in the group-B the analgesic requirement in few patients seen till the end of the week. The study shows that metronidazole used post-operatively effectively reduces the postoperative pain proving its anti-anaerobic affect and anti-inflammatory affect.

All the patients in metronidazole group were discharged by the 5<sup>th</sup> post-operative day but the patients in the non-metronidazole group took longer to get discharged. The mean hospital stay postoperatively was significantly less in metronidazole group.

None of the patients from the metronidazole group had any complications while in the non-metronidazole group three patients had fever and two patients had discharge from the operated site. We noticed that all the patients with complications had grade 4 haemorrhoids. Thus there is a higher rate of complications associated with the non-metronidazole group when the wound size is large. This current study's result strongly recommends that metronidazole should be given routinely to hemorrhoidectomy patients.

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