Capsule Endoscopy as a Diagnostic Tool for Inflammatory Bowel Disease in a Patient with Multiple Myeloma

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ABSTRACT

Capsule endoscopy is an important tool for minimally invasive evaluation of the small bowel, allowing improved diagnostic yield with low complication rates relative to traditional modalities. Here, we present the first case of inflammatory bowel disease (IBD) diagnosed by a capsule endoscopy in Surabaya. There was a case of a patient who suffered chronic diarrhea for four months. When the patient experienced persistent diarrhea, generalized weakness was then reported as a symptom. The patient then received a conventional endoscopy and was planned for a colonoscopy. However, the endoscopy was canceled due to the patient's respiratory distress. The patient underwent capsule endoscopy, where hyperemia and erosion from the small intestine to the colon were found. The diagnosis of IBD was established and the patient was given sulfasalazine 500 mg every 24 hours. In order to image the small intestine endoscopically, capsule endoscopy remains to be the preferred method. This case serves as an example of the advantages of capsule endoscopy, especially in terms of the diagnosis of inflammatory bowel disease.

Keywords: *Bowel disease, Capsule Endoscopy, Diagnosis, Human and Disease*

ABSTRAK

Endoskopi kapsul merupakan sebuah alat diagnostik minimal invasif untuk usus kecil, dan memungkinkan hasil diagnostik yang lebih baik dengan tingkat komplikasi yang rendah dibandingkan modalitas tradisional. Di sini, kami menyajikan kasus pertama Inflammatory Bowel Disease (IBD) yang didiagnosis dengan endoskopi kapsul di Surabaya. Seorang pasien menderita diare kronis selama 4 bulan. Saat pasien mengalami diare persisten, pasien mengatakan merasa lemah. Pasien kemudian endoskopi konvensional dan akan dilakukan kolonoskopi. Namun, saat endoskopi konvensional pasien mengalami distress nafas dan endoskopi dihentikan. Pasien lalu menjalani endoskopi kapsul, dan ditemukan hiperemia dan erosi dari usus kecil sampai ke kolon. Diagnosa IBD ditegakkan dan pasien diberikan sulfasalazine 500mg tiap 24jam. Untuk mendapatkan gambaran usus kecil secara endoskopi, endoskopi kapsul merupakan metode yang dianjurkan. Kasus ini merupakan contoh keuntungan endoskopi kapsul, terutama pada diagnosis Inflammatory Bowel Disease.

Kata Kunci: *Penyakit Usus, Endoskopi Kapsul, Diagnosis, Manusia dan Penyakit*

INTRODUCTION

Capsule endoscopy was first introduced 15 years ago and is now the first line of to diagnose pathological condition of small intestine, and recently specific capsule endoscopy to view the esophagus and colon has begun to be developed, therefore the application of capsule endoscopy extends to include upper and lower gastrointestinal diseases. Nowadays, the popularity of capsule endoscopy among gastroenterologists is increasing with more than 2 million examinations worldwide.[1] Meanwhile in Indonesia, capsule endoscopy use was first reported in 2017 especially in Jakarta gastroenterology center.[2] There is currently no report of capsule endoscopy use in Surabaya. Hence, we need to understand the outlines of capsule endoscopy use in clinical practice as clinicians.

Crohn's disease is one of Inflammatory Bowel Diseases (IBDs) where the etiology is unclear. Meanwhile, multiple myeloma and Crohn's disease are uncommon. One study reported only 11 cases that have been reported in the literature.[2,3] One mechanism that is believed to be its underlying causes is chronic B-lymphocyte disorder. Here, we report a case of a patient with IBD who had a history of Multiple Myeloma who underwent a capsule endoscopy procedure.

CASE ILLUSTRATION

A 50 years-old man came with a main complaint of intermittent watery diarrhea which had been felt since 4 months ago. The patient reported watery diarrhea without stool, approximately 100 ml for each defecation, and a frequency of approximately 5-6 times a day. These complaints were felt intermittently with uncertain time intervals. The patient reported that the diarrhea occurred immediately after eating. No abdominal pain was felt. The patient also felt nauseous but with no vomit, had a decrease in appetite, and a weight loss of approximately 17 kg in the past 10 months. There was no history of cough, shortness of breath, or fever. No complaint in urination. The patient had an endoscopy examination performed before, but respiratory distress occurred which led to the halt of the examination process.

The patient had a history of multiple myeloma since 2016, had been on chemo, and was declared in remission. The patient had a history of hypokalemia with a history of potassium level 2.1 after the patient had diarrhea for seven times. The patient also had a history of GERD and regularly took PPI medication. History of diabetes and high blood pressure was denied by the patient. Allergy history was also denied.

Physical examination revealed that the patient's general condition was moderately ill but fully alert. Blood pressure was 130/80 mmHg, pulse rate was 63 beats per minute, respiratory rate was 20 beats per minute, and body temperature was 36.5^{o}C. Body weight was 49 kg, body height was 160 cm, therefore the BMI was 19.14 kg/m^2 with an impression of adequate nutrition. On head examination, the conjunctiva was not anemic, the sclera was not icteric, and the pupil was isochorous. Tonsils were normal and no sore throat was found. In the neck area no dilated veins were found; The trachea was centrally located, no increase in jugular venous pressure was found. Examination of the chest revealed symmetrical chest in static and dynamic state, normal left and right lung fremitus, sonor sound in both lungs, and no crackles or wheezing was found. On cardiac examination, ictus cordis was not visible nor palpable; the left border of the heart was at the fourth intercostal space and one cm lateral to the left mid-clavicular line and the right border of the heart was at the fourth intercostal space of the right sternal line. The first and second heart sounds were within normal limits with regular beats, no murmurs nor galops was found. On abdominal examination, flat abdomen was found during inspection, tenderness was found at epigastric area which radiated to the umbilicus during palpation, no enlargement of the liver and spleen was found, no mass was palpable, and no kidney ballotement was found. On percussion, tympanic sounds were found and on auscultation bowel sounds were within normal limits. Extremities were warm and no edema was found.

The initial laboratory examination results during admission were as follow: Hb 10.6 g/dL, HCT 30%, MCV 91 fL, MCH 32 pg, MCHC 32.4 g/dL, Leukocytes 4100/uL, Neutrophils 55%, Lymphocytes 14%, Platelets 303,000. Random blood sugar 113 mg/dL, BUN 10.0 mg/dL, Serum Creatinine 1.3 mg/dL, SGOT 10 u/L, SGPT 20 u/L, albumin 3.84 g/dL, direct bilirubin 0.12 mg/dL, total bilirubin 0.33 mg/dL, Sodium 132 mmol/l, Potassium 2.3 mmol/L, Chloride 103 mmol/L, Calcium 8.6 mg/dL, CRP 65.27 mg/L. HbsAg, Anti HCV, three-methods HIV test were found to be non-reactive. COVID-19 polymerase chain reaction (PCR) examination revealed negative result. Radiological examination with postero-anterior chest x-ray revealed no abnormalities.

Based on the patient's history, physical examination, and additional examinations, the patient's assessment was chronic diarrhea pro-evaluation and hypokalemia.

The patient was hospitalized and received intravenous (IV) fluid of Wida KN2 1000 ml/24 hours, two tablets of diagit each time the patient had diarrhea, and 600 mg of KSR tablets every 8 hours. The patient was planned to undergo endoscopy and colonoscopy for further evaluation and diagnosis.

COURSE OF DISEASE

Second Day of Treatment

The patient reported that the diarrhea had decreased and the patient's appetite had slightly improved. The patient's general condition seemed adequate and fully alert with GCS 456. Vital signs showed blood pressure of 120/60 mmHg, pulse rate of 98 beats/minute, respiratory rate of 20 beats/minute, temperature of 36.5^{o}C, oxygen saturation of 98% with room air. The patient underwent endoscopy on the second day, however the patient experienced respiratory distress during the endoscopy with a RR up to 40 times/minute. Hence, the patient was canceled for colonoscopy.

Third Day of Treatment

The patient was planned for capsule endoscopy examination. The patient's general condition seemed adequate and fully alert with GCS 456. Vital signs showed blood pressure of 127/70 mmHg, pulse rate of 72 beats/minute, respiratory rate of 20 beats/minute, temperature of 36.^{o}5C, and oxygen saturation of 98% with room air. Preparations were performed, starting from taking essential drugs two hours before the procedure or delaying it until four hours post-examination. One tablet of Xepaym was taken 30 minutes before the examination. While wearing the belt, antenna was attached to the recorder and the recorder was connected to the capsule **(Figure 1).**

The patient was asked to fast 12 hours before the procedure. After preparation had been completed, the patient was asked to swallow the capsule endoscopy with 150 ml of water **(Figure 1).** Before swallowing the capsule, the examinator ensure the capsules to be flashing and ready to record.

During the examination, the patient was not allowed to be close to magnetic area and perform any exercise to ensure that the tool could record properly. If the capsule was in the gastric area for more than one hour, prokinetic 10 mg and metoclopramide could be considered. The patient could drink clear liquids two hours after the examination. The patient received a light meal six hours after the examination. Capsule endoscopy could record up to 12 hours post-examination.

Fourth Day of Treatment

The patient's general condition seemed adequate and fully alert with GCS 456. Vital signs examination showed blood pressure of 121/71 mmHg, pulse rate of 82 beats/minute, respiratory rate of 20 beats/minute, temperature of 36.5^{o}C, and oxygen saturation of 98% with room air. The patient reported no complaint and the examination record had been obtained. At night, the patient said the endoscopic capsule had come out.

Fifth Day of Treatment

Patient complaints had decreased and reported no diarrhea occured. The patient's general condition seemed adequate and fully alert with GCS 456. Vital signs showed blood pressure of 130/60 mmHg, pulse rate of 87 beats/minute, respiratory rate of 20 beats/minute, temperature of 36.^{o}5C and oxygen saturation of 98% with room air. Endoscopic capsule results revealed hyperemia with erosion that was observed from the small intestine to the colon **(Figure 2 & 3).**

Figure 1. Patient is using the endoscopy capsule's recorder and endoscopy capsule is being swallowed by the patient and

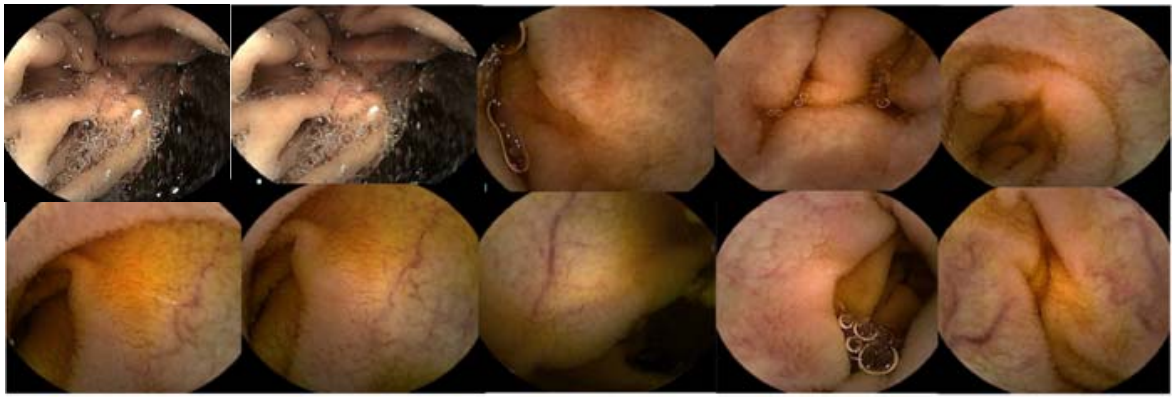

Figure 2. Telangectasia and Erythema was found on small intestine

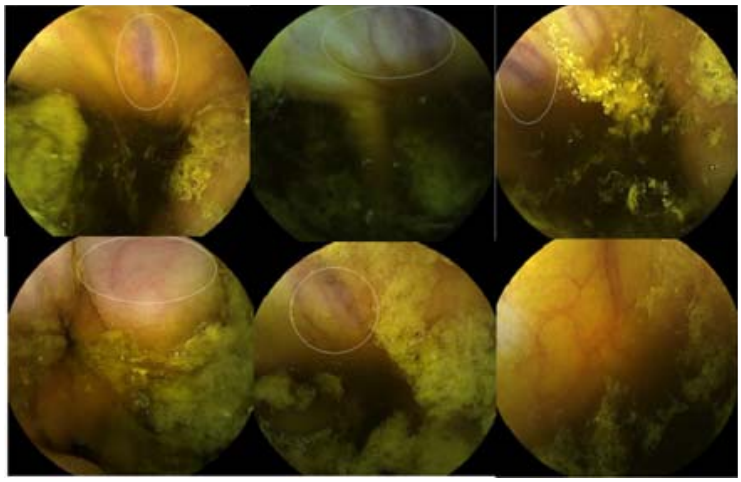

Figure 3. Angioectasia and Erosion was found on Colon

The patient was then sent home and received oral therapy of sulfasalazine 1x500 mg. The patient was scheduled for follow-up visit in gastroenterology outpatient clinic.

DISCUSSION

To date, the etiology of Crohn's disease and multiple myeloma has not been established, but one of the proposed pathogeneses of both diseases is impaired immunity and excessive proinflammatory cytokines production, especially interleukin 6 (IL-6) and interleukin 1b (IL-1b).[4,5] In Irritable Bowel Disease (IBD), secretory IgA and mucosal production as first line ofl mucosal protection is often suppressed. This causes a systemic response to antigen that could penetrate the intestinal mucosal barrier and activate B-lymphocytes and plasmocytes.[6] Chronic B-lymphocyte stimulation triggers monoclonal PC antibodies proliferation which could develop into monoclonal gammopathy ofl undetermined significance (MGUS).[7] It needs to be highlighted that inflammation that infiltrates the intestinal wall in Crohn's Disease does not only consist ofl lymphocyte, but mostly consists ofl plasma cells. In contrast, a genetic disorder is found in the form ofl MGUS in most cases ofl Multiple Myeloma.[8] This is consistent with the present case in which the patient had a history ofl multiple myeloma. The establishment ofl IBD diagnosis in this case was proven through capsule endoscopy examination results, where hyperemia and erosion from small intestine to the colon were found.

Capsule endoscopy is a non-invasive procedure that uses a swallowed and capsule-shaped miniature camera and is a diagnostic imaging tool ofl the small intestine. Gavriel Iddan, an electro-optical engineer from Israel, and Paul Swain, a Gastroenterologist from England, independently investigated the possibility ofl transmitting images from the digestive tract to an extracorporeal receiver by ingesting a wireless camera capsule .[9] In 1996, Paul Swain demonstrated that an ingested wireless capsule could wirelessly transmit images from a pig's stomach to an external

receiver. In 1996, an internal review by the board ofl the Royal Hospital in England allowed trials ofl capsule endoscopy prototype in humans. The first capsule endoscopy was introduced in 2001 by Iddan et al.[9] Since then, many new capsules have been introduced with better battery life, field ofl vision, and sharpness.

The capsule endoscopy system consists ofl (1) the capsule, (2) a wirelessly attached data recorder, and (3) computer software dedicated to downloading and processing the images recorded from the capsule. The capsule consists ofl (1) optical dome (2) lens support, (3) lens, (4) six LEDs, (5) metal-oxide silicon sensor, (6) two silver oxide batteries, (7) transmitter, and (8) antenna **(Figure 4).**

Patients should fast for 12 hours prior to capsule endoscopy. Laxatives will help to clear food debris, air bubbles, and bile. A meta-analysis ofl 12 studies comparing capsule endoscopy with and without laxatives revealed that patients on laxative preparations had better visualization and diagnostic performance compared to drinking clear liquids alone .[10] Another study concluded that laxatives were not recommended for routine administration ofl capsule endoscopy, except in certain conditions such as viewing the distal small intestine and diseases such as Crohn's disease (CD), where there is often fecalization proximal to the diseased area. It was also performed on the patient before the capsule endoscopy. The patient was fasted for 12 hours before the procedure. Xepaym, a class ofl laxative drug, was consumed 30 minutes before the procedure.

Current indications for capsule endoscopy in adults include the diagnosis ofl unexplained GI bleeding, chronic iron deficiency anemia, small bowel tumors, NSAID gastropathy, and for the diagnosis and assessment ofl treatment outcomes ofl celiac and Crohn's disease as seen in **Table 1.** Endoscopy is also used in the screening and surveillance ofl several syndromes such as familial adenomatous polyposis, Barrett's esophagus, and esophageal varices. In colon, capsule endoscopy is indicated when colonoscopy could not be completed and the patient is at moderate to high risk for sedation or has cardiopulmonary disease (12–14). In this case, we found that the patient met the criteria for capsule endoscopy. One ofl the indications was that conventional endoscopy could not be performed because the patient suffered from respiratory distress during conventional endoscopy process.

Table 1. Capsule Endoscopy Indication

In small intestine
• Investigate the source ofl unclear bleeding
• Evaluate iron deficiency anemia where a gastrointestinal source is suspected and conventional upper and lower endoscopy results are negative
• Crohn's disease: diagnosis and monitoring ofl disease activity
• Celiac disease: diagnosis and evaluation ofl refractory disease
• Assess mucosal recovery
• Polyposis syndrome surveillance
• Diagnosis ofl small intestine tumors
• Detects arteriovenous malformations
• Evaluating drug-induced injuries, i.e NSAID drugs
In esophagus
• Diagnosing Barrett's Esophagus
• Diagnosing variceal bleeding
In colon
• Screening ifl colonoscopy could not be completed
• Screening ofl patients with high risk ofl sedation
• Conventional upper endoscopy could not be performed

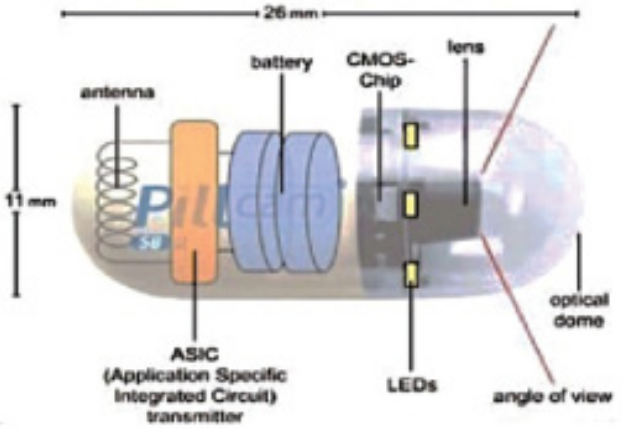

Figure 4. Capsule Endoscopy Scheme

Capsule endoscopy offers several advantages over conventional endoscopy procedure. This procedure could examine the small intestine, which could be difficult to reach during an upper endoscopy or colonoscopy.[11] Capsular endoscopy procedure could also detect intestinal abnormalities that do not appear on imaging tests such as CT scans or X-rays. In addition, this examination does not require anesthetic preparation. Conventional endoscopy procedure uses a flexible tube with a video camera that is passed through the digestive tract and involves some level of sedation. On the other hand, the capsule endoscopy procedure is as easy as swallowing a pill .[15] In this case, the advantage ofl endoscopy was no anesthetic preparation that was required. In addition, abnormalities in the small intestine could be found that could not be identified by conventional endoscopy.

Although capsule endoscopy is a safe and painless procedure, this procedure has several limitations. Capsule endoscopy could not be controlled by operator, biopsies could not be performed, and no treatment that could be conducted. In addition, capsule endoscopy has limited battery life and inability to accurately measure and localize lesions. Interpretation ofl capsule endoscopy is time consuming and requires extra attention, as abnormalities might be present in only a few frames .[16] On average, it takes about one hour to visualize all the images, where in general there could be more than 50,000 images .[17] In contrast to conventional endoscopy, patients could immediately receive endoscopy results right after the procedure. In capsule endoscopy, endoscopy results require a longer time because the images from capsule endoscopy still have to be edited, which takes longer time.

There is a risk ofl capsule retention in the small intestine, resulting in intestinal obstruction. This event could occur in areas where the small intestine is narrowed (stricture) .[18] Signs ofl small bowel obstruction include bloating, abdominal pain, nausea, vomiting, fever, difficulty swallowing and chest pain. Small bowel obstruction requires emergency medical treatment and might require surgery. Retention rates in suspected or known patients are approximately 4% to 8%, respectively.[19] Hence, it is important to know the contraindications ofl this procedure. In addition, we summarize some contraindications for using capsule endoscopy in **Table 2**.[20] In this case, we found no absolute or relative contraindications, therefore the patient met the requirements for capsule endoscopy.

Table 2. Capsule Endoscopy Contraindications

Absolute	Relative
• Bowel obstruction	• Cardiac pacemaker
• Extensive and active Crohn's disease	• Installed electro medical devices
• Bowel strictures	• Dysphagia
• Intestinal pseudo-obstruction	• Previous abdominal surgery
• Children <10 years	• Pregnancy

In this case, the diagnosis of IBD was established based on the capsule endoscopy findings which revealed mucosal hyperemia, telangiectasia, erythema, and erosion extending from the small intestine to the colon. These findings are consistent with typical endoscopic features of Crohn's disease or other forms of IBD. Therefore, despite the limitations of capsule endoscopy (e.g., no biopsy), the mucosal changes seen were strongly indicative of an inflammatory process involving the gastrointestinal tract, supporting the diagnosis of IBD in this patient.

CONCLUSION

A case has been reported ofl a patient with chronic diarrhea that lasted for four months. Diarrhea was followed by complaints ofl general weakness when the patient had continuous diarrhea. The patient then underwent conventional endoscopy and was planned for colonoscopy, but endoscopy could not be performed because the patient was experiencing respiratory distress. The patient underwent capsule endoscopy, where hyperemia and erosion from the small intestine to the colon were found. The patient was then given sulfasalazine 500 mg every 24 hours and was followed-up further through the outpatient clinic visits.

Conflict of Interest

The authors declare that there is no of any potential conflicts of interest related to this work.

Funding

This research did not obtain any specific financing from public, commercial, or non-profit entities.

Author Contributions

NR and IM contributed to data collection and manuscript drafting.

MR contributed supervised the study, provided critical revision, and approved the final version of the manuscript.

Acknowledgment

The authors acknowledge appreciation to the Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga for providing support in the production of this case report. We also express our gratitude to the patient for allowing us to share this case for educational purposes.

Data Availability Statement

No additional data are available. All relevant information is included within the article.

REFERENCES

1. Singeapl AM, Stanciul C, Trifan A. Capsule endoscopy: The road ahead. World J Gastroenterol. 2016 Jan;22(1):369-78.
2. Maulahela H, Fauzi A. Small bowel malignancy in a patient with obscure gastrointestinal bleeding in Cipto Mangunkusumo Hospital, diagnosed using double balloon enteroscopy: a case series. Indones J Gastroenterol Hepatol Dig Endosc. 2017;18(2):118–212.
3. aratina O v., Makarchuk PA, Vysotskaya LL. Crohn's Disease And Multiple Myeloma: A Clinical Case And Literature REVIEW. Koloproktologia. 2019 Aug 23;18(3(69)):84–95.
4. Brandtzaeg P, Halstensen TS, Kett K, Krajčil P, Kvale D, Rognum TO, et al. Immunobiology and immunopathology of human gut mucosa: humoral immunity and intraepithelial lymphocytes. Gastroenterology. 1989 Dec;97(6):1562–84.
5. Ito H. IL-6 and Crohns disease. Curr Drug Targets Inflamm Allergy. 2003 Jun;2(2):125–30.
6. Brandtzaeg P, Halstensen TS, Kett K, Krajčil P, Kvale D, Rognum TO, et al. Immunobiology and immunopathology of human gut mucosa: humoral immunity and intraepithelial lymphocytes. Gastroenterology. 1989 Dec;97(6):1562–84.
7. Carter A, Tatarsky I. The physiopathological significance ofl benign monoclonal gammopathy: A study ofl 64 cases. Br J Haematol. 1980 Dec;46(4):565–74.
8. Greipp PR, Lust JA. Pathogenetic relation between monoclonal gammopathies ofl undetermined significance and multiple myeloma. Stem Cells. 1995 Aug;13 Suppl 2:10–21.
9. Iddan G, Meron G, Glukhovsky A, Swain P. Wireless capsule endoscopy. Nature. 2000 May;405(6785):417.
10. Rokkas T, Papaxoinis K, Triantafyllou K, Pistiolas D, Ladas SD. Does purgative preparation influence the diagnostic yield of small bowel video capsule endoscopy?: A meta-analysis. Am J Gastroenterol. 2009 Jan;104(1):219–27.
11. Marshall CA, Cave DR. Preparation for video capsule endoscopy: A clear choice? Gastrointest Endosc. 2017 Jan;85(1):194–5.
12. Chetcuti Zammit S, McAlindon ME, Hale MF, Sanders DS, Healy A, Thurston V, et al. Small bowel ulcers on capsule endoscopy and their significance. Inflamm Bowel Dis. 2019 Apr;25(5):e55.
13. Esaki M, Matsumoto T, Ohmiya N, Washio E, Morishita T, Sakamoto K, et al. Capsule endoscopy findings for the diagnosis ofl Crohn's disease: a nationwide case-control study. J Gastroenterol. 2019 Mar;54(3):249–60.
14. Enns RA, Hookey L, Armstrong D, Bernstein CN, Heitman SJ, Teshima C, et al. Clinical practice guidelines for the use ofl video capsule endoscopy. Gastroenterology. 2017 Feb;152(3):497–514.
15. Pomerai D De, Daniells C, David H, Allan J, Duce I, Mutwakil M, et al. Wireless capsule endoscopy. 2000;405(May):417–8.
16. Friedrich K, Gehrke S, Stremmel W, Sieg A. First clinical trial ofl a newly developed capsule endoscope with panoramic side view for small bowel: A pilot study. Journal of Gastroenterology and Hepatology (Australia). 2013;28(9):1496–501.
17. Anastasios , K. Dabos, M. P. Keuche ET and M. How should we do colon capsule endoscopy reading: a practical guide. Therapeutic Advances in Gastrointestinal Endoscopy Review. 2021;14(6):1–15.
18. Gheorghe C, Iacob R, Bancila I. Olympus capsule endoscopy for small bowel examination. Journal ofl Gastrointestinal and Liver Diseases. 2007;16(3):309–13.
19. Rezapour M, Amadi C, Gerson LB. Retention associated with video capsule endoscopy: systematic review and meta-analysis. Gastrointest Endosc. 2017;85(6):1157-1168. e2.
20. Chauhan V, Tanwar A, Nijhawan S. Capsule Endoscopy: What We Know and What Is New in the Horizon. Journal ofl Digestive Endoscopy. 2019;10(02):083–9.