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ENDOSCOPIC ARGON PLASMA COAGULATOR(APC) IN TREATMENT OF INOPERABLE COLORECTAL CANCER

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Background: *In cases of inoperable colorectal cancer .palliative resection provides good relief of local symptoms but the mortality can be as high as 21%. A simple alternative is a proximal diverting colostomy, which only relieves symptoms due to obstruction & often involves a prolonged recovery period, encroaching on an already limited prognosis. Endoscopic alternatives including laser ablation has a considerable rate of complications . Argon plasma coagulation (APC) has been developed for flexible endoscopic application.*

APC is a new mode of non-contact electrocoagulation where high-frequency energy is transmitted to tissue by an ionized gas (argon plasma).

Aim of the work: This study focuses on the use of Argon Plasma Coagulator (APC) [N.B. which is not a laser] as a new modality in the management of inoperable colorectal cancer.

Patient & method: From January 1998 to March 2000, 16patients with colorectal lesions were referred for treatment with endoscopic Argon Plasma Coagulator (APC). There were 10 males & 6 females, the mean age of 64±6 years They were 13 patients with rectal carcinoma and 3 patients with sigmoid colon carcinoma. Biopsy samples were obtained from all patients and examined histologically. Patients were divided into two groups by the indications for Argon Plasma Coagulator(APC) treatment .Tumor factors included distant metastases, local unresectable recurrent disease these patients comprised (Group A). There were 13 patients in (Group A), of whom 6 had locally unresectable recurrent rectal carcinoma, 7 had distant liver metastases .Host factors included 3 patients and was named (Group B) they had advanced age(1 case), refusal to undergo surgery (1 case), or poor surgical risk due to underlying medical illnesses (1 case) .

Results: The number of Argon Plasma Coagulator(APC) treatments ranged from 2 to nine , with a mean of 4.0 . The total duration of the treatments ranged from 30 to 90 minutes, with a mean of 45 minutes . Each patient had one or more symptom or sign; Blood loss was seen in 12 cases & was completely controlled in eight (66.7%). before endoscopic recanalization could be achieved & was reduced in four patients (33.3%).Obstructive symptoms relieved in 5 out of 6 (83.3%).One patient developed complete obstruction before recanalisation could be achieved and needed urgent colostomy. In the ten patients with diarrhora bowel function returned to close to normal in 7 (70%) and was helped to great extent in the other three.

Faecal incontinence was almost completely controlled in 3 out of four (75%). Out of the 7 patients who complained of tenesmus relief was achieved after treatment in 5 patients(71.4%) and partial relief in two. Average hospital stay of 14 days per patient (range 7-31 days) to complete therapy. Argon Plasma Coagulator(APC) palliation provided satisfactory control of local symptoms in 14 of 16 (87.5%).

Conclusion: Argon Plasma Coagulator (APC) is an effective form of palliative treatment for rectal carcinoma in high-risk surgical patients and in patients with incurable disease.

INTRODUCTION

The primary modality of treatment for colorectal cancer continues to be surgical resection . In a personal series of 896 combined excisions, Goligher performed 710 (79 %) with a chance of cure and an operative mortality of only 2.8% [7], although in a more representative survey covering a large number of surgeons, the mortality for curative surgery was close to 10%[22].

However, in the remaining patients the disease is incurable owing to metastases or local invasion. Palliative resection provides good relief of local symptoms (obstruction, diarrhea, constipation, bleeding, pain, tenesmus, and rectal Discharge), but the mortality can be as high as 21%. A simple alternative is a proximal diverting colostomy, but this can only relieve symptoms due to obstruction. These procedures often involve a prolonged recovery period, encroaching on an already limited prognosis and may leave patients with a permanent colostomy with which they may not be able to cope [2].

Over the last 50 years in attempts to relieve the local symptoms in these high risk patients without subjecting them to major surgical intervention a range of non-surgical techniques has been explored.

These include radiotherapy, cryotherapy [14] and electrocoagulations [11] and Endoscopic transrectal resection [15] which have proved effective in many cases but all methods have their risks and limitaions.Endoscopic laser treatment is a modality that prooved its efficasy over the last decade using the ND:YAG laser [12,13]. Yet it has many disadvantages such as its high cost, its lack of easy portability, the need for protective glasses and its variable depth of penetration which carries a high risk of perforation. So its popularity among the Gastrointestinal endoscopists decreased.

This study focuses on the use of **Argon Plasma Coagulator (APC)** as a new modality in the management of inoperable colorectal cancer**.**

PATIENTS AND METHODS

From January 1998 to March 2000, 16 patients with inoperable colorectal lesions were referred for treatment with endoscopic Argon Plasma Coagulator (APC).

There were 10 males & 6 females, the mean age of 64±6 years.

They were 13 patients with rectal carcinoma and 3 patients with sigmoid colon carcinoma. Biopsy samples were obtained from all patients and examined histologically.

These patients were not considered candidates for surgical resection because of either tumor factors or host factors.

Patients were divided into two groups by the indications for laser treatment (Table 1).

Tumor factors included distant metastases, local unresectable recurrent disease these patients comprised (Group A). There were 13 patients in (Group A) of whom 6 had locally unresectable recurrent rectal carcinoma, 7 had distant liver metastases.

Host factors included 3 patients and was named (Group B) they had advanced age (1 case), refusal to undergo surgery (1 case), or poor surgical risk due to underlying medical illnesses (1 case).

An initial sigmoidoscopy was carried out to determine the size, position and consistency of the tumour and the patency of the bowel lumen. For those without obstructive symptoms the bowel was prepared before Argon Plasma Coagulator (APC) therapy with sodium picosulphate and magnesium citrate (Picolax, Nordic Pharmaceuticals). If any degree of obstruction was present, preparation was limited to the administration of a low enema (200 ml) followed by a rectal washout immediately before the procedure. Some patients required sedation with 5-10 ml of Diazepam and 50 mg Pethidine.None required a general anaesthetic.

Equipment & Technique:

Argon Plasma Coagulator (APC) delivery system for flexible endoscopy developed by ERBE, Inc, model APC300, Germany. APC units is easily relocated in operating rooms or endoscopy suites, it is independent of special local protective devices and cannot become maladjusted or lose its calibration due to movement also no eye protection is required. The APC300 controls the Argon gas flow from 2 Argon gas cyliders with automatic change-over, it monitors the available Argon supply through a symbolic display of the connected cylinders & their remaining volumes. (Fig. 1)

Inert Argon gas is delivered into the intestinal lumen through a small flexible catheter which resembles the outer sheath of the polypectomy snare (APC probe for gastrointestinal endoscopy –ERBE, Germany 2.3 mm diameter-length 2.2 M) (Fig.2)

The catheter is passed through the endoscope operating channel, similar to a polypectomy snare or biopsy device. An insulated wire run through the catheter and ends just before the tip of the catheter. Once the gas is flown in & the wire is activated with a standard foot switch through a special electrosurgical genetrator, causing the Argon gas to energize . The ionized gas is called the plasma, which merely dissipates if the plasma forms in the middle of the lumen away from tissue.

The argon plasma delivery system is utilized in a monopolar mode, requiring an electrical return plate to be placed onto the patient's skin, similar to monopolar electrosurgical therapy [9].

When the sheath tip closely approaches conductive tissue, an electrical spark forms from the tip to the bowel wall, completing the circuit for electron flow.The gap across which the spark jumps is dependent on the density of the gas in the lumen (controlled by a flow meter) and on the energy output of the generator. At low settings, the permissible gap is only a few millimeters. This is a non-cont;ct thermal modality which does not require the probe to touch the tissue at any time during its activation.

The depth of coagulum is variable and can , to a large extent, be controlled by the power output of the electrosurgical generator. During use of the heat producing argon plasma coagulator, the generated spark desiccates tissue. As the coagulum forms on the surface, continued application of the argon plasma to the same area will result in a shift of the electrical energy to an adjacent nondesiccated segment as current seeks a return pathway to the external return skin electrode. This results in a safety feedback cycle that does not permit deep tissue injury at one site even if current is given and the probe is not moved during thermal application. With the low power output settings used in the colon (40 watts), the tip of the probe must be relatively close to the bowel wall and will result in a burn depth of approximately 1mm. With higher current settings, a longer spark gap can be achieved along with deeper tissue injruy. The ability to penetrate several millimeters of tissue renders this modality useful for necrosis of carcinomas.

The main aim of therapy was to control local symptoms by debulking the intraluminal growth. ,as tissue necrosed by the Argon Plasma Coagulator(APC) sloughs to a depth of 2-3 mm in the few days after treatment.

In all cases, optimum tumour ablation was not possible in one session and the procedure was repeated (twice/ week) untill resolusion of symptoms.

All patients had their treatment sessions as an in-patient. Once satisfactory symptomatic relief had been achieved. patients were foIlowed up at intervals (once /4weeks)depending on their general condition, and treatment repeated if symptoms recurred.

Tumors were treated in an antegrade fashion until the colononcope could be passed through the lesion at subsequent sessions. Antegrade treatment involved starting at the most proximal edge of the lesion from the anal verge and continuing distally.

Table (1):

Group (A)		*Group (B)*	
Distant secondaries	7	*Poor risk*	1
		Refused surgery	1
Unresectable rec. carcinoma	6	*Old age*	1

Table (2):

Symptoms&signs	*Number of patients*	*Result after laser*
Bleeding per rectum	12	Stopped completely in 8 Reduced in 4
Partial obstruction	6	Relieved in 5 One needed colostomy
Spurious diarrheoa	10	Back to normal in 7 Reduced to great extent in 3
Tenesmus	7	Complete relief in 5 Partial relief in 2
Fecal incotenence due to diarrheoa	4	Controlled in 3 Reduced in 1(invasion of anorectal ring)

Each patient had one or more symptoms or signs

RESULTS

A total of 16 patients with colorectal carcinoma were treated with Argon Plasma Coagulator (APC).

The presenting symptoms & signs are shown in (Table 2).

The level of the lesion from the anal verge ranged from 6 to 25 cm, with a mean of 9.2 cm.

Six lesions were endoscopically polypoid, 2 ulcerated and 8 had both morphologies .

As regards the circumference of the lesion: Six patients presented with a circumferential obstructing carcinoma, which was defined as the inability to pass an 11mm diametere colonoscope beyond the lesion, three patients had tumor involving less than 50% of the lumen, and 7 patients had tumor involving more than 50% of the lumen.

The length of the lesion ranged from 1.5 to 7.5 cm, with a mean of 4.5 cm.

The number of laser treatments ranged from 2 to 9, with a mean of 4.0.

The total duration of the treatments ranged from 30 to 90 minutes, with a mean of 45 minutes.

The followup was done in the out-patient clinic on a monthly basis through proctosigmoidoscopy & any re-growth of tumor was treated eIectively.

Details of the patients symptoms & signs before and after laser therapy are given in (Table 2).

Blood loss was completely controlled in eight (66.7%). before endoscopic recanalization could be achieved& was reduced in four patients (33.3%) (Fig.3)

Obstructive symptoms relieved in 5 out of 6 (83.3%) (Fig.4) .One patient developed complete obstruction before recanalisation could be achieved and needed urgent colostomy.

In the ten patients with diarrhora. bowel function returned to close to normal in 7 (70%) and was helped to great extent in the other three.

Faecal incontinence was almost completely controlled in 3 out of four (75%).

Out of the 7 patients who complained of tenesmus. relief was achieved after treatment in 5 patients(71.4%) and partial relief in two average hospital stay of 14 days per patient (range 7-31 days) to complete therapy.

Laser palliation provided satisfactory control of local symptoms in 14 of 16 (87.5 percent). Of the two unsatisfactory results, one had very extensive local disease, and his frequency of incontinence was only slightly reduced by treatment, although this did help nursing care. The other was the patient who required an urgent colostomy. and died in hospital from disseminated malignancy.

One other patient with an anastomotic recurrence required an urgent laparotomy 10 weeks after treatment for small bowel obstruction due to on examination tumour spread, but the anastomosis was patent.

In the follow-up period: Eight patients had recurrent symptoms. In five of them there was minor bleeding in three in the last 3-4 weeks before dying of disseminated malignancy and brief episodes of pain in two others, which suggested obstruction, but which were short lived and responded to simple measures.

Three patients required further Argon Plasma Coagulator (APC) treatment 10 weeks after initial therapy (one with bleeding &two with obstruction). These responded satisfactorily to further Argon Plasma Coagulator (APC) sessions.

Eleven patients have died, from 2 to 30 weeks after initial Argon Plasma Coagulator (APC) therapy (mean survival 15 weeks). Ten died of advanced malignancy, and one with severe obstructive and restrictive airway disease died of pneumonia. Five patients (all of whom had small, non-circumferential lesions) are still alive and are currently free of bowel symptoms 32-50 weeks (mean 43 weeks) after treatment.

Complications:

Most patients passed small amounts of blood or mucus and a few complained of rectal discomfort after treatment, but thes symptoms settled in a few days. There were no patients with perforation or delayed haemorrhage.

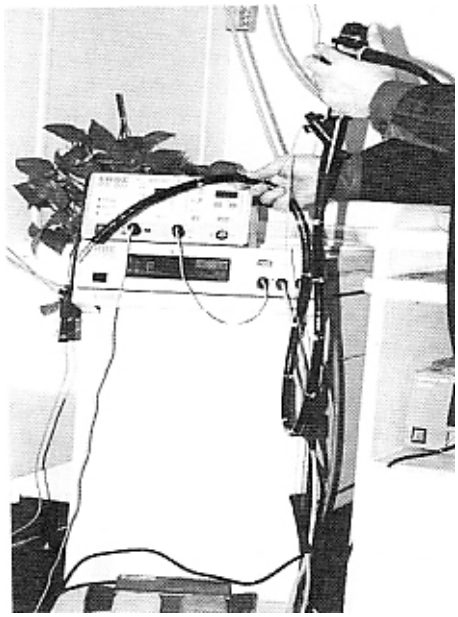

Fig. (1): The ERBE ENDOCUT and APC 300 system . This work station holds two Argon gas cylinders . The electrosurgical generator and Argon gas flow meter are controlled by foot switch application.

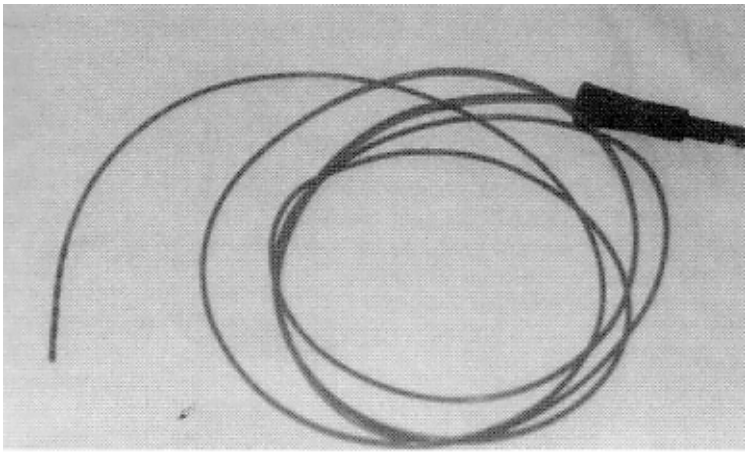

Fig. (2) :The flexible catheter available for introducing Argon into the intestinal tract . This catheter contains an electrically insulated wire to activate the Argon gas.

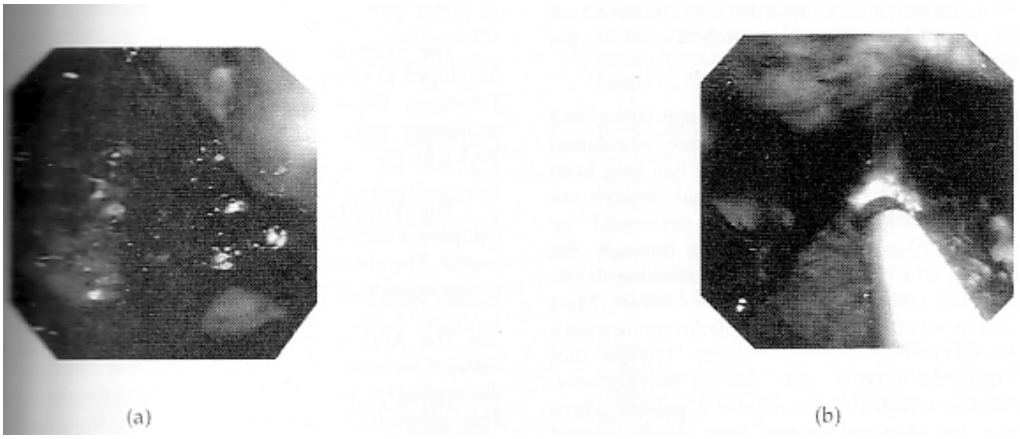

Fig. (3): The catheter for introducing Argon is shown while being used to stop bleeding from a recurrent rectal carcinoma.

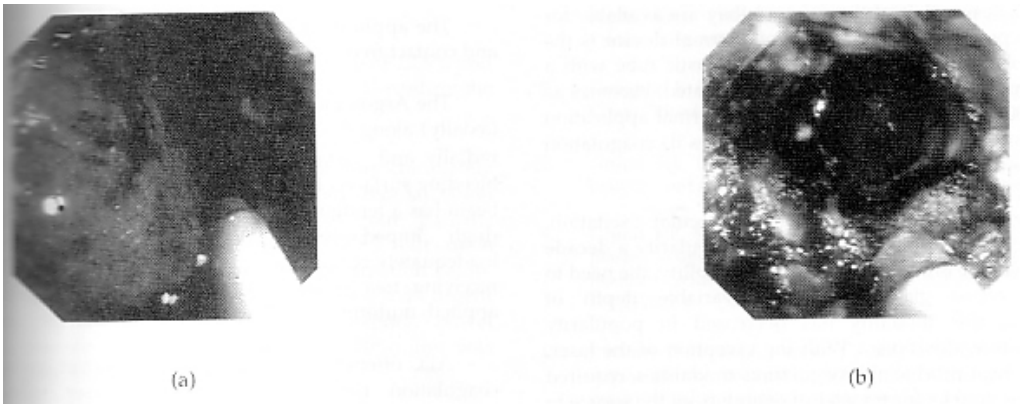

Fig. (4): The (APC) probe while fulgrating a recurrent rectal carcinoma causing partial intestinal obstruction. (a-before & b-after)

DISCUSSION

Although there has been a steady rise in the operability rate for rectal and distal sigmoid cancers over the last six decades there remains a small proportion of patients, about 7 percent, in whom surgical excision is not feasible [7]. For these individuals, the aim of treatment is to control the local symptoms caused by the tumour with the minimum of general upset either at the time of treatment or subsequently. Radiotherapy can produce excellent results for small rectal tumours, but the results for palliation of advanced rectal cancers are much less satisfactory [16-19]. Relief of pelvic pain and reduction of blood loss can be achieved but serious complications including soft tissue necrosis, haemorrhage and fistula.

mortability have been reported in 20% [17]. Others may develop acute problems such as Gl haemorrhage, cystitis, vaginitis and dermatitis which can be severe enough to curtail or modify treatment. In addition, a proximal diverting colostomy may be required during treatment and, although this is only temporary, it adds further to the patient's existing discomfort.

Thermal devices are available for coagulation and tissue destruction. In flexible endoscopy, tissue coagulation or fulguration of lesions is a technique that has long been used in medicine [13]. A variety of thermal devices are available for coagulation of tissues is performed by introducing a supplementary instrument through the accessory channel, which is also used for suctioning debris and fluid from the hollow structure of the GI-tract. Most tissue coagulation is performed in a monopolar mode with a ball-electrode, electrically activated biopsy forceps (hot biopsy), or utilizing a wire snare during polypectomy. Bipolar electrodes, which do not require a patient return plate, but pass the electrical current from closely spaced alternating positive and negative electrodes on the instrument tip, are useful for cautery of bleeding sites and superficial desiccation of tissues, and they are available for snare polypectomy devices. Another thermal device is the heater probe, which consists of a long plastic tube with a Tenon-coated metal tip, which, when activated, becomes as hot as 2000C. This, too, can be used for thermal application directly to tissues of the GI-tract but derives its coagulation power from heat generated in the metal tip.

Laser energy produces heat by molecular excitation. Laser use in the GI-tract enjoyed great popularity a decade ago, but because of its cost, its lack of portability, the need to wear protective glasses, and the variable depth of penetration, this modality has decreased in popularity among gastroendoscopist . With the exception of the laser, all of the heat-producing coagulation modalities required direct tissue contact for transfer of energy from the source to tissues.

When the results of the non surgical therapeutic modalities for treatment of inoperable colorectal carcinoma were reviewed together, certain generalization can be made All can provide symptomatic relief with minimal mortality yet there is a definite morbidity, although less than surgery yet reaching up to 13%[12].

A new thermal modality has recently been introduced to endoscopy : the argon plasma coagulator (APC). This is not a laser, with the only similarity between the APC and the argon laser being the name "Argon". Prior to its introduction to flexible endoscopy, activted Argon gas was used by surgeons to promote hemostasis and has been especially useful for treating the bleeding surface of the diaphragm or the liver following blunt dissection between these two organs during the operative phase of hepatic transplantation, The argon coagulation technique uses high flow Argon generator and a hand-held wand. The activated gas causes spark which effectively seals vascular oozing from a wide area o f the hepatic bed.

The delivery system for flexible endoscopy was developed in Germany in 1994 (ERBE, Inc., model APC300, Tubingen, Germany), and has earned a place in the endoscopy units of Europe and Canada, as well as New York City [9,6].

The Principle of Argon Plasma Coagulation APC equipment combines argon gas with a monopolar power source. The electrode in the argon channel of the applicator is connected to an electrosurgical generator.

The APC applicator ionizes the argon gas where it remains ionized approximately 2-10 mm distal to the tip of the applicator, lonized Argon gas is electrically conductive. This allows the current to flow between the applicator and the tissue. Current density upon arrival at the tissue surface causes coagulation.

The application of the energy to the tissue is uniform, and contact free.

The Argon plasma beam acts not only in a straight line (axially) along the axis of the applicator, but also laterally, radially and "around the corner" as it seeks conductive bleeding surfaces. Following physical principles, the plasma beam has a tendency to turn away from already coagulated (high impedance) areas toward bleeding or still inadequately coagulated (low impedance) tissue in the areas receiving treatment. This automatically results in evenly applied, uniform surface coagulation [21].

APC offers fundamental advantages over conventional coagulation methods including the laser: non-contact coagulation, efficient coagulation of large surface bleeding that shortens procedure time, it has the advantage of

uninterrupted coagulation as the electrosurgical current flows automatically to bleeding surfaces in the treatment area.

Limited maximum penetration depth (typically 3 mm) for better protection against perforation of thin walled anatomy,no vaporization, less carbonization, better wound healing, less smoke, better visualization [23].

The equipment is portable, utilizing a modified electrosurgical generator and a cylinder of argon gas. The apparatus is relatively inexpensive and is a valuable addition to the armamentarium of the gastroarterologist. The delivery catheter was approved by the FDA for flexible endoscopy in 1997. The endoscopic application has been available in Europe for several years and has earned its place in many endoscopy units throughout Europe [20,5].

Some complications may arise with the use of APC. Touching the activated probe to the mucosa may result in sudden and dramatic insumation of the sub-mucosa with gas introduced into the mucosa by a defect created by the spark. This is rapidly resorbed without sequellae.

Abdominal distention is infrequent, appearing especially during a long treatment session. An assistant must monitor the degree of distention by direct palpation of the abdomen. Suction suffices to deflate the distended bowel [10].

The Argon plasma coagulator is a new modality shown to be comparable & superior to the other thermal coagulation devices especially the laser.

The centers that have this capability report relief of symptoms in 80% to 90% of patients, 0% to 1% mortality, and 1% to 19% morbidity. Control of bleeding lesions and relief of obstructing lesions have been reported in 90% and 60% of patients, respectively [12,3,18,2].

Our success rate of 87.5%, morbidity rate of 12.5% and mortality rate in relation to this technique of 0% confirm the results of other centers.

Blood loss was seen in 12 cases & was completely controlled in eight (66.7%). before endoscopic recanalization could be achieved & was reduced in four patients (33.3%).Obstructive symptoms relieved in 5 out of 6 (83.3%).One patient developed complete obstruction before recanalisation could be achieved and needed urgent colostomy. In the ten patients with diarrhora. bowel function returned to close to normal in 7 (70%) and was helped to great extent in the other three.

Faecal incontinence was almost completely controlled in 3 out of four (75%). Out of the 7 patients who complained of tenesmus. relief was achieved after treatment in 5 patients(71.4%) and partial relief in two .The average hospital stay was 14 days per patient (range 7-31 days) to complete therapy. Argon Plasma Coagulator (APC) palliation provided satisfactory control of local symptoms in 14 of 16 (87.5 %).

CONCLUSION

The argon plasma coagulator is a useful device for delivering thermal energy in a noncontact mode to the intestinal wall. its ease of use, low cost, and applicability in several clinical situations will earn it a place in every endoscopic unit.

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