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COMPARISON OF THE EFFICACY OF ARGON PLASMA COAGULATION AND CONVENTIONAL THERAPY IN MANAGEMENT OF BLEEDING SOLITARY RECTAL ULCER

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Abstract

Background and Objective: Solitary rectal ulcer syndrome (SRUS) is an uncommon disorder of evacuation with unsatisfactory outcome by conventional treatments. The aim of this study is to investigate the efficacy of Argon Plasma Coagulation (APC) in controlling bleeding and eventual healing of these ulcers.

Materials and Method: Overall 99 SRUS patients included and randomly divided into 2 groups: group A treated with APC sprayed directly on ulcers with a focused fashion in weekly intervals and group B managed with conventional methods including high fiber regimen, laxative, using of sitting bath and explanation of disease nature. Inclusion criteria was presence of rectal ulcer with histological features of SRUS confirmed by pathologist and exclusion criteria were any history of rectal ulcer that did not match with histological criteria of SRUS, uncontrolled DM and history of cancer.

Results: Response to therapy was 76% in group A and 23% in group B. after 3 months, continued healing in group A and B were 88% and 12% respectively. There was a significantly higher control of bleeding ($P < 0/004$), ulcer healing ($p < 0/0001$) in the APC-treated group.

Conclusion: APC is a useful method for not only bleeding control but also healing of SRUS in comparison with conventional therapy.

Key words: APC, Conventional therapy, RUS, Behavior treatment

Introduction

Solitary Rectal ulcer syndrome (SRUS) is a chronic and benign disease of young people that rectal ulcer is usually occurred due to excessive and abnormal straining during the act of defecation (1, 2). The term SRUS (solitary rectal ulcer syndrome) is a wrong naming, but is common, because several ulcers are seen in 40% of patients, and only 20%

of patients have solitary ulcers, and the waste in terms of shape and size is as a mucosal hyperemia, solitary ulcer, anal ulcers or polypoid lesions pretending like cancer. Histologic states of SRUS is very significant, which include fibro muscular of lamina propria changes, and smooth muscle fibers stretched into hypofid layer of mucosa muscularis of colonic mucosa towards the lumen of colon (3). In the treatment of this disorder, patient training (defecation behavior), preservative acts are fixed and initial points of treatment (4). Studies also have shown that most patients do not give a definite answer to current conventional treatment (behavioral modification, biofeedback and topical treatments and surgery) (4-7). But the use of new methods of treatment such as APC (Argon, plasma, coagulation) has attracted researchers' view in recent years.

In the therapeutic method of APC, a non-contact electrocoagulation means is used where the current monopole with high frequency guided by ionized argon gas for coagulation of tissues and mucosal ulcers. APC may cause ulcer healing by squamous regeneration and Re-epithaliation mechanism (22). Since APC therapy have been performed in the world in just two or three studies (1, 23), therefore this therapeutic method looks very new. Also in Iran, only one case is running by Dr. Falah and colleagues at Tehran University, the results of which have not been published yet. According to a few studies done on the effectiveness of APC compared to current treatments and considering to good effectiveness of APC has been reported in some cases, we decided to conduct a study aimed to compare the effectiveness of APC with current treatments to heal Solitary Rectal ulcer in patients with SRUS. This study aims to examine the impact of APC on bleeding control and ulcer healing in SRUS and innocuous of this type of treatment, and comparing it with conventional therapeutic methods.

Materials and Methods

This study was done in terms of experimental, and in type of Randomized Controlled trial (RCT) on 99 patients with singular rectal ulcer syndrome (SRUS) referred to Ahvaz Imam Hospital, Iran during years of 2010-2013. Patients with malignant ulcers (Malignant) and ulcers that were histologically without SRUS nature were excluded from the study.

Patients were randomly assigned into two groups of conventional treatments (58 persons) and receiving conventional treatments along with APC (41 persons). At first all patients with SRUS eligible to participate in the study, were tested on arrival by laboratory tests of CBC diff, liver tests (AST, ALT, Alk pho), coagulation profile (PT-PTT-INR), (ESR- CRP) and S / E as well as total colonoscopy or rectosigmoidoscopy (if they already have total colonoscopy) to diagnose SRUS as well as other causes of rectal bleeding and comorbidities in this population to be rejected; and after

seeing the nature, size and number of SRUS ulcers, they were assigned randomly and in terms of odd and even in one of the interventional groups (APC plus conventional treatments) or control group (under conventional treatments group).

Conventional treatments in the control group were: behavioral therapy, enema with sucralfate (four tablets of 500 mg powdered in 15 cc of normal saline every night before bedtime), using high-fiber diet and psyllium powder (one to three times a day if having constipation). Then all patients in the control group were visited at four-week intervals in six sessions averagely, and at the end rectosigmoidoscopy were performed on them again to see rectal ulcers, that in case of ulcers healing, this time was considered as End point of Treatment

If ulcers did not heal and there were signs of bleeding on endoscopy performed after six sessions visit, these individuals were considered as people who have not responded to treatment (Non-Responder). Then patients improved by conventional treatments that have reached to the end point of treatment, were examined again by rectosigmoidoscopy in order to prove the continuation of ulcers healing or recurrence of ulcers in 3 months later.

In the group treated by APC along with conventional treatments, APC was performed with four-week intervals in terms of outpatient in order to control bleeding and to heal ulcer. If there were no ulcers healing after six sessions, their ulcer lesion was considered as Failure to treat.

If ulcers healing were achieved before the end of six sessions of APC, this time was considered as Treatment end point for this group of patients. This Group was reassessed within 3 months after response to treatment with rectosigmoidoscopy, and the continuous healing of ulcer or ulcer recurrence were assessed in these patients. Patients Group treated with APC was been comparing in parallel with patients receiving conventional treatment (control group). Information after collected by SPSS software was recorded and analyzed statistically in significance level of 0.05. Description of obtained information was done through frequency tables and related diagrams. Frequency and percentage were used to describe the qualitative characteristics, and chi-square and Mann-Whitney U test were used for qualitative variables.

Before entering the study, while explaining the possible risks of APC therapeutic method, written consent was obtained from all patients. Code of ethics related to research project of number U-90196 is: ETH-307

Results

In this study, 99 patients with rectal bleeding symptoms entered Clinical Randomized Controlled trial for 2.5 years, 58 patients of these numbers were assigned in the control group and 41 patients were assigned in the group receiving AP

and conventional treatments. The average age of patients treated with APC and conventional treatments was 30.73 ± 14.75 , and Group under conventional treatments was 31.78 ± 13.96 . Age range in both treatment groups was 31 to 32 years old. Gender percentage in both treatment groups was 56% male and 43% female. 21% of patients used foreign toilet, and 78% of them used Iranian toilet. About 30% of patients had spiritual-psychological disorders that were under medication therapy. The number of defecation mostly varied between once a day to once in four days. Time of straining for defecation was mostly between three to six minutes, and the average time for straining was about 5.56 minutes, and more than 55% of patients had mucus excretion, and 60% of them used finger in defecation in order to facilitate (Digital Evacuation).

About 76% of the patients had sensation of incomplete defecation, and about half of the patients had pain around the anus. In 58% of cases, patients were using laxative before entering the project, and 67% of patients with SRUS in this study did not use certain drugs such as (NSAIDs, cardiovascular, aspirin, Plavix and anti-depressant). 93% of patients had no comorbidity. The diameter of defecation had been reduced just in 15% of cases (Table 1).

Distance of lesion and rectal ulcer from the anal verge was 5 to 8 cm in 60% of cases, and the ulcer shape in 79% of cases was flat, and in 21% of cases was polypoid. APC performing average in group treated with APC was about five to six sessions, and the onset of symptoms until the diagnosis of solitary rectal ulcer syndrome was one to nine years that in fact, the average time from symptom onset to diagnosis of solitary rectal ulcer syndrome was about four years (4.01 ± 1.89); the frequency of the number of ulcers in patients with SRUS was more than one number in 45% of cases (table 2).

In terms of features of ulcer; 72% of ulcers had clean base, and 16% of cases had bleeding during rectosigmoidoscopy, and only 11% of cases had arrhythmia. Response to treatment in the control group was 29%, and in the group receiving APC was about 76%. Also the continuation of ulcers healing after 3 months in the control group was 10%, and in the group treated with APC was approximately 70% (Table 3).

Chi-square test results showed that there is a statistically significant difference between responses to treatment. Therefore, the APC approach is more efficient for treatment of SRUS than the conventional treatments ($P < 0.001$) (Table 3).

The results of Chi-square test showed statistically significant difference between the two treatment groups in terms of continuity of ulcers healing ($0.05 < 0.05$). The continuity of ulcers healing in the APC group is more than the group receiving the conventional treatments ($P < 0.001$) (Table 4).

Mann-Whitney test results showed that bleeding control percentage showed a significant difference ($P < 0.004$) in both treatment groups. So that control of bleeding was more in the group receiving APC plus conventional treatments in comparison with the group receiving conventional treatments but the results about pain variable that there is no statistically significant difference between the two groups about pain relief ($P < 0.36$) (table 5).

Rectosigmoidoscopy observations in follow-up after treatment did not show any complication caused by APC in 41 patients treated with it. Independent t test results showed that there is no statistically significant difference between the hemoglobin mean ($P < 0.6$), hematocrit ($P < 0.5$), BUN ($P < 0.8$), PT ($P < 0.8$), INR ($P < 0.7$), ESR ($P < 0.7$), CRP ($P < 0.8$), AST ($P < 0.8$), ALT ($P < 0.6$) and OB ($P < 0.9$) in two treatment groups (Table 6).

Discussion

The results of this study showed that response to treatment is 29% in conventional treatment group, and 76% in the group receiving APC plus conventional treatments. Also the continuation of ulcer healing after 3 months in the control group was 10%, and in the group treated with APC was about 70%. Accordingly, chi-square test results showed that there is a statistically significant difference between responding to treatment.

The APC approach, in comparison with conventional treatments, is more efficient for the treatment of SRUS ($P < 0.001$). This finding is consistent with the findings of the Somani et al.'s study (2010). Because they had also assessed the effectiveness of APC in the treatment of SURS, bleeding control and full ulcer healing positively compared to conventional treatments ($p < 0.036$) (1).

In addition, our results are also consistent with the case results' report of Stoppino (2003). They also used APC to treat SRUS in a 64-year-old woman, and assessed its effectiveness in the treatment of ulcer, bleeding reduction, and pain relief positively during follow-up (23). But these findings is inconsistent with the case reports' results of Gopal et al. (2001).

They reported a case that APC was not effective in treating Solitary Rectal ulcer syndrome, and they had to do surgery to treat these lesions. This issue caused their doubt about the effectiveness of APC for the treatment of Solitary Rectal ulcer syndrome (24). In addition, Norton and colleagues demonstrated that APC may even cause injury in propria muscularis layer in laboratory animals (25).

In general, few reports about preference of APC and conventional treatments has been reported compared to mere use of conventional treatments that its reason may be due to the low incidence of this disorder in the general population (1 to 3.5 per 100 thousand people) (26).

Chi-square test results showed that there is a statistically significant difference between continuations of ulcer healing in the two groups. Continuation of ulcer healing in the group treated with APC is more than conventional treatments ($P < 0.001$). These findings are also consistent with the study results of Somani et al. (2010) (1). Because the results of their study showed a significant relationship between full ulcer healing and treatment with APC ($P < 0.036$).

The results of the present study on the better impact of APC compared to conventional treatments on SURS treatment showed that APC stops bleeding ($P < 0.023$). As stopping bleeding in the Group receiving ACP plus conventional treatments had been more than the group receiving conventional treatments

The findings of the present study are consistent with the study findings of Jarrett et al. (2004). Because they found that the amount of rectal mucosal blood flow has been decreased significantly by Laser Doppler Mucosal Flowmetry in patients with SRUS before and after biofeedback therapy (6). in the study of Somani et al. (2010) and case report of Stoppino, the effectiveness of APC to stop the bleeding, rectal pain relief, and lack of using pain reliever could improve the quality of their life (1, 23).

In addition, the results of endoscopy showed depth reduction and ulcer healing in some areas of rectum. Moreover, based on our study results and compare it with the study results of Simsek (2004) and colleagues in Turkey, it can be stated that the efficiency of APC for the treatment of SRUS is comparable to the effectiveness of surgery. Because, according to their study, the surgery had caused full ulcer healing in 74% of patients (5). In our study the effectiveness of APC was about 70%, which is similar to surgery results.

The present study results on the speed of ulcer healing showed that the speed of ulcer healing in the group receiving APC plus conventional treatment is faster than the group receiving conventional treatments ($P < 0.0001$). The findings of the study are also consistent with the study finding of Somani, et al. (2010) (1).

Bu the results showed about the pain variable that there is no statistically significant difference between the two groups about pain relief ($P < 0.36$). This finding is also consistent with the study results of Somani et al. (2010). Of course, the reason of lack of relationship between pain relief and APC is related to research data.

Since from the beginning of the entering samples in the study, pain had been reported in very few cases and there was not any difference between the number of people in the two treatment groups before and after study. On this basis we cannot judge about the lack of impact of APC on pain. Therefore in order to prove this claim, further studies on patients who have pain would be helpful.

Rectosigmoidoscopy observations in follow-up after treatment did not show any complication caused by APC in 41 patients treated with it. Due to the lack of similar research in the field of APC complications on the rectum, cannot claim about rejection of complication being with APC treatment. Therefore, further researches are required in order to prove the lack of complication with APC.

Conclusion

Generally the results showed preference of APC for treatment of SRUS. Previous studies have shown that biofeedback causes SRUS progress compared to high-fiber diet and the use of sucralfate enema. But a recent study shows the more effectiveness of APC than conventional treatments.

Table-1: Frequency distribution of clinical variables to distinguish of treatment groups in patients with SRUS admitted to Imam Hospital in Ahvaz during 2010-2013.

group Variable	Conventional treatments		treatment of APC+Conventional treatments		total	
	Number	percentage	Number	percentage	Number	percentage
Frequency of BMs	0	0	0	0	0	0
More than once per day	13	20.7	10	23.5	23	23.2
once a day	10	17.2	7	17.5	17	17.1
Every other day	8	14.8	7	17.5	15	15.1
Every three days	10	17.2	7	17.5	17	17.1
Every four days	0	0	5	12	5	5.1
Every five days	8	14.8	0	0	8	8.2
Every six days	3	5.1	0	0	3	3
Once a week	3	5.1	5	12	8	8.2
More than a week	3	5.1	0	0	3	3
Total	58	100	41	100	99	100
time of straining for defecation (per minutes)	0	0	0	0	0	0
2	3	5.2	3	5.7	6	6.16
3	8	13	3	5.7	11	11.11
4	8	13	5	12.4	13	13.13
5	15	27.3	9	23.8	24	24.24
6	8	13	0	0	8	8.08
7	8	13	5	12.4	13	13.13
8	0	0	0	0	0	0
10	8	15.5	16	40	24	24.24
Total	58	100	41	100	99	100
drug use related to diseases apart from SRUS	0	0	0	0	0	0
	37	63	27	66	64	61.7
	3	5.4	0	0	3	2.94

Lack of drug use	3	5.4	0	0	3	2.94
NSAIDS	3	5.4	2	4.8	5	5.88
Heart drug	6	10	2	4.8	8	8.82
Aspirin and Plavix	3	5.4	5	12.2	8	8.82
S-ASA antidepressants	3	5.4	5	12.2	8	8.82
Sucralfate	58	100	41	100	99	100
Total						
Mental disorders	0	0.	0	0	0	0.
Yes	15	27.6	15	34.1	30	30.3
No	43	72.4	26	65.9	69	69.7
total	58	100	41	100	99	100
Associated disorders						
having no disease	52	91.4	39	97.7	91	91.50
Diabetes	0	0	0	0	0	0
stroke	0	0	2	2.3	2	2.44
Cardiovascular	6	8.6	0	0	6	6.06
Total	58	100	41	100	99	100
Duration of symptoms (per year)	0	0	0	0	0	0
0	2	12.8	1	6.3	3	8.8
1	3	17.5	2	12.4	5	14.7
2	4	22.9	2	17	7	20.6
3	4	22.9	3	17	7	23.5
4	4	17.5	4	24	8	17.6
5	3	0	3	17	6	2.9
6	0	6.4	1	6.3	1	11.9
7	1	0	3	17	4	0
9	0	0	0	0	0	0
total	17	100	17	100	34	100
Diameter of output feces						
decreased	8	15.5	5	14.6	13	13.13
non-decreased	50	84.5	36	85.4	86	86.87
Total	58	100	41	100	99	100

Table-2: Frequency distribution of Specifications of ulcers in patients with SRUS admitted to Imam Hospital in Ahvaz during the years of 2010-2013

Frequency	Number	percentage
Specifications a wound		
Ulcer diameter (cm)		
1	31	31.3
2	33	33.3
3	19	19.2
4	6	6.1
Circumferential	10	9.1
total	99	100
Form of ulcer		
Flat	79	79.8

Polypoid total	20 99	20.2 100
Number of ulcers		
1	53	53.5
2	24	24.5
3	10	10.5
4	4	4.5
5	6	6.5
7	2	2
total	99	100
Specifications of ulcer		
With bloodshed	16	16.2
Stand cleaning	72	72.2
Erythema	11	11.1
total	99	100
Lesion distance from the anal of Voraj		
2	2	2
5	21	21.2
6	19	19.2
7	24	24.2
8	16	16.2
9	5	5.1
10	10	10.1
12	2	2
total	99	100

Table-3: Comparison of response to treatment between the two treated groups of conventional and APC in patients with SRUS admitted to Imam Hospital in Ahvaz during the years of 2010-2013.

Response to APC of Therapy Group	Yes		No		total		Chi-square test and p-value results
	Number	percent	Number	percent	Number	percent	
Under the conventional treatments	17	29.3	41	70.7	58	100	x ² = 20.61 (P<0.001*)
Under the treatment of APC	31	75.6	10	24.4	41	100	

Table 4: Comparison of ulcer healing continuance between the two treated groups of conventional and APC in patients with SRUS admitted to Imam Hospital in Ahvaz during the years of 2010-2013.

ulcer healing continuance Group Therapy	Yes		No		Total		Chi-square test and p-value results
	Number	percent	Number	percent	Number	Percent	
Under the conventional treatments	6	10.3	52	89.7	58	100	x ² = 38.32 (P<0.001*)
Under the treatment of APC	29	70.7	12	29.3	41	100	
total	35	35.4	64	64.6	99	100	

Table-5: Comparison of some clinical indices of between the two treated groups of conventional and APC in patients with SRUS admitted to Imam Hospital in Ahvaz during the years of 2010-2013.

Group Parameters	APC + conventional treatments	conventional treatments	Mann-Whitney test (p-value)
Bleeding from the rectum	(100%)41	(43.1%) 25	*(z=26 ,P<0.004)
Improvement in pain around the anus	(83.5%)34	(62%)36	*(z=1.2 ,P<0.36)

Table-6: Distribution amount of blood hemoglobin in APC in patients with SRUS admitted to Imam Hospital in Ahvaz during the years of 2010-2013.

Mean±S.D	Amount Laboratory Index
13.406 ± 1.44	Hb
40.254 ± 4.40	Hct
20.01 ± 6.79	Bun

0.993 ± 0.22	Cr
12.646 ± 1.09	PT
1.058 ± 0.11	INR
14.16 ± 4.27	ESR
14.16 ± 7.33	AST
23.11 ± 6.90	ALT

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