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The tissue effect of second generation argon plasma coagulation (VIO APC) in comparison to standard APC and Nd:YAG laser in vitro

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Abstract

Background : **The aim of this study was to evaluate the effect of 2nd generation argon plasma coagulation (VIO APC) with respect to the tissue destruction capacity, and to compare it with standard APC and Nd:YAG laser.**

Methods : **2nd generation APC (VIO APC2, Erbe, Germany), standard APC (APC 300/Erbotom ICC 200, Erbe) and Nd:YAG laser (KTP/YAG XP 800 ; Laserscope, San Jose, California) were applied in 35 porcine livers. Using APC, power settings (30-120 W), application time (2 and 5 sec) and gas flow (1 and 2 l/min) were varied. Using Nd:YAG laser, 30-60 W were applied (flow 2 l/min). Diameter and depth of tissue coagulation were evaluated.**

Results : **Using VIO APC, maximum coagulation depth was 6mm (maximum diameter 15 mm). In comparison to standard APC, the coagulation effect was significantly higher ($p < 0.001$). There was no significant difference in the mean depth achieved by VIO APC and Nd:YAG laser using 30- 60 W and an application time of 2 sec ($p < 0.05$). Using maximum energy available for the 2 systems, maximum depth achieved by VIO APC (6 mm) was higher than the one caused by Nd:YAG laser (4 mm).**

Conclusions : **VIO APC was more effective than standard APC. Using medium power and a limited application time, it was as effective as Nd:YAG laser. The high effectiveness of VIO APC should be a topic of clinical education.** (Acta gastroenterol. belg., **2007**, 70, **352-356**).

Key words : VIO APC, argon plasma coagulation, Nd:YAG laser, porcine liver model.

Introduction

Argon plasma coagulation (APC) is a method of contact-free electrocoagulation in which energy is transmitted to the tissue through ionized argon gas. Initially developed for the surgical arena, this device has seen an ever-expanding role in therapeutic endoscopy (1-5).

Coagulation depth achieved by APC is described to be mainly a function of the power setting, the duration of the application, and the distance from the target tissue (6). Generally, the zone of coagulation is 1-3 mm. The physical properties of the incident tissue also may play a role in determining the depth of tissue injury. Norton *et al.* (7) used a porcine model to compare the incidence of deep tissue injury, respectively the damage of the deep muscle layer for a variety of endoscopically directed thermal devices.

The compact, mobile and easy to handle device, and its relatively low cost favour the choice of APC over comparative treatment modalities, such as Nd :YAG laser, for various forms of gastrointestinal pathology. However, in comparison to the Nd :YAG laser, standard APC appears to be less effective in palliative tumour reduction, which resulted in a high re-treatment rate of up to 21 treatment sessions in stenosing ooesophageal cancer (8). On the other hand, the high efficacy of APC in the treatment of superficial lesions such as vascular lesions has been shown (8-17). Now, an APC system of the second generation (VIO APC) promises to overcome the drawbacks of previously offered APC devices.

In contrast to standard APC and Nd:YAG laser, the thermic effects of VIO APC have not been investigated yet. The aim of this study was to evaluate for the first time the tissue effect of this second generation APC system, and to compare it with a standard APC system and Nd:YAG laser in a parallel-group trial.

Materials and methods

Thirty-five porcine livers were obtained from the slaughter house and were kept in a sealed polythene bag until testing. All specimens were tested within 6 hours of acquiring.

An APC system of the second generation (VIO 300 D with APC 2, Erbe, Tuebingen, Germany), a standard APC device (APC 300/Erbotom ICC 200, Erbe, Tuebingen, Germany), and a Nd:YAG laser system (KTP/YAG XP 800 ; Laserscope, San Jose, California) were used for the study.

Power settings of 30, 40, 50 and 60 W were used during the application of the Nd:YAG laser. 70, 80 and 99 W (maximum energy level available) were used additionally during the application of standard APC (APC 300/ICC 200), and 120 W (maximum energy level available) additionally during the application of VIO APC (VIO 300 D with APC 2).

The argon gas flow was varied (1 and 2 l/min). The power setting from 30 to 40 W was defined as the low energy level, and the power setting from 50 to 70 W was

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defined as the medium energy level. A power setting of at least 80 W was defined as the high energy level.

The 2nd generation APC system offers several modes. The 'Pulsed APC' mode (pulsed 1 and 2) was used for all applications of VIO APC and the comparison in this study. The advantage of this APC mode is that each pulse contains a number of single bursts. The power is set by varying the number of bursts per pulse, and the voltage can be maintained at a high value in order to ensure stable plasma conditions even at a low power setting. The mode 'pulsed 1' had a pulse rate of 1.2/sec. 'Pulsed 2' was defined by a pulse rate of 16/sec. The modes 'pulsed 1' and 'pulsed 2' were used for each individual energy level and gas flow level.

The tested porcine liver was laid on a commercially available disposable return electrode plate (neutral pad). The probe being used had a diameter of 2.3 mm. It was held securely above the tissue in a clamp. The probe tissue distance was constantly 5 mm. A probe tissue angle of 90 degrees was used. The distance from the border of one coagulation area to another was at least 30 mm. The period of time during a coagulation arc was seen to pass from probe to tissue was defined as application time and varied (2 and 5 seconds of constant gas flow). The coagulation arc was noted to be a clearly visible, all or none phenomenon. Using the two APC devices, this was repeated on 35 occasions for each energy level (30-120 W), gas flow level (1 or 2 l/min) and mode (pulsed 1/2 using VIO APC). Using the Nd :YAG laser, this was repeated for 10 occasions for each energy level. Each individual porcine liver was large enough for one application of each combination of power and pulse duration, gas flow and mode (if available, depending on the device used).

The maximum diameter of tissue destruction on the liver surface was analyzed macroscopically using a calliper. Then, after the incision of the liver surface using a surgical knife at a line following the maximum diameter of each individual lesion, the depth of the tissue destruction was evaluated in the same way.

Statistical analysis

The aim of this study was to test the effect of argon plasma coagulation (APC) on porcine liver tissue using a 2nd generation APC system (VIO APC) in comparison to standard APC and Nd :YAG laser in a parallel-group trial. The primary target criteria were depth and diameter of tissue destruction. Arithmetic means, standard deviation, minimum and maximum were reported, depending on the scale level of the characteristics. A repeated measures analysis of variance (tests of hypotheses for between subjects effects) was performed (statistical analysis system, version 8.2, SAS institute Inc., USA) to compare tissue effects of the different devices (VIO APC vs. standard APC), gas flow levels and VIO APC modes (pulsed APC ; pulsed 1 and 2). To compare the tissue effects of the different VIO APC modes 'pulsed 1' and 'pulsed 2' (pulsed APC), the differences between the two modes were checked for normality, and a paired t-test was performed. For the comparison of the effects of VIO APC (pulsed 1 and 2) and Nd:YAG laser, a standard two-sample t-test was performed.

Results

Second generation APC system (VIO 300 D with APC 2)

Using the high power level (80-120 W) for an application duration of 5 sec, 2nd generation APC led to a maximum depth of tissue coagulation of 6 mm. The maximum diameter of tissue destruction was 15 mm.

In comparison to the mode 'pulsed 1', 'pulsed 2' had a significantly higher tissue effect ($p < 0.001$) concerning the mean diameter of lesions and the mean destruction depth achieved using the different gas flow levels of 1 l/min (Table 1) and 2 l/min, a varied application time of 2 and 5 sec and a power setting above 30 W. Using 30 W for 2 sec, no significant difference concerning the diameter of lesions or the destruction depth was found. Using both gas flows (1 and 2 l/min), no difference was

Table 1. — **VIO APC pulsed 1 vs. pulsed 2 (flow 1 l/min) : Mean coagulation depth using different application durations (35 samples for each occasion)**

Power setting	VIO APC mode	Mean depth ± SD (mm) 2 sec	Mean depth ± SD (mm) 5 sec
30 W	Pulsed 1	0.9 ± 0.8	1.7 ± 0.5
	Pulsed 2	0.9 ± 0.4	1.9 ± 0.5
40 W	Pulsed 1	1.0 ± 0.4	2.0 ± 0.5
	Pulsed 2	1.2 ± 0.4	2.3 ± 0.5
50 W	Pulsed 1	1.1 ± 0.5	2.3 ± 0.5
	Pulsed 2	1.6 ± 0.3	2.6 ± 0.5
60 W	Pulsed 1	1.3 ± 0.4	2.5 ± 0.6
	Pulsed 2	1.7 ± 0.4	3.0 ± 0.5
70 W	Pulsed 1	1.5 ± 0.4	2.8 ± 0.6
	Pulsed 2	2.0 ± 0.4	3.3 ± 0.6
80 W	Pulsed 1	1.6 ± 0.5	3.1 ± 0.6
	Pulsed 2	2.1 ± 0.5	3.5 ± 0.7
100 W	Pulsed 1	1.9 ± 0.5	3.4 ± 0.7
	Pulsed 2	2.4 ± 0.5	3.9 ± 0.6
120 W	Pulsed 1	2.2 ± 0.5	3.6 ± 0.7
	Pulsed 2	2.6 ± 0.6	4.2 ± 0.6

Table 2. — **Mean diameter and coagulation depth achieved by second generation APC (flow 1 l/min ; 35 samples for each occasion) in comparison to the Nd:YAG laser (10 samples)**

Setting	Device	Mean diameter ± SD (mm)	Mean depth ± SD (mm)
30 W 2 sec	VIO APC pulsed 1	6.5 ± 0.8	0.9 ± 0.8
	Nd:YAG laser	1.6 ± 0.2	0.9 ± 0.2
	p	< 0.0001	0.8 (n.s.)
30 W 2 sec	VIO APC pulsed 2	6.6 ± 0.9	0.9 ± 0.4
	Nd:YAG laser	1.6 ± 0.2	0.9 ± 0.2
	P	< 0.0001	0.6 (n.s.)
60 W 2 sec	VIO APC pulsed 1	7.3 ± 0.9	1.3 ± 0.4
	Nd :YAG laser	2.1 ± 0.2	1.5 ± 0
	p	< 0.0001	0.2 (n.s.)
60 W 2 sec	VIO APC pulsed 2	7.9 ± 1	1.7 ± 0.4
	Nd:YAG laser	2.1 ± 0.2	1.5 ± 0
	p	< 0.0001	0.1 (n.s.)
60 W 5 sec	VIO APC pulsed 1	9.5 ± 0.9	2.5 ± 0.6
	Nd:YAG laser	2.3 ± 0.3	3.5 ± 0.4
	p	< 0.0001	< 0.0001
60 W 5 sec	VIO APC pulsed 2	10.2 ± 1	3.0 ± 0.5
	Nd:YAG laser	2.3 ± 0.3	3.5 ± 0.4
	p	< 0.0001	0.008

found in the maximum tissue destruction depth achieved using each of the APC modes ‘pulsed 1’ and ‘pulsed 2’.

Standard APC system (APC 300/ICC 200)

The maximum destruction depth achieved was 3.5 mm, and the maximum coagulation diameter was 11 mm.

In comparison to the tissue effects of standard APC, the maximum destruction depth achieved by 2nd generation APC using the power range of 30-99 W was significantly higher ($p < 0.0001$). The maximum diameter of lesions was significantly larger ($p < 0.001$).

Nd:YAG laser

Using the range of wattages from 30 to 60 W, the Nd:YAG laser led to a maximum tissue destruction depth of 1.5 mm (application time 2 sec) and 4 mm (5 sec).

2nd generation APC caused an up to 100% higher maximum destruction depth using the same energy range for a duration of 2 sec in comparison to the Nd:YAG laser. Using increasing energy levels from 30 to 50 W for a duration of 5 sec, the maximum destruction depth was maximally 33% higher (2.5-4 mm vs. 2.5-3 mm). Applying 60 W for 5 sec, maximum destruction depth was equal for both of the systems (4 mm).

The two-sample t-test showed a significantly higher mean diameter of lesions caused by 2nd generation APC using the power range from 30-60 W, a varied application time of 2 and 5 sec, different pulse rates (‘pulsed 1’ vs. ‘pulsed 2’) and a gas flow level of 1 l/min (Table 2). Using 30 and 60 W for 2 sec, VIO APC and Nd:YAG laser led to similar results in the mean destruction depth achieved (no significant difference).
Using the maximum energy levels available for both of the systems, the maximum destruction depth achieved by VIO APC (6 mm) was higher than that caused by the Nd :YAG laser (4 mm).

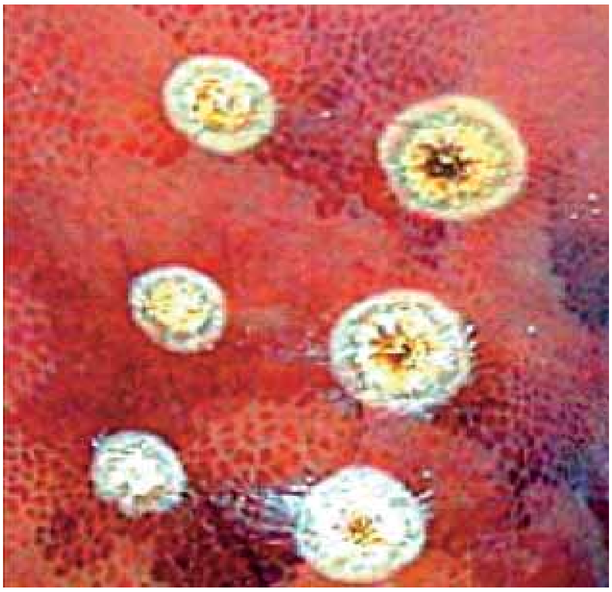

Fig. 1. — Lesions on liver surface after VIO APC application

Discussion

The aim of the present study was to evaluate the effectiveness of a 2nd generation APC system by using different power settings, gas flow levels and modes of ‘pulsed APC’ and to compare it to standard APC and Nd:YAG laser.

Our data confirm that the coagulation depth and diameter of lesions achieved by APC are mainly a function of the power setting chosen and the duration of application (6). In comparison to a maximum destruction depth of 1-3 mm described in literature for the ICC 200 argon plasma coagulator, we achieved a maximum depth of 6 mm using the 2nd generation APC device at a high power setting.

Our data show that the mode ‘pulsed 2’ of pulsed APC was more effective than the mode ‘pulsed 1’ concerning the diameter of lesions and the destruction depth achieved. Therefore, the mode 'pulsed 2' might be useful for the treatment of larger mucosal areas in the gastrointestinal tract, for example during the ablation of Barrett's ooesophagus or in palliative tumour ablation. On the other hand, the mode 'pulsed 1', causing a smaller diameter of lesions in comparison to 'pulsed 2', might be of use for indications like the treatment of Zenker's diverticulum, where a tissue bridge between the diverticulum's lumen and the ooesophageal lumen is divided (18,19).

The results of the present study also show that, in comparison to standard APC, the tissue effect of 2nd generation APC was significantly higher concerning the depth of tissue destruction and the diameter of lesions even when using comparative power settings of 30-99 W. A possible explanation might be the different physical properties of the two APC systems used for the study. The power setting for the APC devices is defined for a load (electrical resistance of the tissue between the electrodes) of 500 Ohm. However, higher loads are quite common in real applications. For those, the actually delivered power decreases below the nominal value. The VIO generator (2nd generation APC) is able to maintain the nominal power for higher loads than the ICC (standard APC) system (e.g. 1000 Ohm). This property of the generator might be the main reason for the higher efficacy of 2nd generation APC.

The 2nd generation APC system offers several modes. Among these, the 'Forced APC' mode is similar to standard APC, but with improved plasma stability. Additionally, a new 'Pulsed APC' mode is offered which has been used for the comparison in this study. The advantage of this APC mode is that each pulse contains a number of single bursts.

In the ICC-System (standard APC), the APC power is set by regulating the voltage. This results in stability problems of the plasma for low power settings (< 40 W). As our data show, a high tissue effect can be achieved by 2nd generation APC even using the low energy level of 30 or 40 W.

The maximum destruction depth of 3.5 mm actually seen for the APC 300 device was achieved by VIO APC using only 30 W for a duration of 5 sec. These data suggest that 2nd generation APC might be useful for various clinical indications where energy of low wattage is wanted. In general, it can be assumed that, due to its higher effectiveness, and without knowing before, 2nd generation APC might lead to an increasing rate of side effects and complications during clinical application. Therefore, the higher effectiveness of VIO APC should be a topic of clinical education before using in clinical practice.

Two studies previously published by our group (20, 21) have shown that the number of complications observed during clinical application of VIO APC is low. 2nd generation APC was applied in various forms of gastrointestinal pathology, and using the whole range of power settings available (20,21). Nevertheless, a prospective randomized trial comparing the effects of VIO APC, standard APC and Nd :YAG laser during clinical application would be desirable. Keeping in mind that the experiences on the use of VIO APC are still limited, the present results might be a basis for all further clinical application of second generation APC, showing its high tissue destruction capacity in vitro.

A possible limitation of the present study might be that no living animal model and histological evaluation of the destruction depth were used. Nevertheless, the aim of the present study was to compare the destruction capacity of three different thermal devices, and our results have proven the higher effectiveness of second generation APC in comparison to standard APC. The question arises whether it would have been helpful to choose a GI tract model to evaluate the tissue destruction capacity of APC systems and Nd :YAG laser. In the present study, the decision was made to use a porcine liver model, because the wall thickness of the GI tract is limited. For example, for the evaluation of the high power level of VIO APC of up to 120 W, the GI wall would not have been an adequate model. The maximum destruction depth observed was 6 mm. In a GI model, this would have led to perforation, and the "true destruction depth" would not have been measured.

The present study shows that 2nd generation APC led to a larger diameter of tissue destruction in comparison to the Nd:YAG laser. Concerning the destruction depth, VIO APC was as effective as the Nd :YAG laser using up to 60 W and a limited application time. Using the maximum levels available for both of the systems, the maximum destruction depth achieved using 2nd second generation APC (6 mm) was higher than the maximum depth caused by the Nd:YAG laser (4 mm).

Regarding the laser application in clinical practice, it has to be remarked that the laser is an absolutely contact-free method. That means that, in comparison to the APC devices, using a laser device is technically much more difficult, especially in ooesophageal strictures or in the area of the ooesophagogastric junction. It can be assumed that during clinical application, the laser energy would be absorbed more intensively by the tissue treated due to blood perfusion, depending on the characteristics of each individual type of tissue. Therefore, the present data are transferable to clinical application only to a limited extent.

Wahab *et al.* (8) reported that APC was successful in tumour debulking, but many treatment sessions were necessary in the patients treated. Due to its higher effectiveness in tissue coagulation, the 2nd generation APC system might be useful for tumour debulking, and it might replace the Nd :YAG laser in clinical practice. Clinical trials comparing VIO APC to the Nd:YAG laser are required to answer this question.

In conclusion, it can be noted that 2nd generation APC was more effective in tissue coagulation than standard APC, even when using comparative power settings.

Using power settings of up to 60 W and a limited application time, VIO APC was as effective as the Nd:YAG laser. Using the maximum energy levels available for both of the systems, the maximum coagulation depth achieved by VIO APC was higher. The high effectiveness of VIO APC should be a topic of clinical education.

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