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Editorial

Argon plasma coagulator – *"primum non nocere"*

More than 10 years ago I wondered whether argon plasma coagulation (APC) would prove revolutionary for therapeutic endoscopy (1). Now, time has settled the question. We now know that APC sources are essential in all endoscopy units around the world, but their use is basically restricted to hemostatic procedures. Ablative applications have been relegated to mere "touch-ups" to finish off other techniques, which today anew seem revolutionary.

APC has also evolved, and second-generation sources are now available that provide several application modes: forced, pulsed, and precise, with various coagulation effects (2).

The forced modality is characterized by continuous monopolar current, which is delivered to the target tissue through a conductive flow of ionized argon gas (argon plasma), and represents the energy dispensed by present-day sources. In pulsed mode discontinuous current is delivered to provide one of two effects: effect one with higher intensity current and longer pauses, and effect two with a higher number of lower-energy pulses. Finally, with the precise mode argon plasma may be regulated using an electronic setup regardless of system impedance and target distance, provided the latter is shorter than 5 mm (3). The effectiveness of second-generation APC is 50% higher than that of original generators (4).

The primary benefit attributed to argon plasma is its capability to cause limited damage in superficial layers, since current moves from treated, dried-up areas with a higher resistance to untreated areas with a lower resistance, with this drift protecting patients from potential perforation by deep burns (5,6). In contrast, more recent studies in experimental models show significant damage to the muscularis propria with severity increasing with dispensed energy amount, pulse duration, and target area; the layer is hit by 86% of 40W shots or 69% of applications longer than 5 seconds using both traditional (7) or second-generation sources (8), the latter requiring greater caution given their increased energetic yield by nearly 50%.

Obviously, continuous gas flow during delivery results in gastrointestinal tract distension and patient discomfort, an adverse effect that may be easily countered by repeat aspirations during therapy pauses.

The most devastating, feared effect is no doubt a deflagration of inflammable gases within the colon. This is why patients scheduled to undergo argon plasma therapy must be fully prepared in an anterograde manner using a sugar-free solution regardless of the target area for APC. Just because actinic proctitis is the condition to be treated, as is the case with Tormo et al. (9), it does not mean that full preparation (using phosphates in our case) to prevent gases from exploding may be overlooked.

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Additional caution must also be exerted with patients carrying pacemakers or defibrillators; a cardiologist should be consulted if in doubt, and the neutral electrode must be positioned as far as possible from the implanted device.

The uses of plasma coagulation for Barrett's esophagus are currently restricted to the elimination of tissue remnants – both neoplastic or otherwise – following other technologies, including the HALO system. This is so because APC cannot eliminate the whole of the diseased mucosal area, and metaplastic glands also develop under the newly regenerated squamous epithelium. On the other hand the rate of adverse effects (17%) or even perforations (9%) (10) in multicenter studies render this therapy inacceptable for Barrett's esophagus, a non-neoplastic lesion with limited malignization risk that is readily manageable with endoscopy.

Tumor or polyp ablation at any location is also an off-label indication of APC, as the technique cannot obtain tissue samples for lesion categorization or assess invasion depth. Similarly, palliative therapy for advanced neoplasms with APC (both for mass reduction and tunnelization) is also uncommon given the high number of sessions needed (more than 20) to obtain clinical remission. In contrast, once symptoms have responded, relapse rate is low at 6%, and the higher efficiency of recent APC generators are likely to offer no improved results (4,11). Nevertheless, argon plasma is irreplaceable to destroy adenomatous remnants from endoscopically resected polyps, particularly when piecemeal resection took place, as this technique significantly reduces relapse rates with no associated complications (12).

The ability of argon plasma to cut metal leaving adjacent tissues unscathed and without perforation has been successfully used for biliary self-expanding stent maintenance. APC may adapt the length of biliary stents within the desired range, prevent them from interfering with intestinal transit, avoid damage to the wall opposite to the papilla of Vater by the prosthesis' duodenal end, or trim the length of the intraduodenal segment, and allow for bile tract cannulation in future exams (13). APC has also been used to fenestrate duodenal stents to gain access to the bile tract by opening up a window looking on the papilla of Vater (14). Targeting foreign bodies eroding the gut wall, including Marlex mesh, seems also feasible with good results (15). This characteristic, however, limits its ability to tunnelize stents invaded by neoplastic or hyperplastic tissue – more often than not prostheses become ultimately damaged for an unfavorable outcome.

The combined cutting and coagulating capabilities of APC have been successfully used for the endoscopic management of Zenker's diverticulum in lieu of the traditional "needle-knife sphincterotome", both in the short- and long term, with a very limited number of side effects (16).

Its hemostatic power is undoubtedly unrivalled in the management of antral vascular ectasis in patients both with and without liver cirrhosis, albeit the latter require a higher number of sessions for complete therapy (17). Argon plasma is also considered the gold standard in the treatment of angiodysplasia no matter where (18,19), hence endoscopists take it to whatever target area they may choose – the esophagus, stomach, small bowel, or colon. Regarding the right colon, in view of its thin wall, perforations associated with its use have been reported (19), thus argon plasma must be used with a lower power output setup or together with saline injections at its base to limit the extent of electrical insult to deeper layers (20,21). APC's excellent hemostatic capacity has prompted its use in order to improve results with other techniques in different scenarios, including esophageal varices after band ligation (22) and Dieulafoy lesions to prevent recurrent bleeding once primary hemostasis is achieved with 1/10,000 adrenaline injections (23).

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Finally, as Tormo and colleagues verify in this issue of our journal, APC is useful in the management of bleeding induced by radiation proctitis, a late complication that is relatively common after pelvic radiation. APC reduces rectal bleeding in almost 90% of cases, and frequently helps relieve other accompanying symptoms such as diarrhea or urgency (60%) (24). Appropriate candidate selection is crucial for each therapy: mild proctitis may be medically treated with topical sucralfate and metronidazole in the absence of prior neuropathy signs (25), and patient slowly improve within months or even years. Estrogens, short-chain fatty-acid enemas, pentosan, thalidomide, or oral/topical salicylates, while useful, have not proven their effectiveness in controlled studies.

It is moderate proctitis, as in the study by Tormo (9), that will substantially improve clinically after APC – transfusion requirements and anemia decrease after 2-3 sessions (26-28), and bleeding subsides in the long-term in more than 80% of subjects. In this indication APC has a complication rate of up to 26% in review papers (25) with slowly-healing deep ulcerations and prolonged rectal pain being most common, since radiation proctitis is basically an ischemic condition and epithelial damage should be avoided by focusing endoscopic management on the destruction of bleeding vessels using isolated, short (< 1 sec) electrofulguration pulses, making any efforts to avoid coalescence (24), and delivering low-power current (40 W) (29) except for active bleeding sites, where power may be set up to 60 W. Stringent compliance with these guidelines results in outcomes as good as those reported by Tormo et al. (9).

While a satisfactory response is possible, the rate of potential refractoriness to argon electrofulguration is higher in more severe proctitis with telangiectasia occupying more than 50% of the rectal mucosa, more bleeding, and therefore higher transfusional requirements. Under such circumstances other therapies may be attempted including topical 4% formalin (30), with good results in over 55% of patients. An alternative option is a hyperbaric chamber, where changed oxygen gradients will favor patients with this ischemic pattern disease (31). Unfortunately, availability is limited regarding these chambers, and there is always concern that hyperoxygenation may favor neoplastic proliferation in other sites.

As with any other condition, making sure that symptoms do not derive from a different disease – triggered by radiation therapy or otherwise – is essential in actinic proctitis (25), and clinicians should be aware that these patients often experience other pelvic side effects involving the bladder, sexual functioning, or both, that may be as significant as bleeding and have a strong impact on the social, psychological, and financial spheres. Oncologists have been thus far primarily concerned about response and survival issues, and let adverse events and their management fade into the background. It is now about time that Hippocratic thinking becomes a part of their treatment schemes, and that they learn – as we endoscopists did as our therapeutic abilities progressed – that "in order to be of help, you should first do no harm".

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