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Contents

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EDITORIAL

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EDITORIAL

Role of botulinum toxin a in the management of complex incisional hernias

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Abstract

Despite the technological breakthroughs and discover of abdominal meshes, ventral hernia has always been challenging in therapeutic strategies by the surgeons, with high recurrence rates. The use of botulinum toxin A (BTA) for the management of ventral and incisional hernia (IH) poses an increasingly interesting practice, especially for the intimidating complex one. The preoperative administration of the toxin to the lateral abdominal muscles by use of Ultra-Sound guidance causes muscle paralysis and a reduction of intra-abdominal pressure. Thus, the hernia defect can be primarily closed without tension, if the length of the defect is up to 10 cm. In larger hernia, this method can be combined with component separation techniques or the use of a mesh. The mesh placement seems to be better by laparoscopy. The site of injection and the dosage of BTA are still under discussion amongst authors. The optimal administration is proposed by some authors to be at least 2 weeks before repair. There is also an analgesic effect of BTA to the patients that underwent hernia reconstruction. Ultimately, the role of BTA in the reconstruction of ventral hernia seems to be promising, but there is a necessity for several randomized clinical trials.

Key words: Ventral hernias and botox; Incisional hernias; Botulinum toxin A; Botox

Core tip: Administration of botulinum toxin A (BTA) in the surgical repair of ventral, incisional and complex hernia is a useful method, even for large hernia defects. The toxin is intramuscularly injected under Ultra-Sound guidance, covering all layers of the lateral abdominal muscles. The neurotoxic and analgesic activity of BTA leads to tension-free hernia closure. There is an increasing use of the technique especially in laparoscopic mesh repair. However, future data analysis will demonstrate the results and the benefits of this interesting procedure.

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INTRODUCTION

In the last years, there is an increasing interest concerning the possible advantages that may present in the use of botulinum toxin A (BTA) for the management of ventral hernias and especially the complex ones. BTA is usually known as Botox, although this is a brand name for the BTA produced by Allergan, and contains 100 IU of BTA. Many companies produce and distribute BTA for medical use. The most common brand names of the world market are Botox, Dysport, Neurobloc, Bocouture, Vistabel *etc*[1,2].

STUDY ANALYSIS

Although BTA has been used for many decades for the treatment of spastic related neurological disorders, it became popular and well known after being adopted from plastic surgeons and introduced in the "medical aesthetics industry". Nowadays many different uses of BTA have been proposed and there is an increasing interest for this "poison". The main indications that have been recently established include the treatment of pain syndromes, chronic low back pain, stump pain (phantom pain), arthritis, migraine, periorbital pain and persistent localized muscular pain syndromes, palmar and axillary hyperhidrosis, detrusor hyperreflexia, gastrointestinal smooth muscle and sphincter spasms[3,4].

Even though in many of these indications the results are promising, there is an ongoing active research particularly to identify and clear the exact mechanisms of BTA use. The effect of BTA has many different mechanisms and the classic knowledge of acting via its paralytic properties represents one of them. Arezzo[5] in 2002 collected and proposed various possible mechanisms including direct effects on muscle nociceptors, motor neuron and muscle spindle afferent changes, alteration of neurogenic inflammation and direct effects on pain afferents.

All these seem to be very interesting but the questions that arise is how all these are related to complex ventral hernia treatment and how they might affect or alter our existing knowledge and practice. The aim of the present editorial is to introduce to the readers this new alternative approach and define the possible physiologic and pathophysiologic mechanisms, the indications and contra-indications of the method and to present the existing techniques.

The hernias that are usually more interesting, complex and difficult to manage are the incisional hernias (IH) after laparotomy. They mostly develop, because the abdominal incision and the myofascial tissues fail to heal. Several factors have been proposed to associate with increased or decreased risk for IH incidence and several techniques have been developed to minimize the risk for postoperative hernia occurrence. However, despite the technical modifications, the high-tech instrument and meshes, the clinical studies that identified the risk factors and the best surgical techniques, the risk for IH is still high. Incidence is growing rapidly due to rising laparotomy rates in increasingly older, obese and co-morbid patients. Only in United States, 200000 IH are operated each year. It has also been estimated that 10% of all abdominal operations will be complicated with IH[6].

The treatment of IH is also followed by an increased incidence for recurrence. The recurrence rate in mesh techniques is estimated 2%-36%, while in cases with simple suturing techniques the risk is much higher and ranges from 12%-54%. Although the recurrence rates may have been slightly decreased with laparoscopic techniques, there is a slight difference and the risk still high. The main reason is, that even on laparoscopic hernia treatment, there is a need of closing the defect if that is feasible. Restoration of the continuity and anatomy of the abdominal wall is important to minimize the complications and recurrence rates. Thus, all the recently developed laparoscopic techniques and modifications focus on abdominal component separation (ACST). Among the main factor that associated with IH recurrence is the extreme tension in closing the abdominal wall. The use of Mesh in IH repair is based on free-tension techniques which hopefully will decrease the recurrence rate. Several studies

suggested that even though meshes can be placed by tension free techniques, if the myofascial defect remains open, the recurrence rate is still significant and associated with other factors like infections, hematomas, seromas *etc*[7]. Bridging has traditionally been used where there has been loss of domain of the abdominal wall or where a compartment syndrome is likely. All the above-mentioned observations suggest that mesh placement by laparoscopy is better, and even better if it can be combined with ACST to close the myofascial defect, restoring the anatomical continuity of the abdominal wall. Different methods have been described to achieve primary myofascial defect closure in patients with complex IH with domain loss and to reduce the morbidity of abdominal wall reconstruction by reducing the risk of compartment syndrome. The most popular techniques include release of fascia[8].

Some other authors suggest the progressive preoperative pneumoperitoneum but the available studies suggest increased complication rate. Tissue expanders have also been used to decrease the defect and the available results are also promising although its use presents several significant difficulties[9,10].

As mentioned above, BTA is a protein with known neurotoxic activity produced by Clostridium botulinum. The existing data suggest that BTA binds to specific glycoproteins found in the cholinergic nerve terminal, blocking the signal transmission temporarily in both motor and autonomic neurons. The paralyzing effect starts 3-4 d after the injections, reaches a maximum after 2 wk and declines gradually after 3-4 mo. Although the toxin is dangerous, application of small well calculated doses in specific points avoiding vital muscles and organs are safe[11].

The use of BTA in animal models showed that preoperative paralysis of the lateral abdominal muscles after intramuscular administration reduces the intra-abdominal pressure, allowing the closure of a hernia defect under minimized muscular tension[12].

These initial results suggested that a pharmaceutical achieved temporary preoperative paralysis of the abdominal wall muscles (with BTA) may facilitate the primary hernia defect closure without component separation (CST) need. Up to now only a few studies has been published. Searching the Medline by using the relative terms as "BTA and hernia", "botox and hernia" *etc*. less than 200 published records can be found. From these the relative studies are less than 10 which suggests that research is starting now. Many things had to declare including the optimal dose, the optimal technique of injections, the exact indications that ensure the best effect, the possible adverse effects and complications *etc*.

First of all, we have to develop the criteria for patient selections. Who are the patients that are most likely to benefit from BTA administration? The size and the location of the hernia defect may be an important factor to patient selection. There is no evidence about that but we can presume the following anatomical facts. The mean length of the frontal abdominal musculature forms the linea alba to middle auxiliary line is about 15-18 cm. The mean myofascial length gained by BTA administration according to several studies is estimated to 3-4 cm at least from each side treated, that mean almost 6-8 cm in total. These observations suggest that myofascial defects 6-10 cm are likely to present the best results, as the initial results suggest that we can achieve the primary defect closure without CST or tension. These data are based on our primary observations and the results are only theoretical. More clinical randomized trials are required to extract reliable results[13].

The site of BTA injection is crucial and need to be defined accurately. Four patterns of BTA injection have been proposed, by Elstner, Ibarra-Hurtado, Zielinski and Zandejas. All of them suggest that BTA injection should be performed between the middle clavicle line and the middle auxiliary line in straight line or triangles ranging from superior iliac fossa to below the lower cartilages. These techniques achieve increased length and decreased thickness of the lateral abdominal muscles, allowing the approximation of myofascial tissue and the primary closure of the hernia defect, while they result in a more anatomical appearance and better aesthetic results[14-16].

The dose of BTA is still something that should be defined in future controlled studies. The existing studies present significant differences concerning the dilution, the dose, the number of the treatments required and the time that BTA should be injected. Although several authors suggest that large doses of BTA (*e.g.*, up to 400 IU of Botox) may be safe, we suggest that a more conservative protocol should be applied. We propose that 2 wk prior to the operation an injection of 100 IU Botox or 500IU Dysport should be applied in 3 points to each side (IU equally divided). The injection should be performed under Ultra-Sound guidance to avoid complications and to ensure that all the related muscles were treated[14].

Another very interesting parameter that has been studied by Zendejas *et al*[17] is the analgesic effect of BTA. Patients who treated preoperatively with BTA under Ultra-Sound guidance required significantly less analgesics postoperatively (Figure 1). The BTA injected into the transversus abdominis and internal and external oblique muscles at three sites bilaterally and the U Ultra-Sound guidance required to ensure

the accuracy of the injection and to avoid complications (Figure 2).

Soltanizadeh *et al*[18] evaluated the literature by searching in PubMed and Embase electronic databases in 2016, regarding BTA as an adjunct to abdominal wall reconstruction for IH. This evaluation included six cohort studies with a total of 133 patients, and no randomized or case-control studies were found. Their eligibility criteria were population, intervention, comparison and outcomes. As for the latter, the primary outcome was the rate of primary fascial closure and the secondary outcomes were safety and long-term results. They suggest that preoperative administration of BTA increases muscle length and the optimal administration is at least 2 wk before repair.

BTA effect lasts for 3-4 mo facilitating the healing process postoperatively. The decreased tension of the abdominal muscles decreases significantly the risk for myofascial tissues tear, or mesh transposition secondary to increased muscle forces.

PERSPECTIVE

In conclusion we can assume that the possible advantages of the BTA in the treatment of complex IH have raised the interest of the researchers. The paralyzing effect of BTA in the muscles may facilitate the primary closure without tension of large hernia defects, may decrease the need for opioid analgesics postoperatively and may also facilitate the postoperative healing process by eliminating the muscle forces. All these possible advantages are supported by the existing data, but it is for sure that large randomized prospective clinical trials are required to certify the current initial results.

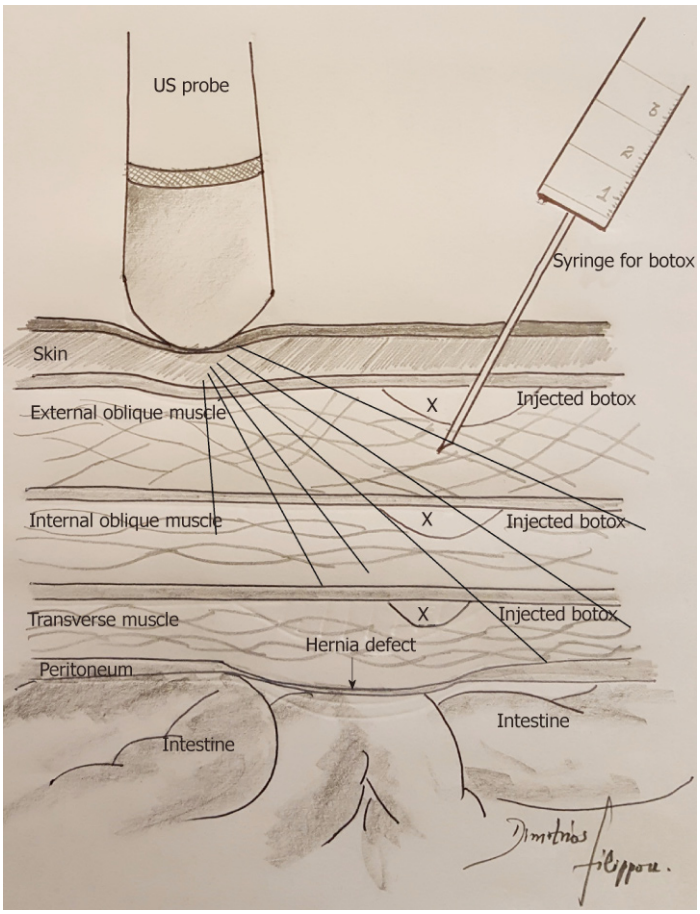

Figure 1 Several protocols concerning the points of injection have been proposed. There is still an ongoing debate about them.

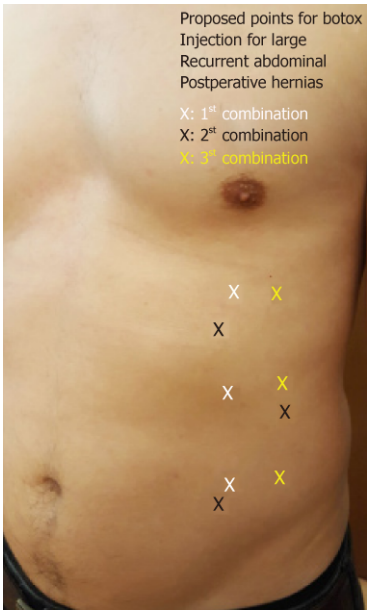

Figure 2 Technique for Botox injection into the abdominal muscles under Ultra-Sound guidance.

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EDITORIAL

Can hyperthermic intraperitoneal chemotherapy effectively control gastric cancer-associated peritoneal carcinomatosis?

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Abstract

Gastric cancer-associated peritoneal carcinomatosis leads to a poor prognosis and low quality of life. The current systemic chemotherapy processes cannot effectively improve survival. Hyperthermic intraperitoneal chemotherapy (HIPEC) has been used as an alternative treatment to control this disease through recurrence prevention, definitive therapeutic modality, and symptom palliation. Although HIPEC has been demonstrated to yield favorable results mainly in some Asian studies, widespread adoption of this treatment is still debatable before larger prospective randomized controlled clinical trials confirm its effectiveness.

Key words: Hyperthermic intraperitoneal chemotherapy; Gastric cancer; Peritoneal carcinomatosis

Core tip: Peritoneal carcinomatosis associated with gastric cancer leads to poor clinical outcomes and low quality of life. Hyperthermic intraperitoneal chemotherapy can potentially be used for the control of this disease.

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INTRODUCTION

Peritoneal carcinomatosis (PC) of gastric cancer origin refers to the spreading of gastric tumor cells in the peritoneum[1]. PC is characterized by extremely poor prognosis with a residual lifespan of approximately 3-7 mo[2-5]. Therefore, the median survival of patients with PC treated with systemic chemotherapy is 9.5-12 mo[6,7]. In addition, intractable ascites may severely affect the quality of life and lead to particularly painful sensations and life-threatening consequences in these patients[8,9].

In the past, these patients have been considered incurable and only received palliative systemic chemotherapy without surgical resection[10,11]. However, systemic chemotherapy, even with targeted agents, has yielded poor responses[12] due to the presence of the "plasma–peritoneal barrier," which separates organs inside the peritoneum from intravenous chemotherapeutic drugs[13]. Notably, in the 1980s, a new concept of a "locoregional disease" in patients with PC led to the identification of a new treatment strategy, cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC)[1]. After complete CRS of macroscopic tumor resection, intraperitoneal chemotherapy (IC) is performed to maximize the dosage and contact time of chemotherapeutic drugs delivered to intraperitoneal microscopic-free tumor cells while minimizing systemic toxicity. Prolonged drug retention in the peritoneal cavity and clearance from the systemic circulation are considered crucial attributes for the intraperitoneal approach[14,15]. Heat has also been proven to be synergistic with the antitumoral effects of chemotherapeutic agents (*e.g.*, mitomycin C, cisplatin, and oxaliplatin)[16,17]. Moreover, the addition of extensive intraoperative peritoneal lavage followed by IC with cisplatin yielded significant improvements in 5-year survival in a Japanese gastric cancer study[18]. The principle underlying this effect is that the use of a large amount of diluent inside the peritoneum before HIPEC could diminish a majority of free tumor cells, and the combined action of physical injury caused by heat and the chemotherapeutic toxin demolishes the remaining tumor cells[19].

HIPEC has been used in three aspects of gastric cancer management. First, it has been used as an adjuvant approach following curative CRS to extend lifespan and reduce the rate of intraperitoneal recurrence in many Asian randomized clinical trials[19]. Second, CRS followed by HIPEC is the sole therapeutic modality in PC management, leading to long-term survival in well-selected patients. Third, HIPEC has been demonstrated to effectively palliate massive ascites and alleviate the need and frequency of paracentesis.

A METHOD OF RECURRENCE PREVENTION

HIPEC is the most appealing prophylactic treatment of gastric cancer for those with a high risk of recurrence in the peritoneum after curative CRS[19]. According to the "tumor cell entrapment hypothesis" proposed by Dr. Sugarbaker, perioperative IC including peroperative HIPEC with or without early postoperative intraperitoneal chemotherapy (EPIC) should be performed to eradicate possible tumor cells released into the peritoneal cavity during cancer resection, transection of lymphatic channels or in cases with close resection margins, and tumor-contaminated blood spillage[20]. Several meta-analyses of prophylactic IC for carcinomatosis prevention have been published. Sun *et al*[21] stated a substantial extent of lifespan after HIPEC despite the use of different chemotherapeutic drugs (mitomycin C or 5-fluorouracil) and irrespective of whether adjuvant intravenous chemotherapy was applied. Mi *et al*[22] reported that HIPEC could reduce the 5-year recurrence rate in the peritoneum even with six different combinations of chemotherapeutic drugs (5-fluorouracil, mitomycin C, cisplatin, cisplatin and 5-fluorouracil, cisplatin and mitomycin C, mitomycin C and 5-fluorouracil). However, neither of these studies demonstrated increased postoperative morbidity after HIPEC[21,22]. Huang e*t al*[23] and Yan *et al*[24] demonstrated a higher incidence of postoperative neutropenia and abscess formation after HIPEC

with four different combinations of chemotherapeutic drugs (5-fluorouracil, mitomycin C, cisplatin and mitomycin C, mitomycin C and 5-fluorouracil) but with no effect on mortality rate. Moreover, sole prophylactic HIPEC or HIPEC combined with EPIC yielded survival benefits. Yonemura *et al*[25] reported a 5-year survival rate reaching 42% in a study group comprising 15 Cy+/P0 patients with combined cisplatin and mitomycin C regimen. Grossly, this prophylaxis strategy in patients with nodal metastasis or serosal invasion has been proven effective and safe. Nevertheless, a large percentage of these randomized clinical trials were conducted in Asian countries, and clinical trials in Western countries were scant[19].

A DEFINITIVE THERAPEUTIC MODALITY

In 1996, Yonemura *et al*[5] reported a 5-year-survival rate of 11% in a study of treatment with HIPEC using regimen of cisplatin and mitomycin C and etoposide, after CRS in 83 patients with PC. The first study of the West reported in 1999 was a phase II study of 42 patients receiving HIPEC with mitomycin C regimen. Sayag-Beaujard *et al*[26] reported an overall median survival of 10.3 mo and a 5-year survival rate of 8%. However, a low tumor load (peritoneal cancer index, PCI) and complete cytoreduction [completeness of cytoreduction (CC) score = 0] would lead to ideal survival. One 49-patient study by Glehen *et al*[27] published in 2004 showed that the median survival reached 21.3 mo and 5-year survival rate increased to 29.4% after CC-0/1 resection and HIPEC with mitomycin C regimen. This improvement in clinical outcomes demonstrated the significance of proper patient selection and technical progress in complete cytoreduction as experience increased.

However, the patients may face risks of complications and mortality. Gill *et al*[28] summarized the results of ten studies and demonstrated a complication risk of 21.5% and average mortality rate of 4.8%. Common complications included ileus, anastomotic leakage, intra-abdominal abscess, digestive fistula, and hematologic toxicity[28-31]. Therefore, appropriate selection of candidates for this treatment is essential. During preoperative evaluation, a low PCI score and low CC score are essential prognostic factors. Moreover, preoperative PCI scores indirectly forecast the possibility of complete cytoreduction during operation. Yonemura *et al*[32] demonstrated complete cytoreduction of 86%, 39%, and 7% in their patients when the PCI score was ≤ 6, >7, and > 13, individually. Suitable indications of CRS and HIPEC for gastric cancer-related PC should include younger age (< 60 years), low PCI scores (lower than 10 points), no para-aortic lymph node involvement, no distant metastasis, and a high possibility of complete cytoreduction[27,30,32-34].

A METHOD OF SYMPTOM PALLIATION

For symptomatic patients with malignant ascites and complete cytoreduction deemed impossible[19], many oncologists have suggested performing HIPEC to relieve the symptoms caused by ascites related to PC[35]. Yonemura *et al*[36] and Fujimoto *et al*[37] advocated effective resolution of ascites in patients after HIPEC treatment. In addition, some studies have reported the successful use of laparoscopic HIPEC to palliate the ascites-related symptoms, to reduce the frequency of repeated paracentesis, and to avoid any significant morbidity or mortality[38]. Moreover, laparoscopic HIPEC could shorten the operation time and length of admission[39,40].

PERSPECTIVE

In the past two decades, the use of CRS and HIPEC in gastric cancer-related PC management has been debatable. Although preliminary data from Asian studies were scrutinized with considerable skepticism, indications of HIPEC in PC treatment remain elusive. Additional large prospective randomized controlled clinical trials are warranted to achieve consensus regarding the use of HIPEC as a gold standard.

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EDITORIAL

Caribbean "substitution culture" is a barrier to effective treatment of persons with diabetic foot infections

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Abstract

Diabetes-related amputation rates are high in the Caribbean. Many authorities have identified independent risk factors for diabetes-related amputations, but cultural factors remain underappreciated. We coined the term "Caribbean substitution culture" to describe the attitude of patients with diabetic foot infections in which they refuse to access medical care, instead voluntarily choosing to substitute "bush medicines" or other alternative therapies in the place of conventional treatment. Recognizing that the Caribbean substitution culture is a barrier to effective treatment of diabetic foot infections is the first step in curbing these practices. In this paper, we discuss the issues related to the Caribbean substitution culture, including the demographics of the population at risk, the alternative therapeutic practices and potential public health strategies to combat this practice.

Key words: Diabetes; Surgery; Infection; Caribbean; Foot

Core tip: Many authorities have identified independent risk factors for diabetes-related amputations, but cultural factors remain underappreciated. We coined the term "Caribbean Substitution Culture" to describe the attitude of patients with diabetic foot infections in which they refuse to access medical care, instead voluntarily choosing to substitute "bush medicines" or other alternative therapies in the place of conventional treatment. We discuss the issues related to the Caribbean Substitution Culture, including the demographics of the population at risk, the alternative therapeutic practices and potential public health strategies to combat this practice.

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INTRODUCTION

In the Caribbean, persons with diabetes have 0.75% annual risk to develop foot infections[1]. Diabetic foot infections rank high among the admission diagnoses in Caribbean hospitals[2-6]. These patients consume significant human and financial resources. The economic burden is illustrated by a report that one Caribbean country spent $85 million United States dollars in just one year solely to treat patients hospitalized with diabetic foot infections[1] – an underestimate since that figure excluded outpatient treatments and treatments in private facilities.

Ideally, we aim to prevent persons with diabetes from developing foot infections. To achieve this, there are many evidence-based recommendations for prevention that are tailored to the needs of the region[2-9]. If these patients do develop foot infections, however, five therapeutic goals should be observed: (1) Achieve glycemic control; (2) Control local infection; (3) Prevent systemic sequlae of sepsis; (4) Prevent amputations; and (5) Preserve life. Despite evidence-based therapeutic guidelines specific to the Caribbean enviroment[2,3,5,8-12], there are still poor clinical outcomes across the region. Since limb salvage is one of the therapeutic goals, we can consider lower limb amputations as a proxy for therapeutic failure. In the Caribbean, the reported annual incidence of lower limb amputations in persons with diabetes ranges from as low as 54 per 100000 persons per year in Trinidad & Tobago[2] to as high as 936 per 100000 persons per year in Barbados[9] – ranking among the highest in the world[9].

DEFINITION OF THE PROBLEM

Many authorities have attempted to determine the reason such poor outcomes exist in the Caribbean. They have identified several independent risk factors for diabetes-related amputations, including: Low socioeconomic status[13], inadequate footwear[5-9], improper nail care[5,6], poor diabetes control[6,9,14], sensory neuropathy[7,9,15], peripheral arterial occlusive disease[9,15], previous ulceration[14,15], late clinical presentation[3,6,12,14], delayed medical intervention[3,8] and infection with resistant microbes[11]. But the Caribbean "substitution culture" is a risk factor that is underappreciated. This is where patients with diabetic foot infections refuse to access medical care, instead voluntarily choosing to "watch it" while substituting "bush medicines" or other alternative therapies in the place of conventional treatment. These alternative therapies are regimes that are not used in conventional medicine, for which there is a paucity of data on safety, efficacy and effectiveness[16]. Most doctors practicing in the Caribbean have encountered variations of the substitution culture, but scientific literature has paid little attention to this practice.

There are many forms of alternative therapies used in the subsitution culture. The commonest method encountered is to apply topical "medicinal" agents to wounds that are then enclosed in improvised, and often unsterile, dressings. A variety of substances are used, but the most common is parrafin wax heated over a flame and poured directly onto open wounds[17]. In persons with diabetes who have neuropathy, this could result in devastating thermal injury. In order of frequency, other agents encountered include honey, wonder of world (Kalanchoe Pinnata) leaves[18], ichthammol ointment, aloe vera, hot oil (may cause direct injury), hot cooking grease (may cause direct injury), vaseline, iodex, epsom salts, methylated spirits, black salve, hydrogen peroxide and green papaya. In our experience, we have found that there is no standardized agent, dosing, frequency of application or duration of therapy.

Oral agents are also used, with bush teas being the most common. These are prepared by boiling water with a variety of ingredients including: leaves from cerasee (momordica charantia), fever grass (cymbopogon), noni (morinda citrifolia), guinea hen weed (petiveria alliacea), periwinkle (catharanthus roseus), soursop (annona muricata), arrowroot (maranta arundinacea), black mint (tagetes minuta), ganga (cannabis satira), aloe vera, lime (citrus aurantifolia), milk thistle (silymarin) and dandelion (taraxacum). Other parts of vegetation are also used, such as the root of

ginger (zingiber officinale), vines or bark from guaco (mikania guaco), bark or fruit from annatto (bixa orellana), coconut shell (cocos nucifera) and cashew bark (anacardium occidentale).

An uncommon but disturbing practice uncovered in some Caribbean countries is for persons to consume "left over tablets prescribed for other persons" to treat other diseases[14]. But even more disturbing is the practice of purchasing "pills" from streetside vendors[14]. These are dangerous practices because there is no instruction on the dose, frequency or duration of the drugs. And, in the latter case, persons were not even aware of the drug they were taking. Technically, these were not alternative therapies because conventional medicines were used[16], but they were delivered in a reckless manner. This demonstrates the popularity of the substitution culture.

We performed a literature review to determine whether similar practices existed in other countries. We encountered reports from India[19,20], Bangladesh[21,22], China[23-27], Maylasia[28], Iran[29,30], Turkey[31] and the African continent[32-35] in which persons with diabetes used non-medical remedies attempting to control their glucose levels. Few reports detailed persons with diabetes using alternative strategies specifically to treat foot infections[17,18,36-38] and none demonstrated any benefit derived from the use of these remedies.

SCOPE OF THE PROBLEM

The reason the substitution culture is so prominent in the Caribbean remains uncertain, but we believe that it is a wider societal issue where there is an ingrained reverence for traditional healers, a low perceived value of conventional medical therapy, an under-estimation of the consequences of foot infections and an element of non-compliance. Whatever the cause, the substitution culture can undermine the primary and secondary prevention strategies that Caribbean policy makers have put in place. If the alternative therapies are not effective, it may cause patients to seek conventional care late in the disease course, only after they admit that their alternative therapies have failed. The trickle-down effect is that infections may be allowed to progress unchecked, increasing the risk of amputation, sepsis and death.

A few investigators attempted to determine the value of alternative therapies specifically with relation to the treatment of diabetic foot infections. Carrington *et al*[36] studied the benefits of a plant known as bloodroot (Justicia secunda) applied topically to treat diabetic foot infections. They incubated bacteria extracted from infected foot wounds (Staphylococcus aureus, Pseudomonas aeruginosa and Enterococcus feacalis) and tested them against bloodroot, using ciprofloxacin as a control and dimethyl sulfoxide solutions as a negative control. In this study, bloodroot had no activity against the organisms tested. Carrington *et al*[36] were able to show that this practice was ineffective, but the study design did not allow them to comment on its safety.

In a previous publication, we sought to determine whether the substitution cultute was harmful[39]. We identified 695 patients who were admitted for diabetic foot infections. The outcomes of 382 patients who presented for conventional medical treatment as soon as their foot infections were identified were compared to 313 patients who made a conscious decision to delay medical therapy in favour of alternative therapies. This study[39] demonstrated just how strong the Caribbean subsitution culture was: 45% of patients voluntarily selected non-medical therapy as their first choice, although 75% had previous hospitalizations for foot infections and 54% had previous amputations and/or operative debridements. It may be expected that more patients would have presented for early medical therapy, considering that they had prior experience with, and were acutely aware of, the dangers of diabetic foot infections. It took an average of nine days for these patients to admit that their alternative therapies failed, and only then presented to hospitals for conventional medical care[39]. But the most important finding was that, for the first time, it was conclusively demonstrated that this practice was harmful. The patients who voluntarily chose to delay their presentations had significantly more surgical debridements, longer hospitalization by an average of nine days and increased health care expenditure of United States $10821.72 per patient[39]. There was also a notable trend toward more major amputations (9.3% *vs* 5.2%; P = 0.073) in the patients who self treated[39]. Although this did not achieve statistical significance, we suggest that it was clinically important because amputees have been shown to have significantly reduced quality of life, independence and life expectancy[2,3,5,7].

POLICY IMPLICATIONS

Govermnents in the Caribbean recognized that diabetes was one of the non-communicable diseases that places a high demand on health care resources in the region. In response to this growing problem, the Heads of Government in the Caribbean convened in Trinidad and Tobago in 2007[4]. They formulated the CARICOM Port of Spain Declaration[4] that aimed to create and implement regional policies to improve the management of non-communicable diseases.

A three-tiered approach was adopted to address diabetic foot infections[39]: The first tier focused on primary prevention, attempting to promote healthy lifestyles, optimize metabolic control and educate persons with diabetes about foot care[3,4]; The next tier focused on secondary prevention, promoting early detection and prompt treatment of foot infections when they did occur[8-10]; and the final tier focused on creating evidenced-based treatment protocols suited to the Caribbean environment[11,12]. The Caribbean substitution culture directly impacts the first and second tiers of these public health policies.

From the point of view of primary prevention, dedicated diabetes clinics were opened at strategic high-traffic areas within the community that were easy to access[8]. These were state-funded facilities with no user fees generated at these points of care. This ensured that patients had unimpeded access to care. Additionally, these clinics were staffed by local nurses and medical practitioners. The healthcare workers were mostly Caribbean natives and were trained at the University of the West Indies, a regional medical training institution providing secondary and tertiary medical education that was geared to training practitioners for all 17 countries in the English-speaking Caribbean[40]. This was important because these healthcare workers could relate to persons with diabetes by using colloquial language, demonstrating knowledge of local culture and discussing common practices. In this way, the healthcare workers could build rapport and gain patient trust.

From the secondary prevention point of view, a network of public health centres were establised across the nation with no user fees generated at the points of service[39]. A national referral policy was also implemented to ensure that patients were routinely evaluated by specialists at tertiary referral facilities in a timely fashion. Clear therapeutic protocols were also established[1-3] as a part of this national policy document.

The Caribbean substitution culture has the potential to underutilize these policies. Therefore creative solutions are required because these are different problems than those in developing countries.

NEXT STEPS / RECOMMENDATIONS

Most Caribbean countries have implemented the above listed mechanisms to ensure that patients with diabetic foot infections have unimpeded access to medical care. Despite this, the "substitution culture" is evident in modern reports from Trinidad & Tobago[14,39], Jamaica[41], Barbados[6,9,42] and Guyana[43] documenting that patients still do not access medical care early. These reports suggest that the existing preventative strategies fall short of their expectations. It may now be necessary to re-think these strategies, taking into account the Caribbean substitution culture.

In order to address these practices, policy makers should be aware of the demographics of these persons and document the practices that exist. Harnarayan *et al*[14] examined 344 patients with diabetic foot infections who chose not to access medical care in favour of alternative therapies. They identified middle-aged, afro-Caribbean males at a mean age of 56.4 ± 12.4 years as the typical persons in whom the substitution culture is manifest[14]. Surprisingly, it was experienced patients who lived with diabetes for a mean duration of 13 years, that engaged in these practices[14]. This study is important because it allows policy makers to identify a specific target population to work with. Additional demographic information that would be useful to target this problem include the educational level of the persons with diabetes who engage in this practice. This should be a focus of future studies.

Patient education is already practiced in these settings as a part of the "three tier approach" described above. Persons with diabetes were counseled in state-funded diabetes clinics that were strategically placed in high-traffic areas in the community. Harnarayan *et al*[14] reported that the persons with diabetes who engaged in these practices were informed patients, 100% having been previously counseled on the dangers of diabetic foot infections. However, it was not stated whether medical practitioners who counseled these individuals had specific training in counseling methods. Therefore, it was unclear whether they were able to build rapport with patients. For example, the counselors could inadvertently build distrust if they maligned traditional practices or spoke down to patients in language they could not

understand. Alternatively, it would have been appropriate for the counselors to address these practices by distinguishing ones that seemed effective from those that were not and/or distinguishing practices that were harmful from those that might have some value and warrant respect.

Another way that the educational process could be improved would be to have pre and post-counseling surveys to determine whether the activity was successful in curbing patient beliefs and practices. If an intervention is not proven to be successful, then early change can be implemented.

Policy makers should always be aware of the alternative strategies that are in common use and study their outcomes. In this way, patient education can be directed. Ongoing research into this would also allow medical practitioners to identify specific practices that may be harmful to patients and distinguish them from those that may be beneficial. Patients may be appreciative of this approach. A good example is when patients pour hot parrafin wax, cooking oil or grease directly onto an infected wound. In persons with diabetes who have neuropathy, this could result in devastating thermal injury. In addition, we can point out that there is no standardized agent, dosing, frequency of applications or duration of therapy.

In some cases, legal means can be used. For example, we detailed a disturbing practice where persons with diabetes were able to purchase "pills" from unregulated streetside vendors with no awareness of the name of the drug or instruction on dose, frequency or duration of the drugs[14]. This demonstrates the severity of the problem because the persons engaging in this practice had such indifference for conventional medicine, that they were willing to pay "alternative healers" even though state-funded conventional health care was available to them free of charge. This could be curbed by policing and imposing penalties via the respective regulatory bodies.

CONCLUSION

Although the Caribbean substitution culture appears to be a barrier to effective treatment of diabetic foot infections, there is little or no data on the driving forces behind these practices. Continued directed research is required to understand the substitution culture before it can be addressed effectively.

Conventional medical practitioners should start with the premise that these alternative therapies can be an important complement to the treatment of Caribbean persons. We should reassure these patients that the treatments need not be mutually exclusive and encourage them to simultaneously seek medical advice as a part of holistic care.

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