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Hemostatic disorders induced by skin contact with *Lonomia obliqua* (Lepidoptera, Saturniidae) caterpillars

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ABSTRACT

Patients envenomed by *Lonomia* sp caterpillars initially experience a mild burning pain, headache, nausea, vomiting, and skin and mucosal hemorrhages. Some patients can rapidly progress to a severe coagulopathy that presents as visceral or intracerebral hemorrhaging. We studied the hemostatic alterations that occurred in 14 patients who were envenomed by *Lonomia obliqua* in Southern Brazil and presented at the Hospital *São Vicente de Paulo* (Passo Fundo, RS), Brazil during the summers of 1993 and 1994 when *Lonomia* antivenom was not yet available for treatment. The patients were classified into to 4 clinical groups: 0 (two patients), I (eight patients), II (two patients), and III (two patients). The patients were admitted to the hospital between 4 hours and five days after contact with the caterpillars. In this study, the coagulation parameters of the patients were followed up for up to 172 hours after the accidents. The patients received no treatment with the exceptions of two patients who received blood transfusions and antifibrinolytic treatment. The observed abnormalities related to blood coagulation and fibrinolytic factors were similar regardless of the severity of the bleeding symptoms. These findings suggest that alterations in hemostatic parameters without thrombocytopenia are not predictors of the seriousness of such accidents. Thus, consumptive disorder and reactive fibrinolysis are not proportional to mild coagulopathy. Furthermore, these patients recovered. The hemostatic parameters of most of the patients normalized between 96 and 120 h after the accident.

KEYWORDS: *Lonomia obliqua* caterpillar. Hemorrhagic syndrome. Coagulopathy. Fibrinolysis.

INTRODUCTION

A bleeding syndrome induced by skin contact with Lepidoptera (Saturniidae) caterpillars was described for the first time in Brazil by Alvarenga in 1912[1]. At this time the responsible caterpillar genus was not known. A similar bleeding syndrome caused by the *Lonomia achelous* moth caterpillar (Saturniidae) was first described in Venezuela in 1967[2,3] and was later reported in the North of Brazil[4]. Accidents with *Lonomia obliqua*[5] caterpillars were observed for the first time in the South of Brazil in 1989 around the municipal districts of Passo Fundo (RS) and *Chapecó* (SC). By 1992, accidents with the caterpillars assumed epidemic proportions as incidence of such accidents grew annually. The main clinical characteristic of *Lonomia (L) obliqua* accidents is a hemorrhagic syndrome associated with acute renal failure[6,7]. In general, the symptoms include local pain and burning, headache, nausea and vomiting, extensive ecchymosis in the contact areas, hematomas, gingival

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bleeding, epistaxis, hematemesis, melena, hematuria and metrorrhagia[8,9]. Acute renal failure and intracerebral bleeding are among the most severe complications of *L. obliqua* accidents and are also among the principal causes of death[7,10,11].

Two procoagulant toxins have been identified in *L. obliqua* bristle extract, i.e., a factor X activator[12] and a prothrombin activator serine protease[13], and these toxins are most likely responsible for the intravascular thrombin formation that directly consumes the coagulation factors[14].

The lethality of lonomic envenomation in the absence of specific treatment is 1.5 to 2.0%, which is approximately 3 to 4 times greater than the lethality of snakebites[15]. Before serum therapy, previous experiences in Venezuela showed that replacement therapies with whole blood, fresh or frozen plasma, or cryoprecipitates contribute to the adverse clinical consequences of envenomation most likely because this type of treatment provides additional clotting factors that exacerbate the intravascular coagulation induced by the circulating toxins. The cessation of clinical evidence of bleeding has been reported following treatment with purified human fibrinogen and antifibrinolytic drugs, such as aprotinin and ε-amino caproic acid (EACA)[3,16].

In Venezuela, skin contact with *Lonomia* caterpillars is mainly treated using Trasylol (aprotinin), and in Brazil, this condition is successfully managed using antilonomic serum therapy, which is effective in normalizing coagulation disturbances and hemorrhagic syndrome[17,18,19]. Moreover, the number of fatal cases is reduced with the use of serum therapy[15]. Studies of patients envenomed by *L. obliqua* caterpillars have shown that at the time of arrival at the hospital, a consumption coagulopathy associated with intravascular thrombin generation triggering secondary fibrinolysis[9]. In contrast, patients envenomed by *Lonomia achelus* caterpillars exhibit a primary fibrinolytic action[16] due to their fibrinolytic enzymes. Despite these results, the complex pathological mechanism by which the hemorrhagic syndrome is caused by *L. obliqua* envenomation remains incompletely elucidated. The presence of high amounts of dimer-D in some patients in combination with nearly normal level of fibrinogen is still not well explained and neither are the rare thrombocytopenia events in patients with moderate and severe coagulopathies. The majority of reports present only the coagulation factor levels at admission. Here, we present a long-term follow-up clinical and laboratory data study concerning hemostatic disturbances in patients who had been envenomed by *L. obliqua* in Brazil. Our results show that the majority of patients who present with incoagulable blood without bleeding can normalize within 96-120 h after contact with the caterpillars. In contrast, patients who are treated with *Lonomia* antivenom recover within 20 h of treatment[19] and thus avoid the considerable risks of bleeding and some systemic complications.

MATERIAL AND METHODS

Patients

The study was performed with 14 patients (Ps) who were admitted to the Hospital *São Vicente de Paulo* (HSVP), Passo Fundo, Rio Grande do Sul, Brazil, during the summers of 1993 and 1994 when *Lonomia* antivenom was not yet available for treatment. Patients with a history of contact with caterpillars and with some clinical evidence of envenomation (local pain, edema, bleeding, hematomas, etc.) and patients who brought the caterpillars to the clinic were considered in this study. These caterpillars were sent to the Instituto Butantan (IBu), *São Paulo*, Brazil for species identification. The patients were classified into the following four clinical groups based on the treatment experience at the hospital: Grade 0 patients were asymptomatic with no blood coagulation changes or bleeding of any type during 72 h of follow-up; Grade I patients exhibited bleeding symptoms with blood coagulation changes (i.e., incoagulable blood or prolonged clotting times); Grade II patients experienced ecchymosis, epistaxis, gingival bleeding, hematomas, bleeding from scars or recent wounds with no hemodynamic changes, and altered blood coagulation parameters; and Grade III patients exhibited macroscopic hematuria and hemorrhages in the digestive tract, lungs, peritoneum and central nervous system. The bleeding was occasionally accompanied by hemodynamic disturbances, acute renal failure, respiratory failure, adynamic ileum, changes in cognition, and/or altered blood coagulation parameters (Table 1).

This study was approved by the Ethics Committee of the HSVP (RS), Brazil. Written informed consent to participate was obtained from the patients or their relatives.

Blood samples

The first venous blood sample was either obtained shortly after admission (P01, P03, P04, P05, P11, P12, and P14), after the patient was under observation at the hospital for 5, 13, or 16 h (P06, P07, and P08), or 1 (P02 and P13), 3 or 4 days (P09 and P10,) before being included in the study. The delay times between blood collection and the assays are indicated in Table 2.

Blood was collected in 10% EDTA-Na_2 with 10 µL of antilonomic serum produced by the IBu (SP) for the laboratory analyses. For the biochemical analysis, serum samples were routinely collected and assayed in the HSVP laboratory. The coagulation assays were performed

Table 1 - Background information on 14 patients on admission to HSVP

Patient	Site of contact, age, sex	Interval* (hours)	Grade	Developed symptoms
01	R. hand (fingers), 25, M.	7	0	-
02	- 3, M	24	0	-
03	Back, 12, M	6	I	L. pain, erythema, cephalea, GID, dizziness
04	R. hand, 7, M	7	I	L. pain, edema
05	R. hand, 36, M	7	I	L. pain, cephalea, dizziness
06	Le. forearm, 13, F	7	I	L. pain, edema, cephalea
07	Le. hand (finger), 8, M	8	I	L. pain, erythema, cephalea, GID
08	R. hand (finger), 71, F	24	I	L. pain, erythema, cephalea, GID
09	Le fingers, 63, F	4	I	L. and general pain, edema, cephalea, GID, dizziness
10	R. hand, 8, F	24	I	L. pain, erythema, edema, arthralgia
11	R. hand, 3, M	48	II	L. pain, ecchymosis, bleeding, hematomas
12	R. thigh, 12, M	120	II	L. pain, ecchymosis, dizziness, gingivorrhagia, hematomas
13	R. hand (fingers), 11, M	< 24	III	L. pain, erythema, macroscopic hematuria, hematoma (R. arm), arthropathy (R. elbow)
14	R. hand, 14, F	48	III	L. pain, edema, post-trauma: pulmonary and peritoneal hemorrhagia., vomiting, hypotension

GID- gastrointestinal disturbance, M-male, F–female, R-right, Le-left, L-local. *- Time elapsed between accident and blood collection; HSVP- Hospital São Vicente de Paulo

Table 2 - Blood coagulation and fibrinolytic parameters in 12 patients after the accidents with *Lonomia oblique* caterpillar, on admission

Assays	Patients X±SEM	Min-max values	(Normal X±SEM)
Fibrinogen (g/L)	0.7±0.6	0.1-1.9	2.1±0.1
FII (%)	91.4±35.7	50-189	100±4
FV (%)	60.6±56.0	11-211	111±9
FVII (%)	130.8±98.1	56-371	132±34
FVIII (%)	137.1±129.9	51-529	135±8
FIX (%)	63.7±20.7	28-95	100±4
FX (%)	112.7±54.8	63-232	128±24
FXI (%)	107.9±34.5	70-177	131±6
FXII (%)	73.1±43.3	12-148	113±14
FXIII act (%)	45.8±18.8	25-75	100
FXIII ag (%)	79.5±18.4	66-105	60-150
vWF (%)	105.0±66.1	46-210	50–150
T-AT (µg/mL)	63.3±23.8	25-93	4±0
Protein C (%)	41.1±38.1	2-109	89±7
AT-III act (%)	111.1±26.8	73-163	94
PLG (%)	45.2±13.0	30-78	76±9
α_2-AP (%)	51.4±21.3	28-96	106±9
PAI (AU/mL)	18.0±10.2	2-33	12±4
FDP (µg/mL)	70.0±107.3	3-384	3±0
D-Di (µg/mL)	26.6±38.8	1-128	0.5±0

Number of volunteers = (5-7), F-factor, vW = von Willebrand, T-thrombin, AT = Antithrombin, act = activity, ag = antigen

on citrated plasma (160 mM sodium citrate with 2% antilonomic serum). This serum was added to prevent further *in vitro* activity of the venom. Plasma aliquots for fibrinogen determination were mixed with 50 µL of 10% EACA (Ipsilon, *Química e Farmacêutica*, NIKKHO Brazil LTDA, RJ, Brazil) before freezing. The plasma was immediately stored at -20 °C. Frozen aliquots were transported on dry ice to the IBu (SP) and maintained at -70 °C until testing. All plasma samples were examined within three months of collection.

Assays

At the HSVP, the whole blood clotting time (WBCT)[20], activated partial thromboplastin time (APTT) (Roche Diagnostics, Switzerland), and prothrombin time (PT) (Baxter Healthcare Corporation, Morgantown, WV, USA) were assayed. Additionally, hematological and biochemical assays were performed, and the platelet count was determined using conventional methods.

Human plasma samples deficient in the following factors were used for the clotting factor assays: II, VIII, X, and XI (Behringwerke, Brazil); VII and IX (Baxter Healthcare Corporation, USA); XII (American Diagnostics, Germany); and V (prepared in the laboratory)[21]. The factor XIII level, antithrombin III activity, protein C (PC; Staclot protein C assay) level, plasminogen (PLG; Stachrom PLG) level, and alpha$_2$-antiplasmin (α_2-AP; Stachrom antiplasmin) level were tested using Diagnostica Stago kits (Asnieres, France). Plasminogen activator inhibitor- 1 (PAI-1; Spectrolyse - enzymatic) was measured with an American Diagnostics kit. Immunological tests were used to measure the degradation products of fibrin/fibrinogen (FnDP/FgDP), and thrombin-antithrombin antigen (T-AT) was measured using an EIA kit system (Behringwerke, Brazil). Cross-linked fibrin fragments (D-dimer–[D-Di]) were measured using a latex agglutination immunoassay (Diagnostica Stago), and fibrinogen levels were assayed using the colorimetric method[22]. Total plasma protein was assayed via the method of Markwell *et al.*[23] and haptoglobin was measured by electrophoresis on cellulose acetate[24].

RESULTS

The majority of the 14 patients (Ps) were classified as Grade I (n=8), two were classified as grade II, two as Grade III, and two as Grade 0 (Table 1). After admission, the patients did not receive any specific treatment with the exceptions of P12 who had received a blood transfusion before she arrived at HSVP and P14 who received a transfusion of erythrocytes and the antifibrinolytic drug ε-amino-caproic acid (EACA). Two asymptomatic patients were excluded. Thus, the recoveries of the hemostatic parameters were assayed in 12 patients.

The time that elapsed from the accident to admission to the hospital varied between 4 and 120 h. There was no relationship between this period and the seriousness of the envenomation, although the more severe cases were the patients who arrived at the hospital less than 24 h or more than 48 h after the accident (Table 1). Bleeding ceased without treatment within 48 h in all GII cases and in one GIII patient.

An overview of the envenomation kinetics (Figures 1, 2) of these patients revealed accentuated fibrinogen reductions during the first hours after the accident that increased the hemostatic levels, but these levels did not reach the normal values. The coagulation and fibrinolytic factor assays of the 12 patients upon admission are presented in Table 2. Marked decreases in the levels of factors V and XIII and Protein C (PC) in the patients were observed during the initial hours after envenomation (Table 2). The FXIII activity levels remained at 50% even after 192 h. In contrast, the FXIII antigen levels remained within the normal range. The majority of the patients presented with FV levels between 70 and 100% at 72 h after envenomation. Accentuated decreases in PC were observed in all envenomation grades, and these values remained below normal during the analysis period (Figure 1). The recuperations were slower in the GII and GIII patients (> 120 h) than in the GI (> 72 h) patients (data not shown). Factor II was decreased upon admission in one mild case (58%) and one severe case (50%), and these levels remained decreased for 3 to 5 days (60 and 70%). Similarly, factor VIII levels were also decreased in three patients (51%), whereas two patients exhibited increased levels (529% and 151%). The majority of the patients exhibited slightly reduced FIX levels (44-81%) with the exception of one patient who had a normal level (102%) 120 h after the accident. Regarding FXII, there were no changes with the exceptions two patients who presented with low levels (12 and 15%). Von Willebrand factor and ATIII activity levels were normal in most of the patients, but one patient presented with an increased vWF level at 29 h (210%). Furthermore, the ATIII antigen levels were increased in 6/11 patients (between 196 and 200%). The T-AT complex levels were increased upon admission in all patients (25-93 µg/mL); however, these levels normalized during the evolutions of the conditions (Figure 2).

The plasminogen and α_2-antiplasmin levels were reduced upon admission. Both parameters increased but did not reach normal levels during the analysis period. Slight increases in the PAI-1 levels were observed at 6 and 24 h, PAI-I levels returned to normal after these time points (Figure 2). The

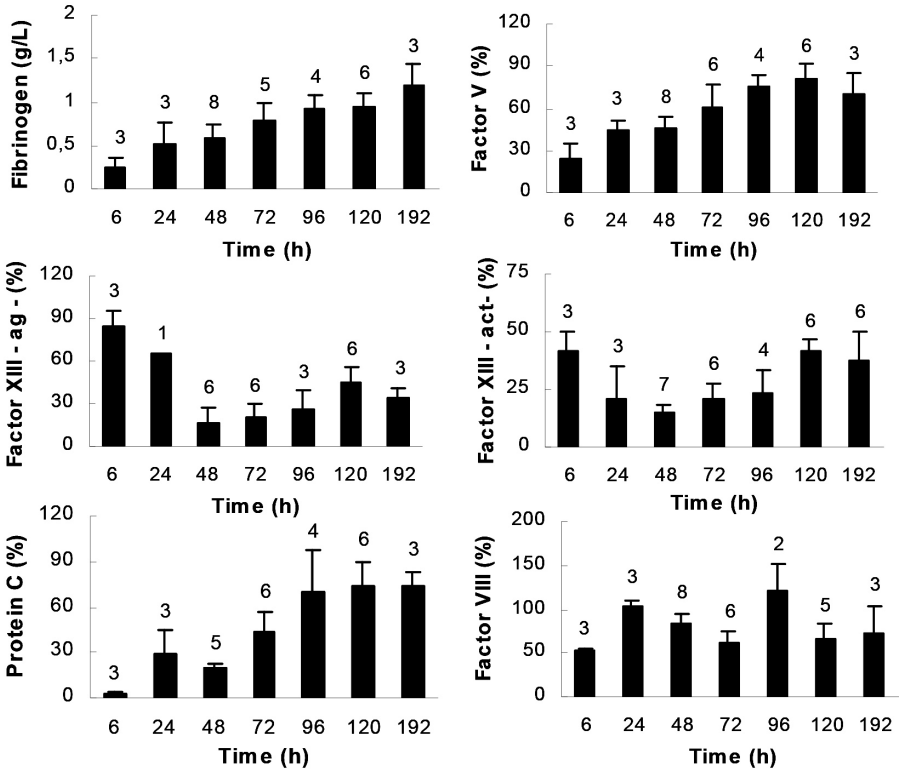

Figure 1 - Time-course of fibrinogen, factor V, factor XIII-ag, factor XIII-act, factor VIII and protein C consumption of 10 patients after contact with the Lonomia obliqua caterpillar. ag- antigen, act- activity, Bars represent the mean ± SEM. Numbers over bars = number of patients.

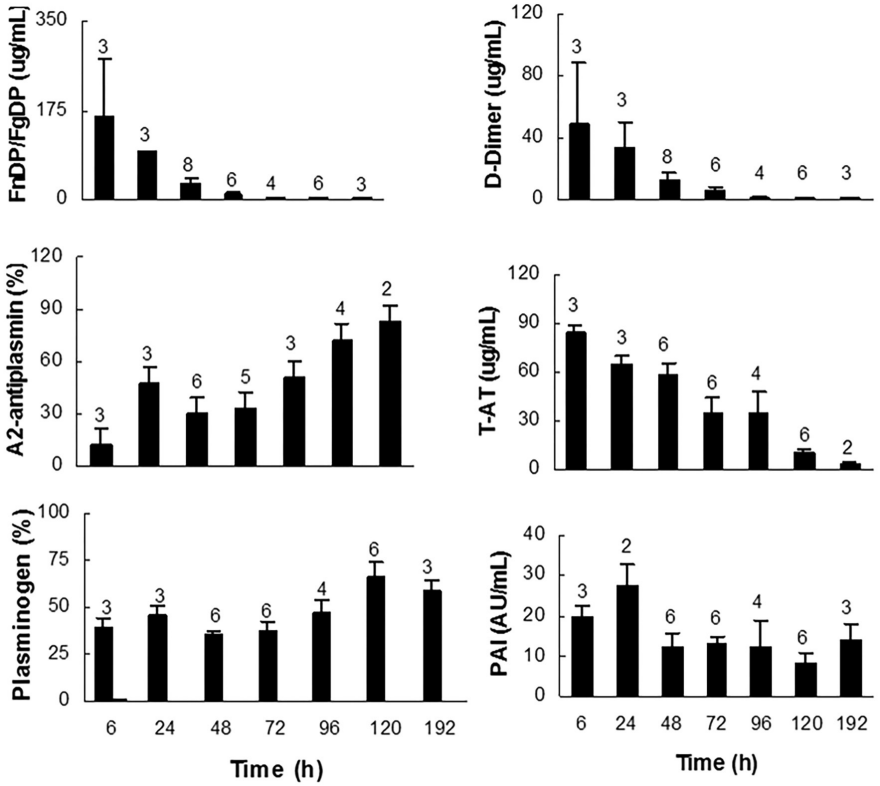

Figure 2 - Time-course of fibrin/fibrinogen degradation products (FnDP/FgDP), cross-linked fibrin fragment (D-Dimer), α_2-antiplasmin, thrombin-antithrombin antigen (T-AT), plasminogen and plasminogen activator inhibitor (PAI) consumption of 10 patients after contact with the *Lonomia obliqua* caterpillar. Bars represent the mean ± SEM. Numbers over bars – number of patients

FnDP/FgDP and D-Di levels were increased in nearly all patients primarily at 6-7 h after the accidents. Higher levels (FnDP/FgDP: -384 µg/mL and D-Di-128: µg/mL) were observed in one patient. All patients returned to normal levels after 120 h (Figure 2).

The hematological patient data that were collected upon admission (n=8) revealed only one anemic patient with internal bleeding (2.5 x 10^{12} red cells, 22% hematocrit and 7.6 g/L hemoglobin). Slight leukocytosis with differential counts that remained within normal limits was observed. Three of the patients presented with moderate leukocytosis (12-14.0x10^9/L) without any significant alterations, and only a single patient presented with neutrophilia without a leftward deviation. Thrombocytopenia was observed in only one patient at 40 h after admission (51 x 10^9/L), and the platelet level remained below normal (65 x 10^9/L) even after 72 h. One patient who was admitted with normal platelet levels exhibited a slight decrease at 120 h after the accident (131 x 10^9/L). Four patients exhibited reduced total protein levels (4.9 – 5.8 g/dL) that did not return to normal (7.0 ± 0.5) until they were discharged, and the other patients exhibited levels between 6.0 and 7.4 g/dL during the analysis period. Low haptoglobin levels (1.3-1.7 g/L) were observed in 3 of 5 studied patients and probably resulted from subclinical hemolysis.

DISCUSSION

This is the first study of patients (n=12) who had been envenomed by contact with the *L. obliqua* caterpillar to conduct monitoring and long-term follow-up of the clinical and (laboratory) coagulation parameters until discharge.

The patients bleeding disorders following contact with the caterpillars were spontaneous and occurred in any part of the body but generally occurred in areas that were injured or had previous wounds.

The patients with low fibrinogen levels also presented with low FV, PC, FXIII, PLG and α_2-AP levels. In contrast, these patients exhibited higher T-AT, FnDP/FgPD, and D-Di levels, which suggests the occurrence of disseminated intravascular coagulation (DIC) and fibrinolysis activation. Our follow-up laboratory data indicated that there was no relationship of the time elapsed from the accident until hospital admission with the severity of the condition. However, the GI patients who were admitted between 7 and 29 h after the accident exhibited higher levels of FnDP/FgDP and D-Di than the patients who were admitted 96 h after the accident and presented with near normal levels. Additionally, the patients who were in critical condition (GII and GIII) an arrived at the hospital 48 h after the accident exhibited lower levels of FnDP/FgDP and D-Di, which suggests that these alterations are more strongly related to the time of the accident than to the seriousness of the envenomation. Similar results have been observed in patients who were poisoned by *L. achelous* caterpillars and presented with low FnDp/FgDP levels during the first days after envenomation[16]. These consumption coagulopathies seem to be induced mainly by the FII and FX procoagulant activators that are present in both *L. obliqua* bristle extracts[12,13] and *Lonomia achelous*[25,26] as previously proposed elsewhere[8,14]. Despite the formation of intravascular thrombin, which is detected as an elevation in the T-AT complex, moderate thrombocytopenia (138 x 10^9/L) was observed in only one patient. In Venezuela, patients poisoned by *L. achelous* were treated with purified human fibrinogen with aprotinin, and in some cases, EACA was administered after aprotinin. In our study, one patient (Grade III) was treated with an antifibrinolytic drug (EACA) in Ringer solution for three days (total of 15 g), received packed red blood cells over four days (1.5 L) and was discharged ten days after admission in a normal condition. Since 1995, there has been a reduction in the mortality rate due to the introduction of an antilonomic serum for the treatment of *L. obliqua* envenomation[19,27]. Our present study revealed a severe consumption coagulopathy characterized by hypofibrinogenemia and activation of the fibrinolytic system that was prolonged for more than eight days during recovery. The abnormalities related to blood coagulation and fibrinolytic factors were similar in all the patients in the study, which indicates that the severity of the accident could not be predicted by changes in the hemostatic parameters. Consequently, alterations of coagulation without thrombocytopenia do not define the seriousness of the accident; however, these parameters are relevant when evaluating the patient recovery, and treatment efficacy.

The comparative study between the patient who received blood and EACA treatment and the patients who did not receive any treatment after admission suggested that blood transfusion, even at 120 h, was responsible for the significantly lower levels of FV, FXIII, PC and PLG and the higher levels of T-AT, which suggests that whole blood infusion can be responsible for blood coagulation activation as has been found in cases hemorrhagic diathesis induced by contact with *L. achelous*[16]. However, 240 h after the accidents, there were no differences in the fibrinogen levels, which were at hemostatic levels. Moreover, the FXIII levels remained below normal values in all patients.

Material obtained from the venomous fluid of the secretory system of *L. obliqua* has been shown to contain an enzyme with fibrinolytic action[28]. Consequently, in the

patients in this study, fibrinolysis could have occurred due to the direct action of this enzyme (lonofibrase), which may have been responsible for both the primary fibrinolytic activity and the secondary fibrinolysis activation that were induced by procoagulant activities[29]. The decrease in PLG was not related to the interval between the accident and the analysis. In contrast, the PAI-1 levels at 7 and 29 h after the accidents were greater than the levels at 48 and 96 h. Interestingly, all patients, including the asymptomatic ones, exhibited FXIII levels that were below normal values during the analyzed period. Studies of *L. achelous* hemolymph and its fractions (i.e., lonomin V) have shown that this enzyme has a dose-dependent relationship with FXIII inactivation, and this effect may play a major role in the bleeding syndrome induced in humans[30]. This mechanism could be one of the factors that are involved in the hemorrhagic syndrome that occurs following *L. obliqua* exposure, which is also associated with a decrease in FXIII. *In vitro* studies and experimental envenomations of rats and rabbits with *L. achelous* caterpillar bristle extract as well as studies in patients indicate that FXIII reduction is related to the cleavage of subunit A of the factor XIII molecule associated with the inhibitor of crosslinking[30]. Consequently, the formation of D-Di is not substantially increased. These results suggest that, *in vivo*, the hemorrhagic syndrome can also be provoked by the proteolysis of FXIII. In contrast, Zannin *et al*.[9], who obtained data only upon patient arrival at the hospital, reported high levels of D-Di in the majority of the patients, although some of these patients presented with normal levels of fibrinogen. Thus, it is important to consider that although some groups have reported that no fibrinolytic activity is induced by *L. obliqua* exposure and that any fibrinolytic activities are secondary[26], another group presented clear evidence of fibrinogenolytic activity[28,29]. Thus, the mechanism of this envenomation is not yet entirely understood. Some components, such as fibrinogenolytic agents, kininogen, serpins, lectins, and PLA_2, which have been described in a catalog of *L. obliqua* cDNAs and proteins[29], may also contribute to the symptoms manifested by patients who experience this type of accident. Moreover, kininogens have been shown to possess antithrombotic properties *in vivo* at low concentrations of thrombin[31]. *Lonomia obliqua* bristle extract actives human platelets to induce adhesion and aggregation through a calcium-dependent mechanism that is triggered by the phospholipase A2 that is present in this extract[32]. Most severely affected patients present thrombocytopenia, which is related to morbidity and bleeding events. Rats that are experimentally envenomed with *Lonomia obliqua* extract have been shown to present with slight thrombocytopenia, but significant hypoaggregation induced by intravascular nitric oxide and fibrin/ fibrinogen degradation products can be elicited by hemostatic disturbances[33].

Approximately 2% of patients envenomed via contact with *L. obliqua* caterpillars develop acute renal failure, and the administration of antilonomic serum reduces the mortality due to the severity of renal impairment; however, antilonomic serum does not decrease this incidence[27]. An experimental research has shown that treatment with *Lonomia* antivenom within 2 h of envenomation normalizes biochemical alterations, whereas treatment after 6 h does not elicit the recovery of these parameters despite the efficacy of specific antivenom therapy in reversing hemostatic disturbances[34].These results may explain the observations in 286 patients. The patients who received care more than 48 h after the contact exhibited a greater probability (11%) of progressing to acute renal failure than those who arrived at the hospital within the first 48 h (2.9%) indicating that the time elapsed between the contact and the hospital care is an important factor in terms of the occurrence of acute renal failure (HSVP, Passo Fundo, 1989/02 to 1995/07, unpublished data, Duarte AC). The mechanism responsible for renal dysfunction following the accidental exposure in humans is not yet well understood, but hemodynamic changes secondary to bleeding or direct nephrotoxicity are possible explanations. It has been suggested that renal dysfunction could be related to a disseminated intravascular coagulation with a massive deposition of fibrin in the glomerular capillaries. Cortical and tubular necrosis resulting from intravascular coagulation is also possible because, in previous studies, 4 of 39 acute renal failure cases have never recovered renal function[11,27]. In our study, only one patient, who was admitted to the hospital 48 h after the accident, presented with an increased creatinine (2.7 mg/ dL) level, which normalized after 24 h. Experimental *L. obliqua* envenomation in rats has been shown to elicit acute kidney injury with tubular necrosis associated with renal inflammation, fibrosis and increased vascular permeability. Additionally, the presence of *Lonomia* venom in the renal tissue is associated with morphological and functional alterations that are suggestive of a direct nephrotoxic action[35].

The patients in this study presented with different levels of envenomation and received palliative treatment without antilonomic serum therapy, and the laboratory parameters normalized after 196 h. However, treatment with antilonomic serum must be applied because it is the most efficient treatment and reverses the hemostatic disturbances as well as the bleeding disorders in less than 24 h after treatment[19].

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