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Using peritoneal and blood lactate as predictor of condition type, surgical referral and prognosis in equine colic cases

[*Uso do lactato peritoneal e sanguíneo como preditor do tipo de afecção, encaminhamento cirúrgico e prognóstico em casos de cólica equina*]

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ABSTRACT

It is important to investigate fast and accurate equine colic syndrome diagnostic forms. Lactate results from anaerobic glycolysis; high levels of it may indicate intestinal disorders with tissue hypoperfusion and hypoxia. The current study aims at investigating whether blood and peritoneal lactate values observed when horses with colic syndrome were hospitalized, were associated with condition type, therapeutic referral, and survival rates. Retrospective analysis was applied to 498 medical records of animals with colic syndrome, at EQUIVET Hospital –SP; 89 cases were herein selected. Based on logistic regression, peritoneal lactate played a more significant part than blood in variables like obstruction type and survival rates. Surgical cases comprised 52.8% of analyzed animals; strangulation changes, 26%; and overall survival, 62.9%. Mean blood and peritoneal lactate level in animals showing strangulation changes reached 5.11 and 7.33mmol/L, whereas non-strangulation cases recorded 3.54 and 3.06mmol/L, respectively. On the other hand, mean blood and peritoneal lactate level recorded for survivors reached 3.43 and 2.42mmol/L, whereas non-survivors recorded 4.84 and 7.13mmol/L, respectively. We concluded that peritoneal lactate measured when horses with colic syndrome were hospitalized was a predictor of condition type, and of animal survival and prognosis. However, blood and peritoneal lactate measurements did not contribute to therapeutic referral.

Keywords: portable analyzer, peritoneal fluid lactate, venous lactate, intestinal ischemia, prognosis

RESUMO

O estudo de formas diagnósticas rápidas e precisas é importante na síndrome cólica equina. O lactato, produto da glicólise anaeróbica, quando elevado, pode indicar afecções intestinais com hipoperfusão e hipóxia. O objetivo deste estudo foi verificar se os valores de lactato sanguíneo e peritoneal, na admissão de equinos com síndrome cólica, estão relacionados com o tipo de afecção, com o encaminhamento terapêutico e a sobrevida. Uma análise retrospectiva foi realizada em 498 atendimentos em síndrome cólica, no Hospital EQUIVET-SP, quando 89 casos foram selecionados. A regressão logística indicou que o lactato peritoneal obteve maior significância comparado ao sanguíneo, nas variáveis tipo de obstrução e sobrevida. Casos cirúrgicos foram 52,8%; alterações estrangulativas, 26%; e sobrevivência geral, 62,9%. Em alterações estrangulativas, a média do lactato sanguíneo e peritoneal foi de 5,11 e 7,33mmol/L; em não estrangulativos, 3,54 e 3,06mmol/L. Já os sobreviventes obtiveram 3,43 e 2,42mmol/L, e os não sobreviventes 4,84 e 7,13mmol/L, respectivamente. Conclui-se que a mensuração do lactato peritoneal na admissão de cavalos com cólica foi considerada um preditor do tipo de afecção, bem como da sobrevida e do prognóstico. Porém, as mensurações de lactato sanguíneo e peritoneal não auxiliaram no encaminhamento terapêutico.

Palavras-chave: analisador portátil, lactato líquido peritoneal, lactato venoso, isquemia intestinal, prognóstico

INTRODUCTION

Colic syndrome is the main condition observed in equine emergency care procedures (Cook and Hassel, 2014). Resolutive rates observed in medical clinics range from 80% to 85%; simple obstructive or strangulating diseases requiring surgical intervention account for 2% to 10% of cases (Dukti and White, 2009). However, it is important to emphasize that the shorter the

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clinical evolution time, the better the prognosis (Abutarbush *et al*., 2005), since it helps reducing risks associated with complications, such as ischemia (Suthers *et al*., 2012).

The prognosis of horses treated with colic syndrome is essential to help define the therapeutic approach to be adopted and to provide owners with information about costs with surgery or patient stabilization (Grulke *et al*., 2001). Prognosis can vary depending on animals' condition type and on affected site, clinical evolution time, patients' overall condition and complications (Dukti and White, 2009). Mair and Smith (2005) reported 79.6% survival rate in simple small bowel obstructions cases and 54.8%, in strangulation-related injuries. With respect to the larger colon, Dukti and White (2009) reported 90% survival rate in simple obstruction cases and 52% in strangulation-related cases.

Lactate has been used and validated as systemic marker of poor tissue perfusion and anaerobic metabolism in horses (Southwood and Fehr, 2013); lactate analysis in peritoneal fluid is more sensitive than that of blood for prognostic purposes (Delesalle *et al*., 2007). Therefore, the aim of the current study was to investigate whether blood and peritoneal lactate levels, measured at the time horses with colic syndrome were hospitalized, were associated with animals' condition type, therapeutic referral, and survival rates, in order contribute to the therapeutic management and prognosis of horses affected by this disease.

MATERIALS AND METHODS

Medical records of adult horses with colic syndrome treated at EQÜIVET Hospital, Indaiatuba County-São Paulo State, from January 2016 to September 2020, were retrospectively reviewed. Medical records comprising information about peritoneal and blood lactate measurements performed at hospitalization time, animals' condition diagnosis, treatment type, complications during hospital treatment and case evolution were included in the analysis. Records presenting incomplete medical reports and concomitant illnesses were excluded from the analysis.

Collected data included blood and peritoneal lactate measurements conducted at hospitalization time; condition site; obstruction type (strangulation or non-strangulation); diagnosis; complications before, during, or after surgical or medical treatment; and outcome (hospital discharge, death, or euthanasia). Animals' survival was defined as hospital discharge. Necropsy reports issued for euthanasia or death cases were compiled.

Portable analyzer (Accutrend® Plus) was used to determine lactate concentrations in anticoagulant-free blood samples collected from animals' external jugular vein, as well as in abdominal fluid samples obtained through abdominocentesis and placed in tubes without anticoagulant.

Recommended temperature ranging from 15ºC to 35ºC was used for lactate measurement purposes. Accutrend® Plus analyzer enables measuring lactate levels ranging from 0.8 to 21.7mmol/L blood value and from 0.7 to 26mmol/L plasma value. However, the device's analyzer registers LOW for values lower than the aforementioned, and HIGH for values higher than them. This test must be performed 60 seconds after the sample is placed on the tape (Accutrend…, 2007). Quantitative values observed for blood and peritoneal lactate levels were used for statistical analysis; 0.6 mmol/L of blood lactate was recorded as LOW in the analyzer whereas 0.7mmol of peritoneal lactate was considered LOW and 27mmol/L of it was considered HIGH.

Multiple linear regression, carried out in IBM SPSS Statistics software version 20, was used to compare independent variables (sex, complications, gastrointestinal segment, peritoneal lactate, blood lactate, therapeutic referral, and obstruction type) to the dependent variable (animal's death). Binary logistic regression was carried out in the same software to compare the significance of dependent variables (venous lactate and peritoneal lactate) to that of independent variables (obstruction type, referral, and animal's survival). Both analyses were conducted at 5% significance level. Moreover, descriptive analysis was performed to investigate samples' features.

RESULTS

Medical records of 498 horses presenting abdominal discomfort, which were treated between January 2016 and September 2020 - mean number of 103 cases on a yearly basis - were analyzed. Of this total, 89 adult horses (21 Quarter Horses, 20 Brazilian Equestrians, 18 mixed breed, 11 Mangalarga Marchador, six Thoroughbred Lusitano, five Thoroughbred Arabian, three Thoroughbred English, two Campolina, one Breton, one Polo and one Paint Horse) - 38 females and 51 males (only 1 stallion) - were selected based on the herein adopted inclusion criteria.

Animals' conditions were divided into categories based on the affected site, gastrointestinal segment, obstruction type, need of surgical procedure, survival, and number of complications (Table 1). Regarding condition type, 74% of cases presented non-strangulating obstruction and recorded 77.3% survival rate, whereas 26% of cases presented strangulation changes and recorded 21.7% survival rate. As for digestive segments, gastric disorder cases recorded 100% survival rate; small intestine, 60.9%; large intestine, 66%; small and large intestines, 30%; and other cases, 66.7%. The need for surgical procedure was observed in 52.8% of the 89 included cases. Overall survival rate reached 62.9% - 56 animals survived and 16 out of 33 non-survivors were euthanized.

Among all 89 selected medical records, 7% reported diseases in animals' stomach; 26%, in the small intestine 53%, in the large intestine; 11%, in the small and large intestines; and 3%, in other sites. Animals belonging to the gastric disorder group, which presented gastric distension due to overload or gas, were included in the study. Affections diagnosed in the intestinal segment, listed as small intestine, comprised 14 compactions, five volvulus (three in the mesenteric root, one due to lipoma and one by the omentum), two incarcerations (in the gastrosplenic ligament and in the epiploic foramen), one rupture and one duodenitis-proximal jejunitis. The ones listed as large intestine comprised 10 large colon displacements (one associated with impaction; one, with enterolithiasis in the small colon; and one, with large colon torsion), 19 impactions (six cecal, seven in the large colon (one associated with fecaloma in the small colon), five in the small colon; and one, in the large and small colon), five torsions (four in the large colon and one cecal), five tympany (two in the large colon and three cecal), three colitis, one ceco-colic intussusception, two enteroliths (one enterolith in the transverse colon and small colon and one, in the transverse colon and large colon rupture), and two fecalomas.

Health issues classified as disorders in the small and large intestine comprised five impactions (one of ileum and large colon displacement, two of ileum and large colon, one of small and large colon and colitis, one of large colon and duodenitis-proximal jejunitis), one enteritis and peritonitis, one mesenteric root torsion and small and large colon impaction, one large colon displacement and epiploic foramen entrapment, one cecal entrapment in abdominal hernia, and one inguinal hernia and large colon torsion. The ones named as others comprised one rectal rupture, one peritonitis and one adhesion case.

Table 2 shows information about mean values observed for minimum and maximum lactate concentrations in venous and peritoneal lactate analyses, in each investigated segment, as well as mean values observed for non-strangulating and strangulating obstructions.

Obstruction type – i.e., non-strangulation or strangulation – played a significant part in blood lactate ($p=0.01$) and peritoneal fluid ($p=0.006$) concentrations, based on binary logistic regression analysis. The odds ratio observed for venous lactate, at 95% confidence interval, reached 1.302 (1.065 – 1.592), whereas odds ratio observed for peritoneal lactate concentrations in strangulation injuries reached 1.177 (1.047 – 1.323). Only peritoneal lactate recorded statistically significant difference ($p=0.05$) in the analysis carried out with both lactates.

Blood lactate concentration of 5.11 mmol/L was observed in horses with strangulation changes, on average, whereas the group with non-strangulating obstructions recorded blood lactate concentration of 3.54 mmol/L at hospitalization time, on average. Peritoneal fluid concentration under strangulating obstruction conditions reached 7.33 mmol/L, on average, and the concentrations of it in the non-strangulating obstruction group reached 3.06 mmol/L.

Table 1. Division of 89 adult horses treated with colic syndrome from 2016 to 2020, at Equivet Hospital, Indaiatuba County- São Paulo State, Brazil, based on digestive segments, number of horses, obstruction type, need of surgery, as well as on number of survivors and complications (M=male; F=female)

Digestive segment	Number of horses	Obstruction type	Need of surgery	Number of survivors	Number of complications
Stomach	Total= 6 M=6	Strangulating: 0 Non-strangulating: 6	Yes: 0 No: 6	Survivors: 6 Dead: 0	None
Small intestine	Total=23 F= 7 M= 16	Strangulating: 10 Non-strangulating: 13	Yes: 14 No: 9	Survivors: 14 Dead: 9	2 nasogastric reflux cases 1 diarrhea 3 more than one complication 1 myositis 1 segment necrosis 1 adhesion
Large intestine	Total=47 F= 25 M= 22	Strangulating: 9 Non-strangulating: 38	Yes:23 No: 24	Survivors: 31 Dead: 16	2 diarrheas 2 ruptures 2 deaths in recovery 2 more than one complication 3 colitis/typhlitis 1 euthanasia on the operating table 1 relaparotomy after 5 days 1 laminitis
small and large intestine	Total=10 F= 5 M= 5	Strangulating: 4 Non-strangulating: 6	Yes: 9 No: 1	Survivors: 3 Dead: 7	2 more than one complication 1 shock 1 hemoperitoneum
Others	Total= 3 F= 1 M= 2	Strangulating: 0 Non-strangulating: 3	Yes:1 No:2	Survivors: 2 Dead: 1	1 colitis/typhlitis

Table 2. Mean blood and peritoneal lactate concentrations and their variation in non-strangulating and strangulating obstructions observed in 89 horses treated with colic syndrome, from 2016 to 2020, at Equivet Hospital, Indaiatuba County – SP, distributed based on affected segment (B=blood lactate; PF=peritoneal fluid lactate)

Digestive segment	Mean lactate concentration (minimum-maximum values)	Mean lactate concentration in non-strangulating obstructions	Mean lactate concentration in strangulating obstructions
Stomach	B= 3.31 mmol/L (0.7 to 8.3) PF=1.85 mmol/L (0.6 to 4.6)	B= 3.31 mmol/L PF= 1.85 mmol/L	-
Small intestine	B= 4.12 mmol/L (1.5 to 8.3) PF= 6.43 mmol/L (0.6 to 27)	B= 4.17 mmol/L PF= 4.60 mmol/L	B= 4.05 mmol/L PF= 8.81 mmol/L
Large intestine	B= 3.81 mmol/L (1.2 to 11.7) PF= 3.21 mmol/L (0.6 to 21.1)	B= 3.81 mmol/L PF= 3.21 mmol/L	B= 3.97 mmol/L PF= 3.56 mmol/L
Small and large intestine	B= 5.07 mmol/L (2.8 to 10.2) PF= 5.49 mmol/L (0.6 to 12.4)	B= 4.8 mmol/L PF= 4.83 mmol/L	B= 5.47 mmol/L PF= 6.47 mmol/L
Others	B= 2.33 mmol/L (1.3 to 3.3) PF= 1.8 mmol/L (0.6 to 3.6)	B= 2.33 mmol/L PF= 1.8 mmol/L	-

Analysis conducted for therapeutic, surgical, or medical referral purposes was based on binary logistic regression, according to which, peritoneal (p=0.109) and blood (p=0.879) lactate concentrations were not statistically significant in analyses applied to them, either in combination or in separate. Therapeutic referral was not statistically significant for lactate measurement at hospitalization time.

Based on the binary logistic regression, blood (p=0.01) and peritoneal (p<0.001) lactate values were statistically significant for the survival of horses with colic syndrome. The odds ratio (95%

confidence interval) of blood lactate values describing survival cases reached 1.303 (1.064 - 1.596). The odds ratio of peritoneal fluid lactate recorded for this very same variable reached 1.385 (1.151-1.667). Only peritoneal lactate presented statistical significance (p=0.005) when both lactate sample types were assessed in combination.

Mean blood and peritoneal lactate concentrations observed for survivors' groups reached 3.43mmol/L (they ranged from 0.7 to 8.5mmol/L) and 2.42mmol/L (they ranged from 0.6 to 8.7mmol/L), respectively. On the other hand, mean blood and peritoneal lactate concentrations observed for the non-survivors' group reached 4.84 mmol/L (they ranged from 1.9 to 11.7) and 7.13mmol/L (they ranged from 0.6 to 21.1mmol/L), respectively. Median blood lactate concentration observed for non-surviving horses at hospitalization time reached 3.8mmol/L; it was higher than that observed for survivors in the current study (2.9mmol/L). Median peritoneal lactate concentration observed for non-surviving horses at hospitalization time reached 4.3 mmol/L; it was also higher than that observed for survivors (1.4mmol/L).

Based on the comparison of variables, such as blood lactate, peritoneal lactate, obstruction type, therapeutic referral, complications during treatment, animals' sex and gastrointestinal segment to outcome "death", peritoneal lactate, obstruction type and incidence/lack of complications during treatment recorded statistically significant results (Table 3, 4). This finding has shown that patients with colic syndrome, who were subjected to surgical procedure, did not present risk factor for death, unlike patients undergoing strangulation process. Animals' sex was not a risk factor for lactate measurements at hospitalization time. Complications observed during medical treatment, or after surgical treatment, were associated with risk of death; they were also an important factor for improvements in patients' health condition.

Table 3. Variables (sex, obstruction type, therapy, gastrointestinal segment, and complications) associated with the outcome (death) observed for all 89 horses with colic syndrome treated at EQUIVET Hospital, Indaiatuba County-SP, from 2016 to 2020

Death			
Factors		YES	NO
Sex	Male	16	35
	Female	17	21
Obstruction type *	Non-strangulating	15	51
	Strangulating	18	5
Therapy	Medical clinic	6	36
	Surgical	27	20
Gastrointestinal Segment	Stomach	0	6
	Small intestine	9	14
	Large Intestine	16	31
	Small and Large Intestines	7	3
	Others	1	2
Complications **	None	13	47
	With complications	20	9
	Nasogastric reflux	0	2
	Laminitis	0	1
	Diarrhea	1	3
	Relaparotomy 5 days after the initial procedure	0	1
	More than one complication	5	2
	Adhesion	1	0
	Myositis	1	0
	Colitis/typhlitis	4	0
	Shock	1	0
	Intestinal loop rupture	2	0
	Hemoperitoneum	1	0
	Death at the time of anesthesia recovery	2	0
	Segment necrosis	1	0
	Euthanasia on the operating table	1	0

*statistical significance at p=0.008 **statistical significance at p=0.006

Table 4. Analysis of variables with significance level, odds ratio and 95% confidence interval, based on outcome "death", in 89 adult horses with colic syndrome, who were treated at Equivet hospital, from 2016 to 2020

Variable	p value	Odds ratio	95% Confidence Interval	
Peritoneal lactate	0.002	3.259	0.010	0.043
Obstruction type	0.008	2.714	0.075	0.489
Complications	0.006	2.819	0.007	0.040
Therapeutic referral	0.083	1.752	0.022	0.350
Gastrointestinal segment	0.196	1.305	0.016	0.077
Sex	0.384	0.875	0.229	0.089
Blood lactate	0.988	0.016	0.041	0.042

DISCUSSION

Based on the herein adopted inclusion criteria, 89 out of 498 medical records of horses with colic syndrome, which were treated during the investigated period, were analyzed in the current study. The herein analyzed overall equine colic syndrome profile accounted for surgical rate equal to 52.8%, whereas Laranjeira *et al*. (2009) observed 0.7% surgical rate in three military units in Rio de Janeiro city, which comprised 770 horses, in total. The low need of surgery observed in these military institutions can be explained by the gastric origin of colic causes, which ranged from 78.1 to 86.6%, whereas the one recorded in the present study reached 7%.

Survival rate reached 62.9% in the current study; the main affected sites comprised large intestine (53%), small intestine (26%), small and large intestines (11%), stomach (7%), among others (3%). On the other hand, Northeastern Brazil recorded lower survival rate (36.7% of cases) among 60 horses with colic syndrome. With respect to disease location, the large intestine was the most affected site (70% of cases), the small intestine accounted for 11.7% of cases, nonspecific causes were observed in 11.7% of animals, stomach was affected in 5% of cases, and small and large intestine accounted for 1.6% of cases (Pessoa *et al*., 2012).

Large intestine impaction was the most prevalent condition; it accounted for 19 veterinary medical consultations, 7 of them were associated with large colon. This finding corroborates the study conducted by Pessoa *et al*. (2012), who described large colon impaction as the most observed condition (23 out of 60 colic syndrome cases).

Only peritoneal lactate recorded statistically significant results in the joint analysis applied to peritoneal and blood lactate concentrations. This finding can be explained by the association between the two lactate types in gastrointestinal disorders, since peritoneal lactate levels may increase before blood lactate levels increase. The analysis of both lactate types is better explained by the peritoneal lactate concentration, whose increase is associated with intestinal ischemia.

The comparison between blood and peritoneal lactates based on obstruction type (non-strangulating or strangulating), has shown statistically significant difference in peritoneal lactate levels. Mean peritoneal lactate concentration of 7.33mmol/L was observed in strangulation changes, whereas 3.06 mmol/L of it was observed in the non-strangulation ones. This statistical difference was also reported by Latson *et al*. (2005), who recorded mean peritoneal lactate concentration of 8.45 mmol/L in horses with strangulating obstruction and 2.09 mmol/L of it in animals with non-strangulating obstruction.

Therapeutic referral did not show statistical significance after lactate measurement at hospitalization time; this finding can be explained by conditions other than strangulation cases, which required surgery after patients did not show satisfactory evolution in the medical clinic. Strangulation injuries caused change to blood supply in the affected gastrointestinal segment and resulted in ischemia. Thus, peritoneal lactate levels rose due to anaerobic glycolysis and, subsequently, there was an increase in blood levels. These lactate levels were lower in non-strangulating injuries and their subsequent increase may indicate the need of surgical intervention; however, it would require serial lactate measurements in order to monitor patients' evolution (Latson *et al*., 2005). It may have happened in some horses investigated in the current study; therefore, lactate analysis conducted at hospitalization time was not

statistically significant to indicate the need of surgical intervention. However, strangulation injuries recorded statistically significant lactate concentrations, and they were classified as surgical cases.

Latson *et al*. (2005) did not find association between peritoneal: plasma lactate ratio <1.0 and the need of surgical intervention, except for horses presenting simple intestinal obstruction. Likewise, there was no sensitive way to determine the need of surgical intervention in the herein investigated horses who have presented this lactate ratio, although it was possible to associate it with obstruction type. In contrast, Thoefner *et al*. (2003) reported decrease in the number of surgical treatments at plasma: peritoneal lactate ratio <1.0.

With respect to variable "survival" all animals presenting blood lactate concentrations higher than 8.6mmol/L (from 9.6 to 11.7mmol/L) in the present study have died. The same outcome was observed in the study carried out by Delesalle *et al*. (2007), according to whom, animals with colic syndrome, which presented blood lactate concentrations higher than 8.6 mmol/L did not survive. Moreover, all horses presenting peritoneal lactate concentrations higher than 9.69 mmol/L (from 9.7 to 27 mmol/L) did not survive. According to the aforementioned authors, all horses presenting peritoneal fluid lactate values higher than 16.9 mmol/L have died. However, these findings must be assessed along with patients' clinical condition to enable predicting animals' chance of survival and recovery possibilities. Individual variations may take place depending on the incidence of other complications or on the involved factors.

The herein observed median blood lactate concentration (3.8 mmol/L; it ranged from 1.6 to 11.7mmol/L) at the time non-surviving horses were hospitalized was higher than the one observed for the survivor group (2.9mmol/L; it ranged from 0.7 to 8.5mmol/L). Likewise, according to Tennent-Brown *et al*. (2010), median blood lactate concentration observed for non-survivors was significantly higher at hospitalization time (4.10mmol/L; it ranged from 0.6-18.20mmol/L) than the one observed for the survivor group (1.30 mmol /L; it ranged from 0.30-13.90mmol/L).

Hashimoto-Hill *et al*. (2011) have investigated horses with colitis; they only failed to associate blood lactate concentration at hospitalization time with survival when the analysis was carried out 24 hours after it. However, these researchers did not analyze peritoneal fluid lactate, which could be associated with survival at hospitalization time, since lactate concentrations first increase in this fluid. Moreover, since lactate increase is also observed under non-surgical and non-strangulating conditions, it may take place at lower concentrations.

Animals' sex did not play a significant part in the survival rate of patients with colic syndrome analyzed in the current study. On the other hand, the retrospective analysis of 320 acute equine colic cases conducted by Reeves *et al*. (1989) reported statistically significant difference in surgical survival rates among non-castrated (55.8%), castrated males (24.5%) and females (30.9%).

Based on the comparison between blood and peritoneal lactate concentrations to predict equine colic prognosis, peritoneal lactate was more adequate than blood lactate to predict the likelihood of strangulation injury and death. The higher the peritoneal lactate concentration at hospitalization time, the higher the risk of patients' death. According to Delesalle *et al*. (2007), peritoneal lactate is more adequate and sensitive to diagnose early ischemic intestinal injuries and to predict their outcome.

CONCLUSION

Peritoneal lactate measurements conducted at the time horses with colic syndrome were hospitalized were considered predictors of animals' condition type, survival and prognosis. The higher the peritoneal lactate concentration at hospitalization time, the higher the risk of death for horses with gastrointestinal colic syndrome. Variables, such as peritoneal lactate, strangulation changes and complications, were associated with negative patient's outcome and with increased risk of death. On the other hand, increased blood and peritoneal lactate concentrations did not contribute to the decision-making process associated with therapeutic referral.

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