ORIGINAL ARTICLE

Injection Tranexamic Acid in Preventing Postpartum Hemorrhage Following Vaginal Delivery: A One-year Hospital-based Randomized Placebo-controlled Trial

Kshama Hinchigeri[1], Kamal P Patil[2], Ankita Patil[3], Mrityunjay C Metgud[4]

Received on: 18 March 2024; *Accepted on:* 10 April 2024; *Published on:* 29 April 2024

Abstract

Introduction: Tranexamic acid (TXA) injections, known for their antifibrinolytic properties, are gaining wider acceptance as a treatment for postpartum hemorrhage (PPH) on a global scale.

Aims and objectives: The purpose of this study was to evaluate the effectiveness of TXA and its potential side effects in preventing PPH following vaginal birth.

Materials and methods: This randomized controlled trial, conducted in a multispecialty hospital in Belagavi, India, involved 210 term patients over 1 year from January to December 2019. Subjects were randomly assigned into two cohorts using computer-based randomization. Each cohort received 10 prophylactic units of oxytocin. One group received 1 gm of intravenous TXA, while the other received 10 mL of normal saline intravenously within 2 minutes after delivery. Blood loss was measured using calibrated drapes, and mean changes in hemoglobin (Hb) and packed cell volume (PCV) were assessed from pre-delivery to postnatal day 2. Data assessment was carried out using the statistical program R i386 3.6.3.

Results: Patients in the research had an average age of 23.43 years with a standard deviation (SD) of 3.26 years. The occurrence of PPH was observed in 5 individuals (4.85%) in the TXA group and 12 individuals (11.21%) in the placebo group ($p = 0.0912$). Furthermore, the mean blood loss was significantly lesser in the TXA group, measuring 250.10 mL with an SD of 133.54 mL, compared to 334.2 mL with an SD of 141.78 mL in the placebo group ($p < 0.0001$).

Conclusion: Tranexamic acid can serve as a supplementary treatment alongside uterotonics during the third stage of labor, given its demonstrated clinical effectiveness and safety in preventing PPH.

Keywords: Adverse effects, Blood loss, Postpartum hemorrhage, Tranexamic acid, Uterotonics.

Journal of South Asian Federation of Obstetrics and Gynaecology (2024): 10.5005/jp-journals-10006-2413

Introduction

Postpartum hemorrhage (PPH) is characterized by an "anticipated loss of over 500 mL of blood following a vaginal delivery or 1,000 mL after a cesarean section, or any bleeding significant enough to threaten hemodynamics stability".[1] Over 25% of the maternal fatalities worldwide result from PPH. Its occurrence ranges between 3 and 15% of childbirths globally, with rates of 2–4% following vaginal delivery and 6% after cesarean section in India.[1]

Factors that increase the threat of PPH include a history of previous PPH, being a first-time mother, being overweight or obese, experiencing long-lasting labor, carrying multiple pregnancies, having had a previous cesarean section, and giving birth to a large baby.[2] Visual inspection of PPH is indeed a crude method of estimating the severity of blood loss. A more definitive and realistic measure is using a calibrated drape to correctly estimate in mL the amount of blood loss.[3]

Due to blood loss allogenic blood commodities are transfused, which may expose patients to an increased risk of transfusion-related adverse effects which have increased the interest in lowering the necessity of transfusions during delivery.[4]

Complications during childbirth, such as placenta previa, abruption, retained placenta, ruptured uterus, adherent placenta, vaginal and cervical trauma responsible for most maternal deaths. Therefore, it's crucial to use a hemostatic agent alongside uterotonics to minimize bleeding during vaginal delivery.[5]

Oxytocin injections are part of Active Management of Third Stage Labor (AMTSL) accompanied by controlled cord traction. Prohemostatic medications are necessary to uphold the hemostatic alterations that could potentially result in PPH. [6]

[1,3]Department of Obstetrics & Gynaecology, SDM College of Medical Sciences & Hospital, Dharwad, Karnataka, India

[2,4]Department of Obstetrics & Gynaecology, Jawaharlal Nehru Medical College, KLE University, Belgaum, Karnataka, India

Corresponding Author: Kshama Hinchigeri, Department of Obstetrics & Gynaecology, SDM College of Medical Sciences & Hospital, Dharwad, Karnataka, India, Phone: +91 9886159337, e-mail: kshamah92@gmail.com

How to cite this article: Hinchigeri K, Patil KP, Patil A, *et al*. Injection Tranexamic Acid in Preventing Postpartum Hemorrhage Following Vaginal Delivery: A One-year Hospital-based Randomized Placebo-controlled Trial. J South Asian Feder Obst Gynae 2024;16(3):239–242.

Source of support: Nil

Conflict of interest: None

Coagulopathy characterizes severe PPH, yet IV TXA, with its antifibrinolytic traits, is globally utilized for PPH treatment.[7]

Tranexamic acid (TXA) has been shown in trials to reduce trauma and obstetrics patient mortality by one-third due to bleeding. It could be a valuable tool in preventing PPH, being accessible, straightforward, cost-effective, and easily integrated into delivery procedures.[7]

Administering TXA alongside preventive oxytocin during the third stage of labor can enhance clotting, and reduce transfusions in surgery, mortality in bleeding patients, and menstrual bleeding in menorrhagia.[8]

This analysis aimed to assess TXA's efficacy and side effects in preventing postpartum hemorrhage after vaginal delivery.

Materials and Methods

A randomized controlled experiment conducted from January to December 2019 included 210 term pregnant women at a multispecialty hospital in Belagavi, Karnataka, India, aiming for vaginal delivery. Exclusions comprised patients with specific medical conditions or a history of certain diseases were excluded from the study. Participants meeting the inclusion criteria were enrolled after obtaining written informed consent. They were randomly assigned to two groups, each comprising 105 patients. Both groups received 10 units of prophylactic oxytocin injection intramuscularly as part of AMTSL. One group received a 1-gm intravenous dose of TXA, while the other received a slow infusion of 10 milliliters of normal saline over 30–60 seconds within 2 minutes after delivery. A graduated brass V drape bag was placed under the woman's buttocks to collect blood loss, measured in milliliters at 30 minutes and 2 hours post-delivery. Hemodynamic parameters were monitored every 15 minutes for the 1st hour and again at the end of the 2nd hour. Immediate minor adverse effects of TXA were recorded. Participants were followed-up until discharge to determine if they required blood transfusion or additional interventions such as peripartum hysterectomy or arterial embolization to control bleeding. On post-natal day 2, we checked laboratory parameters [hemoglobin (Hb), packed cell volume (PCV)]. Two groups were followed-up for 3 months. Participants were asked about major adverse effects.

The analysis of data was completed using R I 386 3.6.3. Statistical software.

Results

In a study with 210 participants, the average age was 23.43 years (SD = 3.26). Participants aged 18–22 accounted for 46.67% (TXA) and 40.95% (placebo). The 33–37 age group had only 1 participant (0.95%) in each group. Primigravida: TXA (46.6%), placebo (42.06%). Multigravida: TXA (55.34%), placebo (56.07%). No significant difference in primigravida vs multigravida distribution between groups ($p = 0.6537$). In this study, most people had a normal BMI value. Specifically, 63 participants (60%) in the TXA group and 65 participants (61.9%) in the placebo group had normal BMI values ($p = 0.95$), as shown in the Table 1.

In this study, atonic PPH was observed in 3 (2.86%) subjects in the TXA group and 8 (7.62%) subjects in the placebo group ($p = 0.21$). Traumatic PPH was observed in 2 (1.9%) in the TXA group and 3 subjects (2.86%) in the placebo group with a ($p = 0.72$). Further, no occurrence of traumatic and atonic PPH together in the TXA group, whereas in placebo group I (0.95%) subject was observed as revealed in Table 2.

In recent research, the mean blood loss was significantly lower in the TXA group (250.10 ± 133.54 mL) compared to the control group (334.2 ± 141.78 mL) ($p < 0.0001$). Additionally, a lower percentage of participants in the TXA group (3.88%) required blood transfusion compared to the placebo group (9.35%), as shown in Table 3. In the study, Hb change was 1.48 ± 1.22 in TXA vs 1.82 ± 1.20 in controls ($p = 0.0066$). Packed cell volume change was 3.51 ± 3.42 in TXA vs 5.05 ± 4.18 in controls ($p = 0.0015$) (Table 3).

Table 1: Distribution based on mother age, gravidity and BMI

Characteristics	*TXA group*	*Placebo group*	*p-value*
Mother age			
18–22 years	49 (46.67%)	42 (40%)	0.3218[F]
23–27 years	44 (41.9%)	43 (40.95%)	
28–32 years	11 (10.48%)	19 (18.1%)	
33–37 years	1 (0.95%)	1 (0.95%)	
Mean age (in years)	24.11 ± 4.1	23.53 ± 3.06	0.1008[M]
Gravidity			
Primigravida	47 (46.6%)	46 (42.06%)	0.6537
Multigravida	58 (55.34%)	59 (56.07%)	
BMI (Kg/m^2)			
<18.5 (underweight)	4 (3.81%)	3 (2.86%)	0.95
18.5–24.9 (normal weight)	63 (60%)	65 (61.9%)	
25–29.9 (pre-obesity)	26 (24.76%)	28 (26.67%)	
30–34.99 (class I obesity)	12 (11.43%)	9 (8.57%)	
35–39.9 (class II obesity)	0 (0)	0 (0)	
Above 40 (class III obesity)	0 (0)	0 (0)	

[F]Indicates Fisher's exact test; [M] Indicates Mann–Whitney *U*-test

Table 2: Frequency of PPH

Type of PPH	*TXA group*	*Placebo group*	*p-value*
Atonic PPH	3 (2.86%)	8 (7.62%)	0.21
Traumatic PPH	2 (1.9%)	3 (2.86%)	0.72
Atonic + traumatic	0 (0%)	1 (0.95%)	1

Table 3: Mean blood loss and clinical/lab parameters for both groups were within typical ranges

Parameters	*TXA group*	*Placebo group*	*p-value*
Mean blood loss	250.10 ± 133.54	334.2 ± 141.78	<0.0001[M]
Clinical parameters			
Postpartum transfusion	4 (3.88%)	10 (9.35%)	0.1127
Arterial embolization	0	0	0
Emergency hysterectomy	0	0	0
Lab parameters			
Change in hemoglobin	1.48 ± 1.22	1.82 ± 1.20	0.0066[T]
Change in packed cell volume (PCV)	3.51 ± 3.42	5.05 ± 4.18	0.0015[T]

[M]Indicates Mann–Whitney *U*-test; [T]Indicates T-test

Table 4: Mean variation in pulse rate, SBP and DBP among both groups

Characteristics	*TXA group*	*Placebo group*	*p-value among both groups*
Pulse rate (beats per minute)			
Preintervention	81.64 ± 8.54	79.52 ± 6.48	0.13 [M]
Postintervention	76.38 ± 9.67	75.41 ± 5.81	0.86 [M]
Change	−1.35 ± 11.44	−3.33 ± 10.79	0.21 [M]
p-value (within group)	0.09[W]	0.002[W]	
Systolic blood pressure (SBP)			
Preintervention	111.81 ± 10.42	111.25 ± 9.30	0.65 [M]
Postintervention	112.84 ± 8.91	112.38 ± 8.08	0.66 [M]
Change	1.02 ± 12.57	1.12 ± 12.51	0.93 [M]
p-value (within group)	0.25[W]	0.25[W]	
Diastolic blood pressure (DBP)			
Preintervention	76.32 ± 5.87	75.40 ± 4.81	0.33[M]
Postintervention	74.04 ± 5.79	72.52 ± 6.11	0.05[M]
Change	−2.28 ± 7.50	−2.89 ± 7.98	0.71[M]
p-value (within group)	0.003[W]	0.0004[W]	

[M]Indicates Mann–Whitney *U*-test; [W]Indicates Wilcoxon sign test

Table 5: Comparison: Minor negative events, hospital stays, uterotonic drug use in both groups

Parameters	*TXA group*	*Placebo group*	*Among groups p-value*
Minor adverse drug reactions			
Nausea	5 (4.76%)	4 (3.81%)	1
Vomiting	4 (3.81%)	5 (4.76%)	1
dizziness	2 (1.9%)	3 (2.86%)	1
Nausea + vomiting	2 (1.9%)	1 (0.95%)	1
Length of time spent in hospital			
≤3 days	90 (85.7%)	85 (80.95%)	0.2
>3 days	15 (14.29%)	20 (19.05%)	
Additional use of uterotonics			
Yes	4 (3.81%)	14 (13.33%)	0.02
No	101 (96.19%)	91 (86.67%)	

In this study, it was found that the median pulse rate was not significantly different between 2 groups at the base (81.64 ± 8.54, 79.52 ± 6.48) along with postintervention (76.38 ± 9.67, 75.41 ± 5.81) (Table 4).

The median of systolic blood pressure (SBP) was not considerably different between 2 groups at baseline (111.81 ± 10.42, 111.25 ± 9.30) compare to postintervention (112.84 ± 8.91, 112.38 ± 8.08). In the current investigation, the median of diastolic blood pressure (DBP) was not drastically different between 2 groups at baseline (76.32 ± 5.87, 75.40 ± 4.81) along with postintervention (74.04 ± 5.79, 72.52 ± 6.11) as shown in the Table 4.

In the investigation, 5 patients (4.76%) in the TXA test group experienced nausea, compared to 4 subjects (3.81%) in the control group. Vomiting occurred in 4 patients (3.81%) in the TXA test group and 5 subjects (4.76%) in the control group, as shown in Table 5. In the current study, 90 (85.71%) participants in the TXA test group exhibited hospital stay ≤ 3 days as compared to 85 (80.95%) participants in the control group ($p = 0.2$) (Table 5).

In this research, 4 (3.81%) participants in the TXA test group required additional uterotonics whereas 14 (13.33%) participants in the control group required additional uterotonics as shown in Table 5.

Discussion

Obstetric bleeding remains a leading cause of maternal deaths worldwide. Primary PPH has a global prevalence of 6%, it accounts for 35–55% of peripartum maternal fatalities.[9]

In this study, most participants in the TXA and placebo groups were aged 18–22 years (46.67 and 40.95%, respectively), with the fewest in the 33–37 age group (0.95%). The median age didn't significantly differ between groups, indicating age parity. Dahiya et al. found similar mean ages in their investigation: 24.25 ± 4.02 years in group I and 24.23 ± 4.14 years in group II ($p = 0.945$).[10]

The study showed no significant difference in gravidity between the TXA test and control groups ($p = 0.653$). Similarly, Nambiar and Somu found no significant difference in primigravida or multigravida women proportion between the TXA test and control groups ($p = 0.39$, 0.79), consistent with our findings.[11] Mean BMI ranged from 18.5 to 24.9 kg/m^2 in both groups with no discrepancy observed. Al-Garhy et al. also reported no variance in BMI across groups ($p = 0.658$), corroborating our results.[12]

In this trial, PPH occurred in 4.85% of the test group and 11.21% of the control group ($p = 0.0912$). Atonic PPH was 2.86% in the test group and 7.62% in the control group ($p = 0.21$). Traumatic PPH was 1.9% in the test group and 2.8% in the control group ($p = 0.72$). No simultaneous traumatic and atonic PPH cases were observed in the test group, while a 0.95% incidence was noted in the control group. A study by Almutairi WM reported an overall atonic PPH incidence of 2.5%, with a 12% increase between 2017 and 2018 in a Saudi Arabian specialty hospital.[13]

A recent study found that the TXA test group had significantly lower average blood loss compared to the control group. In the TXA test group, the mean blood loss was 250.10 ± 133.54 mL, whereas, in the control group, it was 334.2 ± 141.78 mL ($p < 0.0001$), indicating a significant difference. The median blood loss in the TXA test group was 200 mL, which was lower than that in the control group. Additionally, research by Igboke et al. showed that TXA reduced blood loss after vaginal birth. The TXA test group had a lower mean estimated blood loss than the control group (174.87 ± 119.83 mL vs 341.07 ± 67.97 mL, respectively; $p < 0.0001$).[14]

In this study, TXA didn't significantly reduce PPH. Rates were 4.85% in the TXA group and 11.21% in the control group, showing no significant difference. In contrast, Saccone et al. found that TXA after vaginal delivery decreased primary PPH incidence (8.7% vs 11.4%; relative risk 0.61, 95% CI, 0.41–0.91).[15]

In the trial, there was no significant difference in blood transfusions, peripartum hysterectomy, or arterial embolization between the TXA test and control groups. Although 9.8% of control group patients needed postpartum transfusions, compared to 3% in the TXA test group, the difference wasn't statistically significant. A meta-analysis by Xia et al. also found no significant difference in transfusion needs between control and test groups, consistent with this study's findings (TXA vs control; relative risk: 0.87, 95% CI: 0.46–1.64, $p = 0.66$) in two trials.[16]

Franchini et al. performed a recent meta-analysis at the Italian National Blood Centre on TXA's effectiveness in PPH. They found that the TXA group required fewer transfusions compared to the control groups.[17]

In the current investigation, the test group showed significantly lower changes in laboratory measures, particularly Hb and PCV levels, compared to the control group (1.48 ± 1.22, 1.82 ± 1.20), with a statistically significant difference ($p = 0.0066$). Naeiji et al. also found that the control group had notably lower mean hemoglobin levels compared to the test TXA group (11.77 ± 0.50 vs 11.31 ± 0.56), consistent with our study's results.[18] Oseni et al. discovered that preoperative TXA lowered blood loss during emergency C-sections.[19] In our study, no notable variances were observed in pulse rates or blood pressure between groups pre- and postintervention. Although DBP notably decreased in both groups during the intervention, SBP remained relatively unchanged. Shakur-Still et al. conducted a trial with 167 women, finding no significant vital sign changes post-tranexamic acid injection during and after delivery.[20]

The current study found no statistically significant difference in the side effects of TXA, such as nausea, vomiting, and dizziness, between the two groups. Sentilhes et al. found that nausea, vomiting, and dizziness were prevalent side effects in a multicenter randomized trial.[21]

In this trial, 90 people (85.7%) in the TXA test group were discharged within 3 days of hospitalization, compared to 85 participants (80.95%) in the control group. The length of hospital stay showed no statistically significant differences in this investigation. In this study, the control group (14 participants, 13.33%) needed significantly more uterotonics compared to the test group. Another study by Ifunanya et al. showed that the uterotonic requirement was 7.1% in the TXA test group and 33.3% in the control group, aligning with our current results.[22] Tran et al. found higher uterotonic use in the control group vs the TXA test group, aligning with our study's results.[23]

Conclusion

To manage PPH, prioritize prevention, early detection, and prompt intervention. Prophylactic intravenous TXA during childbirth reduces blood loss without serious side effects. It complements uterotonics in the third stage of labor.

References

1. Nigussie J, Girma B, Molla A, et al. Magnitude of postpartum hemorrhage and its associated factors in Ethiopia: A systematic review and meta-analysis. Reprod Health 2022;19(1):63. DOI: 10.1186/s12978-022-01360-7.
2. Bazirete O, Nzayirambaho M, Umubyeyi A, et al. Risk factors for postpartum haemorrhage in the Northern Province of Rwanda: A case control study. PLoS One 2022;17(2):e0263731. DOI: 10.1371/journal.pone.0263731.
3. McLintock C. Prevention and treatment of postpartum hemorrhage: Focus on hematological aspects of management. Hematology Am Soc Hematol Educ Program 2020;2020(1):542–546. DOI: 10.1182/hematology.2020000139.
4. Muñoz M, Stensballe J, Ducloy-Bouthors AS, et al. Patient blood management in obstetrics: Prevention and treatment of postpartum haemorrhage. A NATA consensus statement. Blood Transfus 2019;17(2):112–136. DOI: 10.2450/2019.0245-18.
5. Schmidt P, Skelly CL, Raines DA. Placental Abruption. StatPearls. Treasure Island (FL): StatPearls Publishing; 2022. PMID: 29493960.
6. Salati JA, Leathersich SJ, Williams MJ, et al. Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. Cochrane Database Syst Rev 2019;4(4):CD001808. DOI: 10.1002/14651858.CD001808.pub3.
7. Mielke RT, Obermeyer S. The use of tranexamic acid to prevent postpartum hemorrhage. J Midwifery Womens Health 2020;65(3):410. DOI: 10.1111/jmwh.13101.
8. Albaz Z. Role of prophylactic tranexamic acid in reducing blood loss during elective cesarean delivery. J Fam Med 2020;7(8):1227. Available from: https://austinpublishinggroup.com/family-medicine/fulltext/jfm-v7-id1227.pdf.
9. Shahbazi Sighaldeh S, Nazari A, Maasoumi R, et al. Prevalence, related factors and maternal outcomes of primary postpartum haemorrhage in governmental hospitals in Kabul-Afghanistan. BMC Pregnancy Childbirth 2020;20(1):1–9. DOI: 10.1186/s12884-020-03123-3.
10. Dahiya K, Shalu. Efficacy and safety of tranexamic acid in the prevention of postpartum haemorrhage after vaginal delivery. Int J Clin Obstet Gynaecol 2021;5(3):377–381. DOI: 10.33545/gynae.2021.v5.i3f.950.
11. Nambiar MJ, Somu K. The effect of tranexamic acid on blood loss after vaginal delivery. Indian Journal of Obstetrics and Gynecology Research 2020;5(4):559–562. DOI: 10.18231/2394-2754.2018.0125.
12. Al-Garhy ET, Mohamed AH, Barakat IA. Effect of tranexamic acid on blood loss in elective cesarean delivery. Egypt J Hosp Med 2019;74(6):1314. DOI: 10.21608/ejhm.2019.26689.
13. Almutairi WM. Incidences of atonic postpartum hemorrhage and related risk factors at a Tertiary Hospital in Saudi Arabia. Nurs Rep 2020;10(2):164. DOI: 10.3390/nursrep10020020.
14. Igboke FN, Obi VO, Dimejesi BI, et al. Tranexamic acid for reducing blood loss following vaginal delivery: A double-blind randomized controlled trial. BMC Pregnancy Childbirth 2022;22(1):1–8. DOI: https://doi.org/10.1186/s12884-022-04462-z.
15. Saccone G, della Corte L, Ardino B, et al. Prophylactic use of tranexamic acid after vaginal delivery reduces the risk of primary postpartum hemorrhage. J Matern Feotal Neonatal Med 2020;33(19):3368–3376. DOI: 10.1080/14767058.2019.1571576.
16. Xia Y, Griffiths BB, Xue Q. Tranexamic acid for postpartum hemorrhage prevention in vaginal delivery: A meta-analysis. Medicine (Baltimore) 2020;99(3):e18792. DOI: 10.1097/MD.0000000000018792.
17. Franchini M, Mengoli C, Cruciani M, et al. Safety and efficacy of tranexamic acid for prevention of obstetric haemorrhage: An updated systematic review and meta-analysis. Blood transfusion 2018;16(4):329. DOI: 10.2450/2018.0026-18.
18. Naeiji Z, Delshadiyan N, Saleh S, et al. Prophylactic use of tranexamic acid for decreasing the blood loss in elective cesarean section: A placebo-controlled randomized clinical trial. J Gynecol Obstet Hum Reprod 2021;50(1):101973. DOI: 10.1016/j.jogoh.2020.10197.
19. Oseni RO, Zakari M, Adamou N, et al. Effectiveness of preoperative tranexamic acid in reducing blood loss during caesarean section at Aminu Kano Teaching Hospital, Kano: A randomized controlled trial. Pan Afr Med J 2021;39:34. DOI: 10.11604/pamj.2021.39.34.21938.
20. Shakur-Still H, Roberts I, Fawole B, et al. Effect of tranexamic acid on coagulation and fibrinolysis in women with postpartum haemorrhage (WOMAN-ETAC): A single-centre, randomised, double-blind, placebo-controlled trial. Wellcome Open Res 2018;3:100. DOI: 10.12688/wellcomeopenres.
21. Sentilhes L, Daniel V, Deneux-Tharaux C. TRAAP2-TRAnexamic acid for preventing postpartum hemorrhage after cesarean delivery: A multicenter randomized, doubleblind, placebo-controlled trial-a study protocol. BMC Pregnancy Childbirth 2020;20:63. DOI: https://doi.org/10.1186/s12884-019-2718-4.
22. Ifunanya NJ, Chukwu IC, Nobert OC, et al. Tranexamic acid versus placebo for prevention of primary postpartum haemorrhage among high risk women undergoing caesarean section in abakaliki: A randomized controlled trial. Open J Obstet Gynecol 2019;9(6):914–922. DOI: 10.4236/ojog.2019.96089.
23. Tran NT, Bar-Zeev S, Schulte-Hillen C, et al. Tranexamic acid for postpartum hemorrhage treatment in low-resource settings: A rapid scoping review. Int J Environ Res Public Health 2022;19(12):7385. DOI: https://doi.org/10.3390/ijerph19127385.