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Data Article

Traces pilot pharmacokinetic study dataset

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ABSTRACT

The dataset displays the pharmacokinetics data obtained from the TRACES pilot study. The nine patients included were undergoing haemorrhagic caesarean section (blood loss > 800 mL) and receiving a single i.v dose of tranexamic acid (0.5, 1 or 2 g over 1 min).

The dataset gathers the tranexamic acid blood and urinary concentrations. With these first elements, a pharmacokinetic compartment model was built as described in Gilliot et al. and the individual pharmacokinetic parameters were estimated. In parallel, the patients anthropometric, biological, and clinical characteristics were collected. The correlation between the patient data and the estimated individual pharmacokinetic parameters were tested.

The correlation tests revealed that the dose, the height, the body weight, and the ideal bodyweight had and impact on the volume of distribution of tranexamic acid. According to these results, these latter covariates were explored using a multi-regression analysis in Gilliot et al.

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Specifications Table

Subject	Pharmaceutical Science
Specific subject area	Pharmacokinetics of tranexamic acid in obstetrics
Type of data	Dataset, table
How data were acquired	The toxicological data were obtained from the results of tranexamic acid concentration dosage. Concentration measurement used a liquid chromatography system coupled with tandem mass spectrometry (Acquity Xevo-TQ Detector, Waters, Milford, MA, USA). Data acquisition and quantification were performed using MassLynx 4.1 Software (Waters). These concentrations were analysed using the parametric NLMEM software program Monolix 2019R1 (Lixoft, Orsay, France). A pharmacokinetic model was built and the populational pharmacokinetic parameters were estimated in Gilliot et al. [1]. In parallel to the recruitment of the patients, anthropometric, biological, and clinical data were prospectively collected. Correlation tests between the estimated pharmacokinetic parameters and the potential covariates were performed using Monolix 2019R1.
Data format	Raw data, analysed data
Parameters for data collection	Patients were included if they were undergoing haemorrhagic caesarean section (blood loss $>$ 800 mL) and receiving a single i.v dose of TA (0.5, 1 or 2 g over 1 min). Non-inclusion criteria used were presented in the TRACES pilot study protocol [2].
Description of data collection	The toxicological data collected were tranexamic blood concentrations measured at T0 (time of inclusion, when bleeding $\geq$ 800 mL is diagnosed), T1 (at the end of the tranexamic acid injection), T15, T30, T60, T120, T180, and T360 (respectively 15, 30, 60, 120, 180 and 360 min after the injection), and the tranexamic acid urinary concentrations measured in the urinary samples collected within 6 h after treatment. The anthropometric data collected were the height and bodyweight of each patient. The body surface area, the body mass index and the ideal weight were secondarily calculated. In the dataset, the anthropometric data were divided by the administrated dose. The biological data reported were urea and the creatininemia, from which were deducted the corrected glomerular filtration rate and the renal clearance according to several formulas. The age, the initial blood loss volume and the volume of injected intravenous fluids were also reported.
Data source location	Institution: Lille Hospital City/Town/Region: Lille, Hauts-de-France Country: France Lille Hospital geographically is at GPS coordinates: 50°36′21.4″ North Latitude and 3°01′55.7″East Longitude, and with google maps: https://www.google.com/maps/place/50%C2%B036′21.4%22N+3%C2%B001′55.7%22E/@50.6059404,3.0299553,17z/
Data accessibility	Repository name: Mendeley data Data identification number: doi:10.17632/z5mhfckr29.2 Direct URL to data: https://data.mendeley.com/datasets/z5mhfckr29/2
Related research article	S. Gilliot, A.S. Ducloy-Bouthors, B. Hennart, F. Loingeville, M. Jeanne, G. Lebuffe, P. Odou. Hypothesis for a partially non urinary elimination of tranexamic acid in haemorrhagic caesarean section: Traces pilot pharmacokinetic study: Pharmacokinetics of tranexamic acid in obstetrics. European Journal of Pharmaceutical Sciences, Volume 153, 2020, 105,486, ISSN 0928–0987, https://doi.org/10.1016/j.ejps.2020.105486 [1]

Value of the Data

- These data provide the dataset of the original pharmacokinetics and patient characteristics that were used for the population pharmacokinetic model presented in Gilliot et al. [1].

- Those data may be used as comparative data for any further study investigating the pharmacokinetic/pharmacodynamic profile of tranexamic acid in haemorrhagic post-partum, as TRACES study, for which recruitment is now complete.
- The patient dataset can be useful to anyone who studies the pharmacokinetics of tranexamic acid or the evolution of biological parameters during a haemorrhagic caesarean section.

1. Data Description

The presented data provide complementary elements to the original research article Gilliot et al. [1].

1.1. Dataset

The dataset presents the pharmacokinetic data and the covariate data, displayed to be analysed on Monolix2019R1 as performed in Gilliot et al. [1]. The nine patients included in this latter study were undergoing haemorrhagic caesarean section (blood loss > 800 mL) and receiving a single i.v dose of TA (0.5, 1 or 2 g over 1 min).

The seven first columns (at the left) of the dataset describe the administration and the results of tranexamic acid concentration dosage. The blood samples were collected immediately after injection T0, and T15, T30, T60, T120, T180, and T360 (respectively 15, 30, 60, 120, 180 and 360 min after the injection). The tranexamic acid urinary concentrations measured in the urinary samples collected within 6 h after treatment.

Each line of the dataset describes either the administration of tranexamic acid (administration line), the concentration measurement (on a urinary or a blood sample) or the beginning of the urinary collection (from the injection of tranexamic acid for each patient).

The first column named “ID” correspond to the patient identification number. The second column named “TIME” correspond to the time of the dose for the administration lines, the time of the concentration recording for the observation lines, or the time of the start of the urinary collection for the urinary collection lines. In the third column “CONC” are indicated the recorded blood and urinary concentrations in tranexamic acid in mg/L. For the line corresponding to the administration or the start of the urinary collection, the cells are filled with dots.

The “EVID” column provides the information whether the line corresponds to an observation line (coded “0″) or an “other event” (administration or start of urinary collection, coded “1″). The “Amount” column corresponds to the dose of tranexamid acid in mg given via a bolus i.v administration and is only completed for the when the EVID cells are coded by “1″. For the observation lines, the cells are filled with a dot.

The “ADM” column is coded “1″ if the event correspond to a dose administration or “2″ if the event to the start of the urinary collection. For the observation lines, the cells are filled with a dot.

The “DVID” column indicates if the observation line corresponds to a blood concentration (coded “1″) or a urinary concentration (coded “2″). For the “other event” lines, the cells are filled with a dot

The anthropometric (height in cm, bodyweight [BW] in kg), the biological (creatininemia in mg/L, uremia in g/L) data were prospectively collected as described in the study protocol [2].

The volume of intravenous fluids in L consists in the cumulated filling volumes in gelatin or crystalloids administered from the beginning of the caesaran section to the end of the study period.

The anthropometric parameters were obtained as follows:

- The bodymass index (BMI, in kg/m²) was calculated as BMI = (BW in kg) / (height in m)²
- The body surface area (BSA, in m²) was calculated as $BSA = 0.20247 * (\text{height in m})^{0.725} * (\text{BW in kg})^{0.425}$

Table 1
Estimated individual parameters for the base model presented in Gilliot et al. [1].

ID	Cl	V1	Q	V2	p_urine
1	0.27	24.21	0.53	22.25	0.46
2	0.12	16.49	0.54	10.98	0.26
3	0.20	5.70	0.54	9.1	0.18
4	0.14	3.88	0.55	16.61	0.21
5	0.12	13.04	0.51	25.09	0.33
6	0.12	18.08	0.53	12.72	0.24
7	0.24	14.03	0.54	19.44	0.21
8	0.20	13.52	0.53	25.06	0.48
9	0.20	18.31	0.53	14.54	0.16

Legend: identification number for the study patients (ID), clearance in L/min (Cl), the volume in L of central (V1) and peripheral (V2) compartments, diffusional clearance in L/min (Q), urinary excretion fraction (p_{urine}).

- The ideal bodyweight (IW, in kg) was calculated using the Devine formula (1974), $IW = 45.5 + 0.9 \times (\text{height (cm)} - 152)$

The height, the BW and the IW were divided by the dose in a second step of the correlation tests.

Concerning the renal parameters, we used several formula to estimate the glomerular filtration rate with correction to the body surface area (GFRc in mL/min/1.73m²) or the creatinemia clearance (Clcr in mL/min), as there is no current recommended formula in parturient women. For each equation, the creatinemia used was the one collected at inclusion (T0) called SCr1 in the dataset. Concerning the Chiou formula, the equation provides a calculation of unstable creatinine clearance; for this formula, we used either the creatinemia collected at inclusion (T0) and at T360, called SCr2.

The equations used fo each estimation of Clcr or GFR were the following:

- According to Jellife formula (1973), $Clcr = \frac{(98-16)*\frac{Age-20}{20}}{SCr}$, with SCr in mg/dL
- According to Chiou formula (1975),

$$Clcr = \frac{2*IW*(22.4-(0.16*Age))}{SCr1+SCr2} + \frac{2*(0.6*IW)*(SCr1-SCr2)}{SCr1+SCr2)*\Delta Time(hrs)} - 0.0286*0.6*IW, \text{ with SCr in mg/dL}$$

- According to Cockroft and Gault (CG) formula (1976), $Clcr = \frac{(140-Age)*BW}{72*SCr} * 0.85$.
- According to CKD-EPI formula, $GFR = 144 * (\frac{(SCr}{0.7})^{-A} * 0.993^{Age} * BSA/1.73$, with SCr in mg/dL, and $A = 0.329$ if SCr≤0.7 mg/dL or 1.209 if SCr> 0.7 mg/dL
- According to MDRD formula, $GFR = 175 * SCr^{-1.154} * Age^{-0.203} * 0,742 * BSA/1.73$ with SCr in mg/dL

The initial blood loss volume (Vs1, in mL) was calculated by additing the weights of the vaginal blood flow collected by a delivery bag through the caesarean section and the volume the weight of drapes and pads, as described in Ducloy-Bouthors et al. [2]. A cell saver aspiration bag was used for only one patient.

In Table 1 are presented the individual estimated pharmacokinetic parameters, rounded to two decimal places, obtained from the base model described in Gilliot et al. [1].

Every characteristic collected for each patient and presented in the dataset was tested as a potential covariate for the PK model. The correlation tests were performed between the individual PK parameters estimated by the model validated in Gilliot et al. [1] (rounded to two decimal places in Table 1) and the continuous covariates described in the dataset: dose, age, BW, IW, height, BMI, BSA, SCr at inclusion, uremia, volume of intravenous fluids, Vs1, Clcr and GFR calculated using the different formulas described above (displayed in the dataset). Table 2 summarizes the results of the correlation tests, performed preliminary to the multiple sequential regression analysis.

The results presented are the coefficient of correlation r² and the p-value.

Table 2
Results for the correlation test between the individual estimated parameters and the tested covariates.

Covariate	Cl	V1	Q	V2	p_urine
Age	$r^2 = 0.027$ p-value=0.95	r^2=0.20 p-value=0.61	r^2=0.14 p-value=0.71	r^2=−0.19 p-value=0.63	r^2=0.074 p-value=0.85
Dose (mg)	r^2= 0.15 p-value = 0.69	$r^2 = 0.84$ p-value = 0.0046*	$r^2 = -0.086$ p-value =0.82	$r^2 = -0.029$ p-value =0.94	r^2 =−0.012 p-value =0.98
Ideal weight (kg)	$r^2 = -0.80$ p-value=0.0089*	r^2 = - 0.14 p-value = 0.73	$r^2 = 0.084$ p-value =0.83	$r^2 = 0.19$ p-value = 0.62	$r^2 = -0.16$ p-value =0.69
Ideal weight/dose (kg)	$r^2 = -0.25$ p-value = 0.51	r^2 = - 0.95 p-value=8.8×10^{-5}*	$r^2 = 0.25$ p-value =0.51	$r^2 = -0.073$ p-value =0.85	$r^2 = -0.19$ p-value =0.63
Body weight (kg)	$r^2 = -0.12$ p-value = 0.75	r^2 = - 0.33 p-value = 0.38	$r^2 = 0.31$ p-value =0.41	$r^2 = 0.44$ p-value = 0.23	$r^2 = 0.30$ p-value =0.43
Body weight/dose (kg/mg)	$r^2 = -0.22$ p-value = 0.57	r^2 = - 0.89 p-value=0.0014*	$r^2 = 0.33$ p-value =0.38	$r^2 = 0.049$ p-value = 0.90	$r^2 = -0.11$ p-value =0.77
Body mass index (kg/m²)	r^2=0.24 p-value=0.54	r^2=−0.26 p-value = 0.50	r^2=0.34 p-value=0.37	r^2=0.30 p-value=0.43	r^2=0.26 p-value=0.50
Body surface area (m²)	r^2=−0.17 p-value=0.67	r^2=−0.36 p-value=0.34	r^2=0.38 p-value=0.32	r^2=0.34 p-value=0.37	r^2=0.16 p-value=0.68
Height (cm)	$r^2 = -0.80$ p-value = 0.0089*	r^2 = - 0.14 p-value = 0.73	$r^2 = 0.084$ p-value =0.83	$r^2 = 0.19$ p-value =0.62	r^2 = - 0.16 p-value =0.69
Height/dose (cm/mg)	$r^2 = -0.17$ p-value=0.67	$r^2 = -0.96$ p-value=5.8×10^{-5}*	$r^2 = 0.25$ p-value =0.52	r^2 = - 0.15 p-value = 0.71	$r^2 = -0.20$ p-value =0.60
Serum Creatininemia at T0, SCr1	$r^2 = -0.26$ p-value = 0.50	$r^2 = -0.22$ p-value = 0.56	$r^2 = -0.043$ p-value= 0.91	$r^2 = 0.016$ p-value = 0.97	$r^2 = -0.16$ p-value = 0.68
Clcr CG (mL/min)	$r^2 = 0.30$ p-value = 0.43	$r^2 = -0.47$ p-value =0.22	$r^2 = 0.14$ p-value= 0.73	$r^2 = 0.44$ p-value = 0.24	$r^2 = 0.14$ p-value = 0.73
Clcr Jeliffe (mL/min)	r^2=−0.39 p-value=0.30	r^2=−0.56 p-value=0.12	r^2=0.097 p-value=0.80	r^2=0.13 p-value=0.74	r^2=−0.37 p-value=0.33
Clcr Chiou (mL/min)	r^2=−0.27 p-value=0.49	r^2=−0.19 p-value=0.63	r^2=−0.17 p-value=0.65	r^2=−0.22 p-value=0.57	r^2=−0.45 p-value=0.22
Corrected GFR (CKD-EPI formula, mL/min/1.73m²)	$r^2 = 0.36$ p-value = 0.35	$r^2 = -0.30$ p-value =0.43	$r^2 = -0.12$ p-value= 0.75	$r^2 = 0.52$ p-value = 0.15	$r^2 = 0.19$ p-value =0.63
Corrected GFR (MDRD formula, mL/min/1.73m²)	$r^2 = 0.35$ p-value = 0.35	$r^2 = -0.32$ p-value =0.40	$r^2 = -0.017$ p-value= 0.97	$r^2 = 0.073$ p-value = 0.85	$r^2 = -0.19$ p-value = 0.63
Uremia (g/L)	$r^2 = -0.20$ p-value =0.61	$r^2 = -0.53$ p-value =0.15	$r^2 = 0.30$ p-value= 0.44	$r^2 = 0.063$ p-value = 0.87	$r^2 = -0.20$ p-value = 0.61
Vs1 (mL)	r^2=−0.019 p-value=0.96	r^2=−0.080 p-value=0.84	r^2=0.21 p-value = 0.59	r^2=0.64 p-value=0.06	r^2=0.19 p-value=0.63

Legend: volume of blood loss before inclusion (Vs1), glomerular filtration rate (GFR), clearance of creatinine (Clcr), Cockroft & Gault(CG), clearance in /.min (Cl), the volume in L of central (V1) and peripheral (V2) compartments, diffusional clearance in L/min (Q), urinary excretion fraction (p_{urine}),.

* for significant correlation (p-value≤0.05).

Only the covariates significantly correlated with at least one PK parameter with a risk of 5% (Table 1) were included in the multiple regression analysis in Gilliot *et al.* [1].

2. Experimental Design, Materials and Methods

The data presented in the dataset were propesctively collected during the TRACES pilot study as described in the study protocol [2].

Concentration measurement used a liquid chromatography system coupled with tandem mass spectrometry (Acquity Xevo-TQ Detector, Waters, Milford, MA, USA). Data acquisition and quantification were performed using MassLynx 4.1 Software (Waters) as described in the study protocol [2].

The patient characteristics were collected before inclusion (or at T0 for SCr, uremia, Vs1, the volume of intravenous fluids).

The collected concentrations were analysedwith the parametric NLMEM software program Monolix 2019R1 (Lixoft, Orsay, France) using a Stochastic Approximation Expectation-Maximization algorithm as described in Gilliot et al. [1]. In this previous study, several two-compartment models and one compartment model were compared to determine which one would better fit with the tranexamic acid pharmacokinetics. The individual parameters estimated by the chosen base model described in this latter study are described in Table 1.

The correlation tests between the estimated individual pharmacokinetic parameters and the potential covariates were performed using Monolix 2019R1 (Table 2).

Ethics Statement

TRACES trial obtained approval from the competent national authorities (ANSM 201500249926) and the Ethics Committee (CPP 15/50 020216) before beginning the study, in accordance with article L1121–4 of the Public Healthcare Code. This trial has been declared on the clinical trials registration on 13 of June 2016 under the number CT 02797119. Registration will be performed in accordance with decree dated November 14, 2006 about gathering data in the national register of individuals participating in biomedical research.

All study patients received complete information and gave their written consent.

Declaration of Competing Interest

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The authors declare that they have no known competing financial interests or personal relationships which have, or could be perceived to have, influenced the work reported in this article.

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