UNIVERSIDADE FEDERAL DE SANTA CATARINA

CENTRO DE CIÊNCIAS DA SAÚDE

CURSO DE GRADUAÇÃO EM FARMÁCIA

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EVALUATION OF THE EFFICIENCY OF A TOXICOLOGY LABORATORY

Florianópolis,

2020

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Trabalho de Conclusão de Curso apresentado à disciplina de TCC II como requisito parcial para a conclusão do Curso de Graduação em Farmácia do Centro de Ciências da Saúde da Universidade Federal de Santa Catarina.

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Florianópolis,

2020

Ficha de identificação da obra elaborada pelo autor,
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Neves, Mariah Bonelli Roussenq
Evaluation of the efficiency of a toxicology laboratory / Mariah Bonelli Roussenq Neves ; orientador, Flávia Martinello, coorientador, Angela Somavilla Higioka, 2020.
36 p.

Trabalho de Conclusão de Curso (graduação) - Universidade Federal de Santa Catarina, Centro de Ciências da Saúde, Graduação em Farmácia, Florianópolis, 2020.

Inclui referências.

1. Farmácia. 2. Toxicologia . 3. Gestão da Qualidade . 4. Análises clínicas. 5. Turnaround time. I. Martinello, Flávia . II. Higioka, Angela Somavilla. III. Universidade Federal de Santa Catarina. Graduação em Farmácia. IV. Título.

Mariah Bonelli Roussenq Neves

EVALUATION OF THE EFFICIENCY OF A TOXICOLOGY LABORATORY

Este Trabalho de Conclusão de Curso foi julgado adequado para obtenção do grau de Bacharel em Farmácia, e aprovado em sua forma final pelo Curso Graduação em Farmácia do Centro de Ciências da Saúde da Universidade Federal de Santa Catarina.

Florianópolis, 27 de agosto de 2020.

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Agradecimentos

Em primeiro lugar, gostaria de agradecer ao universo por me permitir estar e evoluir nesta jornada, sendo sempre tão bom comigo, a ponto de me fazer cruzar com as pessoas que serão aqui citadas.

Em segundo lugar, agradeço aos meus pais, **Rose Bonelli** e **Julio Cesar**, por diversas vezes abrirem mão dos seus sonhos para que fosse possível realizar o meu. Mãe, minha melhor amiga, lembro-me de uma frase de nosso livro preferido que me remete muito a você. No Pequeno Príncipe, o livro diz: "todos já fomos criança um dia, alguns de nós apenas esqueceram-se disso". Obrigada por ser você quem me lembra diariamente a minha essência e como é importante honrar nossa criança interior. Tenho muito orgulho de ser parecida com você, a melhor pessoa que já habitou este mundo. Pai, obrigada por ser meu alicerce e nunca me negar palavras de conforto e acalento. A forma com que você confia e se orgulha de mim faz com que eu me sinta capaz de qualquer coisa, você é meu herói.

Minhas irmãs, **Bruna** e **Carolina**. Obrigada por todo apoio, seja ele financeiro ou emocional. Carol, obrigada por me possibilitar conhecer um outro mundo e me deparar com outras qualidades que não teria descoberto sem seu apoio. Bru, obrigada por se fazer presente em todos os momentos e vibrar comigo em todas as minhas vitórias, não importa quais elas sejam – sinto teu amor e cuidado de longe.

À tia **Geni**, minha segunda mãe, meu muito obrigada. Você me ensinou o significado da palavra "incondicional" e a gostosura da independência. Você é uma mulher forte e incrível.

Aos meus amigos de Blumenau, que carrego há muitos anos e sempre se fizeram presentes, mesmo nos momentos em que a faculdade me fez ausente. Em especial, **Bruno** e **Julia**, que aceitaram embarcar nessa trajetória comigo. Vocês me inspiram. À minha melhor amiga, **Tatiele**, a quem me faltam palavras para descrever a ligação e o amor incondicional que temos uma pela outra.

Aos meus amigos que Florianópolis me apresentou, em especial aos que dividiram o teto comigo, **Gustavo Izídio, Paula Tribéss, Julia Neckel** e **Rangel Lidani**. À minha primeira amiga do curso que me cuidou com tanto amor e me ensinou tanto, **Victória Hess**. Para os que dividiram a rotina de uma maneira tão leve, **Amanda**, **Cris**, **Fani**, **Gabriela**, **Henrique**, **João**, **Regiane**, **Bruna** e **Jéssica**. Vocês fazem parte de quem eu sou, obrigada por me fazerem sentir tão amada.

Ao Hospital Universitário, especificamente ao Laboratório de Análises Clínicas, por ter sido minha segunda casa durante três anos e meio da minha jornada acadêmica. Em especial, à **Cida**, por me ensinar o significado de caridade e amor ao que se faz. À **Elayne Rateke** e professora **Cláudia Regina**, por terem me proporcionado tanto crescimento – tenho muito orgulho de ser chamada de "pupila" de vocês.

Gostaria de agradecer à minha orientadora, **Flávia Martinello**, por toda dedicação e paciência. Fica claro quanto gosta do que faz. Ficarei honrada em dividir a profissão com você. À minha coorientadora, **Angela Higioka**, que está embarcando em uma nova e maravilhosa jornada (a de ser mãe), pela parceria no laboratório e no congresso.

Por fim, agradeço à **Universidade Federal de Santa Catarina**, que possibilita diariamente que tantas histórias sejam mudadas e que os alunos retornem à sociedade buscando um mundo melhor.

Este Trabalho de Conclusão de curso é apresentado na forma de manuscrito que será submetido para publicação na revista **Basic & Clinical Pharmacology & Toxicology**, cujas instruções aos autores podem ser encontradas na página https://onlinelibrary.wiley.com/journal/17427843 e no anexo.

ISSN (online): 1742-7843

Qualis Capes para Farmácia: A2

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Title:

Evaluation of the efficiency of a toxicology laboratory

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Abstract

Laboratory turnaround time (TAT) has been used as an indicator of efficiency. Prolonged TAT causes delay on treatment, increases patient waiting time on emergency department and the risk for patient safety. Short TAT is important in poisoning cases. To decrease the time of the clinical decision, report of critical values is also important. To evaluate the efficiency of a public toxicology laboratory a user satisfaction survey was applied and TAT data collected. This laboratory serves the demands of a Brazilian Center for Information and Toxicological Assistance. The observed TAT met the laboratory's own deadline but not the user's expectations and the one predicted by the UK guideline. Almost half of the users reported not being informed of the critical values. While everyone considered that communication is important, half of the users reported that it is not necessary. Although all users reported good satisfaction on laboratory results, opportunities for efficiency improvement were observed,

such as reducing the test deadline, improving the test menu, and the communication of critical values.

Keywords: Turnaround time (TAT), toxicology laboratory, user satisfaction, sigma metric, quality assurance.

Introduction

Laboratory tests are essential for clinical management in situations of prevention, diagnosis, prognosis, treatment decision and monitoring. It has been estimated that laboratory results are responsible for 60-70% of clinical decisions[1], so the laboratory should provide accurate and timely results. The timeliness can be measured and expressed as turnaround time (TAT)[2] and have been used as an indicator of efficiency. However, studies demonstrate that, in most cases, laboratories do not meet clinician's expectations about the time that take the tests results[3,4].

Despite the widespread use of TAT, a comparison among studies is difficult due to the use of different definitions to the indicator. A study proposed a term harmonization and defined turnaround time (TAT) as a generic term; laboratory turnaround time (LTAT) as a laboratory process that starts on the receipt of the specimen and ends when the result is available; and medication turnaround time (MTAT) as a specific term covering the laboratory processes and medication turnaround time, which includes therapeutic conduct. The MTAT has been defined as the golden pattern, but LTAT is the most used because the internal processing time is considered the most accessible measure[5].

According to the International Organization for Standardization, TAT can be defined as two specific points between pre-examination, examination and/or post-examination processes. The use of different TAT as a quality indicator can be used as an evaluation strategy of each stage of the process if they are precisely defined[6]. The optimal time should be defined by a multidisciplinary team reflecting the clinical needs and must be periodically evaluated through satisfaction survey[4].

A small TAT for toxicological tests is important in poisoning cases admitted in emergency departments (EDs) of hospitals. A timely result can provide information that can direct the clinician's conduct towards optimal life support and possibly of administering the

antidote in time. A prolonged TAT has caused delay on 43% of treatments, increased 61% patient waiting time in the ED, and increased the risk for patient safety[7,8].

The current concern of the health institutions to improve patient security involves decreasing the time of clinical decision, and raising the interest in definition and report of critical values. According to the Institute of Medicine, critical values report is an indicator of safety and timeliness[9]. This procedure reduces the time of diagnosis and treatment, reflecting in clinical and logistic efficiency of service, according to the immediate action that results can generate[10,11].

Toxicology laboratories are responsible for performing the analysis of toxic agents and/or their metabolites in biological fluids for diagnosis of suspected poisoning, management of patients on drug therapy and forensic reasons[7,12,13]. The substances variability limits the possibility to provide a full spectrum of toxicological analyses. In this sense, a multidisciplinary team is necessary to define the menu of toxicological tests, if the assay should be qualitative or quantitative, when and what specimen should be analyzed and what TAT is acceptable[7].

The Brazilian Toxicological Information and Assistance Centers (CIATox) are responsible for providing support and guidance on possible substances involved in the intoxication, orientations on test requests, and the ideal clinical management. Since 2011, exogenous intoxication is a notifiable disease and requires laboratory tests as confirmation criteria. Medicines are the most prevalent cause of intoxication[14]. Our public toxicology laboratory (Labtox) offers 14 tests including Paracetamol, Salicylate, Paraquat (qualitative test), Methaemoglobin, Toxicology screen, Cholinesterase (plasma and erythrocyte), Iron, Lithium, Valproate, Carbamazepine, Digoxin, Phenytoin and Phenobarbital, and primarily serves the demands of the CIATox of the State of Santa Catarina (CIATox/SC). In this context, the purpose of this study was assessing the service efficiency offered by the toxicology laboratory through analysis of the turnaround time and CIATox/SC user's satisfaction.

Methods

The study was conducted at the Hospital of the Federal University of Santa Catarina from 2019 August to 2020 May. The research was approved by the Research Ethics Committee of the UFSC (CAAE 21467119.4.0000.0121) and followed the recommendations of Resolution no. 466/2012 of the National Health Council.

The study was carried out in two steps. The first one assessed the CIATox/SC user's satisfaction in relation to the service offered by the Labtox. The following step measured the turnaround time of the toxicological tests.

CIATox/SC professional's satisfaction with the Labtox assistance

A questionnaire was used to assess the CIATox/SC professional`s satisfaction with the assistance provided by Labtox. The questionnaire was developed by grouping 14 questions (Chart 1).

The answers were used as quality indicators, compared to the literature, and evaluated by the Sigma metric. Answers checked as "below average", "regular" and that "do not trust the results", which characterizes dissatisfaction, were considered non-conformities.

The Sigma level was calculated considering the number of defects (non-conformities) in a million opportunities (DPMO), using the Six Sigma Calculator[15]. A Sigma lower than 3.0 was considered unacceptable; between 3.0 and 4.0, acceptable; above 4.0, a good process performance, and Sigma 6.0, the desired goal[16,17].

TAT analysis

The monitored tests were Paracetamol, Salicylate, Paraquat (qualitative test), Methaemoglobin, Toxicology screen, Butyrylcholinesterase and Acetylcholinesterase. The Paracetamol, Toxicology screen and Cholinesterases tests, that are requested on average once a week or more, had the TAT monitored from 2017 to 2019. The Salicylate, Paraquat and Methaemoglobin tests, which are requested less than once a week, were monitored from 2014 to 2019.

The data were obtained using the laboratory scheduling system and also from CIATox/SC form. The time of laboratory scheduling, sample receiving, the release of results and the access of results by CIATox/SC professionals were registered in an Excel spreadsheet.

LTAT was calculated as the difference between the time of result release and the time of sample receiving and expressed in minutes.

MTAT was calculated as the difference between the time of result access and the time of sample receiving and expressed in minutes.

The TAT was compared to the recommended by UK guideline for laboratory analyses of poisoned patients[13], to the laboratory deadline, and the users' expectations. The period that the guideline[13] takes into account was not specified, so for the research, it was considered the same period as the LTAT. Each non-compliance with the requirements was considered non-conformity. The non-conformities were evaluated using Sigma metric as previously described.

The data distribution was analyzed using Microsoft Excel program version Professional Plus 2013, Redmond (EUA). The results not showing normal distribution were expressed as a median.

Results

The CIATox/SC has 29 professionals, which are physicians, pharmacists, biologists, laboratory techniques, administrators and nurses. Among these professionals, 20 use the service and could have evaluated it. From the 13 (65%) professionals that answered the questionnaire (Chart 1), 9 (69%) are physicians and 4 (31%) pharmacists, with a median time of work in CIATox/SC of 5 years (1 month-23 years).

Chart 1. Answers (number) to the satisfaction questionnaire applied to CIATox professional's users of the toxicology laboratory (Labtox).

Question 1. In your opinion, the elapsed time between toxicology test order and result release is:

Excellent	Good	Regular	Bad	Never used the service
(3)	*(9)*	*(1)*	*(0)*	*(0)*

Question 2. In your opinion, what would be the ideal deadline, in minutes, for result release of the tests below:

According Table 1

Question 3. In your opinion, which frequency the toxicology test results influence on clinical conduct?

Always	Most times	Few times	Never
(0)	*(10)*	*(3)*	*(0)*

Question 4. How often has toxicology test result release caused delay in patients therapy or discharge?

Always	Most times	Few times	Never
(0)	*(3)*	*(10)*	*(0)*

Question 5. Do you trust test results released by Labtox?

Yes	No. Why?
(13)	*(0)*

Question 6. What is your satisfaction degree with the laboratory workers courtesy, which assists in samples screening?

Excellent	Good	Regular	Bad	Never used the service
(4)	*(6)*	*(2)*	*(0)*	*(0)*

One participant does not answer the question.

Question 7. What is your satisfaction degree with the courtesy of Labtox workers?

Excellent	Good	Regular	Bad	Never used the service
(7)	*(5)*	*(0)*	*(0)*	*(0)*

One participant did not answer the question.

Question 8. In your opinion, the menu of Labtox toxicology tests is enough?

Yes	No
(5)	*(8)*

If not, what new test should be implemented?

- "*Blood alcohol (Methanol e Ethanol)"* (*7)*
- *"Dosage of Amitriptyline" (1)*
- *"Carboxyhemoglobin" (1)*
- *"Fentanyl" (1)*
- *"Midazolam" (1)*
- *"Metoclopramide" (1)*
- *"LSD" (1)*
- *"MDMA" (1)*
- *"NBOMe" (1)*
- *"New substances psicoatives (NSP) like synthetic cathinones, tryptamine derivatives" (1)*

According to Rocha and collaborators (2016), critical values are laboratory results that represent risk or threats to the patient's life

Question 9. Have you been notified of critical toxicology tests values by Labtox?

Yes	No
(7)	*(6)*

Question 10. Considering the definition above, is the notification of critical value important to CIATox?

Yes	No
(13)	*(0)*

Question 11. Currently, not all Toxicology Screen (TS) results are reported. Do you think this notification is important?

Yes, for all the TS results	Yes, only for TS positive results	No, it is not necessary. We use to consult the result on the schedule system.
(4)	*(2)*	*(7)*

Question 12. What is your overall satisfaction degree with the Labtox service?

Excellent	Good	On average	Below average	Bad
(3)	*(10)*	*(0)*	*(0)*	*(0)*

Question 13. In your opinion, what is the Labtox major problem?

- "*Not offer all the tests 24 hours a day 7 days a week*" (*9)*
- *"Delay to release reports"(1)*
- "*No problem*" *(1)*

Two users did not answer this question.

Question 14. Do you have any suggestion for Labtox improvement?

- "*Offer all the tests 24 hours a day 7 days a week*" (3*)*
- *"Increase the number of workers in the laboratory" (2)*
- "*Increase the menu of tests available*" *(2)*
- *"Greater agility to release the results"(1)*

- *"Improve the communication between Labtox and CIATox/SC"(1)*
- *"The service is great and doesn't need any improvement"(1)*

Seven users did not answer this question.

(n), number of answers.

Ten (77%) professionals considered that the laboratory results on most of the times influence clinical management. 3 (23%) professionals stated that on few times the current TAT of the toxicology tests has caused a delay in treatment and hospital discharge of ED, leading to a sigma indicator level 2.3, considered unacceptable[16,17].

About the LTAT, 3 (23%) users considered it as excellent, 9 (69%) as good and 1 (8%) as regular. The last answer reflected non-conformity and presents a sigma level 3, considered acceptable[16,17]. The ideal deadline suggested by professionals for the different tests available on Labtox is presented in Table 1.

Table 1. Time considered acceptable by users and described in the UK guideline for releasing test results.

	Time for releasing test results (minutes)						
Laboratory test	Acceptable by users (n)						UK guideline
Acetylcholinesterase	30 (1)	40 (1)	**60 (6)**	90 (3)	180 (1)	2880 (1)	360
Butyrylcholinesterase	30 (1)	40 (1)	**60 (4)**	**90 (3)**	**120 (4)**		180
Methaemoglobin	30 (2)	40 (2)	**60 (3)**	**90 (3)**	**120 (3)**		120
Paracetamol	30 (1)	40 (1)	45 (1)	60 (4)	90 (1)	**120 (5)**	120
Paraquat	15 (1)	**30 (5)**	40 (1)	**60 (5)**	120 (1)		120
Salicylate	30 (1)	40 (1)	**60 (7)**	90 (2)	120 (2)		120
Toxicology screen	15 (1)	**30 (8)**	40 (1)	60 (3)			-

n, number of professionals; -, not specified by UK guideline.

Most professionals (10) classified general satisfaction regarding the service offered by Labtox as good, and 3 (23%) as excellent. All the users affirmed that they trust in the results released by the laboratory.

Most of the professionals (62%) are not satisfied with the menu of tests offered by Labtox. The inclusion of serum ethanol determination was suggested by 6 users (46%), methanol by 3 (23%), amitriptyline by 1 (8%), metoclopramide by 1 (8%), fentanyl by 1 (8%), carboxyhemoglobin by 1 (8%), midazolam by 1 (8%), LSD by 1 (8%), MDMA by 1 (8%), NBOMe by 1 (8%) and new psychoactive substances (NPS) by 1 (8%) user.

When asked about the report of critical values, 54% of users stated that have been receiving calls from laboratory to communicate the critical values and 46% of users denied, but all users considered it important to the CIATox/SC. About toxicology screen specifically, the laboratory only communicates detected results. So, users were asked if they considered important to report all the test results. 54% affirmed that they prefer to access the results directly in the laboratory system, 31% prefer to receive the report of all results and 15% answered that is necessary to report only the detected cases.

According to the majority of the users (10), the biggest problem of the Labtox was not offering all the tests during the night shift, such as Paracetamol, Salicylates, Acetylcholinesterase and Methaemoglobin. One (8%) participant affirmed that Labtox did not have any problem, and two (15%) did not answer the question. Extending the disponibility of the tests for 24 hours and 7 days a week was the most registered suggestion (by 8 users) to improve the service offered by Labtox, followed by increasing the test menu (2), improving communication between CIATox/SC and Labtox (1), improving TAT (1), and using Toxicology screen kit with higher sensibility (1). One participant answered that Labtox did not need improvement and two did not answer the question.

From the total of 3,488 monitored TAT, 87% (3,035) was from external patients (attended outside the hospital). Toxicology screen was responsible for 72% of the tests, followed by Paracetamol (14%). Butyrylcholinesterase was requested twice more (5.4%) when compared to Acetylcholinesterase (2.5%) (Table 2).

Table 2. LTAT, MTAT and deadline stipulated by laboratory to release the results.

Laboratory test (n)	Laboratory's deadline (days)	LTAT (minutes)	MTAT (minutes)
Acetylcholinesterase (88)	3	2557 (4908-1821)	3015 (4408-2021)
Butyrylcholinesterase (188)	2	55 (480-33)	191 (624-90)
Methaemoglobin (25)	3	195 (997-62)	291 (1530-279)
Paracetamol (498)	3	160 (1428-92)	517 (1431-137)
Paraquat (161)	3	58 (1149-29)	721 (1358-213)
Salicylate (13)	3	70 (204-50)	142 (1233-88)
Toxicology screen (2515)	3	35 (219-17)	185 (1316-29)

LTAT, laboratory turnaround time; MTAT, therapeutic turnaround time; n, number of monitored tests. Results are expressed as median (minimum and maximum time).

LTAT was responsible by 85% of Acetylcholinesterase MTAT, 29% of Butyrylcholinesterase MTAT, 19% of Toxicology screen MTAT, 49% of Salicylate MTAT, 31% of Paracetamol MTAT, 67% of Methaemoglobin MTAT, and 8% of Paraquat MTAT (Table 2).

Table 3 presents the number of non-conformities on LTAT according to the laboratory`s deadline and UK guideline[13]. The total of identified errors was 611. Paracetamol (260) and Methaemoglobin (14) were the tests with the highest rate of non-conformities when compared to UK guideline[13], they consequently obtained unacceptable sigma[16,17]. Salicylates and Paraquat also presented unacceptable sigma when analyzed through UK guideline[13,16,17]. Butyrylcholinesterase was the only test to present non-conformity (1) according to the laboratory's deadline.

Table 3. Non-conformities on LTAT according to laboratory`s deadline and according to UK guideline.

	LD / UK								
Laboratory test	2014	2015	2016	2017	2018	2019	**TOTAL**	DPMO	Sigma

Toxicology screen	--	--	--	0 / NA	0 / NA	0 / NA	0 / NA	0 / NA	6/ NA
Methaemoglobin	0 / 5	0 / 1	0 / 4	0 / 2	0 / 2	0 / 0	0 / 14	0 / 560000	6 / 1.4
Salicylate	0 /0	0 / 0	0 / 1	0 / 1	0 / 1	0 / 1	0 / 4	0 / 307692	6 / 2.1
Paraquat	0 / 0	0 / 1	0 / 1	0 / 5	0 / 1	0 / 6	0 / 14	0 / 86957	6 / 2.9
Acetylcholinesterase	--	--	--	0 / --	0 / --	0 / --	0 / --	0 / --	6 / --
Butyrylcholinesterase	--	--	--	0 / 1	1 / 8	0 / 4	1 / 13	5319 / 69149	4.1 / 3.0
Paracetamol	--	--	--	0 / 76	0 / 91	0 / 93	0 / 260	0 / 522088	6 / 1.5
TOTAL	5	2	6	85	103	104	1 / 610	175172	2.5

LD, laboratory`s deadline; UK, United Kingdom guideline; DPMO, defects per million of opportunities; --, not evaluated; NA, not available.

Discussion

Some authors criticize the use of satisfaction research as a quality indicator, considering that the answers can be based on personal expectations, therefore evaluation should be combined with other tools[17]. For other authors, clinician satisfaction, and TAT perceptions can offer guidance to improve performance of laboratory[18,19]. In this way, the application of questionnaires was one strategy to strengthen the relationship between CIATox/SC and Labtox.

Comparing adherence to our study (65%), the percentage of participation of the clinicians was 45% on a similar study performed in the same hospital[3] and in other studies the observed participation was around of 56% and 94%[19,20].

A recent study in a public hospital in Ethiopia showed that the test menu was the main cause of physicians' dissatisfaction (68%)[20]. Corroborating, our study illustrates the same scenario. The complicating factor on the test menu is the situations unpredictability that arises in EDs and the number of cases to justify menu expansion. This point must be discussed between users and laboratory, taking into account economic, personal, and structural barriers.

The tests selected for evaluation were based on the methodology and relevance for emergency department cases. Other automated tests, besides Butyrylcholinesterase, were not studied because they presented similar results. Tests like Lithium and Digoxin are often used for therapeutic follow-up, which was not the focus of our study.

Labtox presented a good performance on user's TAT perception compared to a study in which more than 80% of laboratories received complaints about it[21]. A previous study at our hospital showed regular user satisfaction with the TAT of common biochemical and haematological tests, which was up to three times higher than expected[3]. This comparison demonstrated that Labtox performed better than in other areas. On the other hand, the majority of Labtox users considered that the current TAT has caused a delay in the treatment and discharge of ED, which shows a systematic non-compliance that has not yet been resolved.

We have observed that the TAT suggested by Labtox users was similar to that recommended by the UK guideline[13]. The UK guideline separates toxicological tests into two groups. The first one is composed of tests that must be available 24 hours 7 days a week. For this group, the guideline recommends that results should be available within a maximum of 2 hours or sooner if possible. The second group is composed of tests that are not necessary to be available 24 hours a day. However, the tests must be available when necessary and the deadline varies among them[13] as shown in table 1.

Evaluating through laboratory deadline, only butyrylcholinesterase showed non-conformity for one specimen, which exceeded the preconized time. For any test, LTAT or MTAT meet the deadline defined by Labtox. Consequently, the sigma analysis shows good performance[16,17]. On the other hand, when analyzed through UK guideline[13] deadlines, only Butyrylcholinesterase assay had sigma performance considered acceptable[16,17]. Methaemoglobin, Salicylate, Paraquat and Paracetamol presented unacceptable sigma[16,17]. These facts indicate that the Labtox deadlines are too wide and must be revised to suit

CIATox/SC needs. On the other hand, the UK guideline does not specify, and probably suggests TAT for automated testing, which is not the reality of our Labtox.

Cholinesterase tests were evaluated only in cases of emergency request. The test can also be requested for patients to monitor workers' health for which deadline is 15 days. Butyrylcholinesterase was solicited twice more than acetylcholinesterase which confirms your widespread use to acute poisoning. Plasmatic cholinesterase is inhibited more quickly in case of poisoning and it is easier to measure, although it is less specific, it can be confirmed by erythrocyte cholinesterase[13].

As UK guideline[13] does not report deadline for Toxicology screen, it was not possible to make the comparison with Labtox TAT.

Similarly, acetylcholinesterase has not been evaluated by the UK guideline[13] pattern, because the method is different from Labtox. Our method requires a 24-hour frozen step. According to the user's TAT suggestions, only one participant suggested two days as a feasible proposal. The TAT most proposed were 60 and 90 minutes, which is not enough to carry out the test. These data demonstrate the need to strengthen communication between the laboratory and users, providing information on the tests offered.

The only automated test analyzed was Butyrylcholinesterase. Users have suggested an acceptable TAT between 60 and 120 minutes, which is 180 minutes on UK guideline[13]. Labtox's LTAT (55 minutes) meets both requirements.

For Paracetamol and Salicylates, which use the spectrophotometric method, the users suggested 120 and 60 minutes as TAT, respectively. This corroborates the suggested by UK guideline[13] which is 120 minutes. Labtox's LTAT for Paracetamol was more than double of the Salicylates LTAT and did not comply with the UK recommendations. The LTAT performance for Paracetamol showed level sigma 1.5, considered unacceptable[16,17].

A spectrophotometric method is also used on Labtox for Methaemoglobin. Labtox's LTAT did not meet user and UK requirements[13]. Consequently, the Methaemoglobin LTAT also showed level sigma considered unacceptable[16,17].

Labtox's laboratory information system has enabled evaluate the TAT of tests since 2017. However, most samples are external and they have recorded only the time of entry into Labtox. This fact makes it impossible to include transport time into the TAT, except for Paracetamol. For Paracetamol, the time of collection is registered because this information is essential to analyze the Rumack-Matthew Nomogram, which predicts hepatic damage. It is important to assess the transport time, as the pre-analytical phase is the main responsible for delays in TAT. Moreover, most samples must be transported refrigerated or frozen, even for the most unstable analytes, and kept in this condition until analysis[22].

In general, MTAT was much higher than LTAT, which shows a delay in results accessing. This may be occurring because the results are not essential for clinical management or due to the delays in the reports. The inconsistency in the communication of critical values can also make users wait longer to access the system. This situation can be solved by the communication of critical values, or automatically printing the results for emergency patients[23,24].

The perception of the report of critical values was not uniform among users. The users stated that it is important to be communicated, on the other hand, over half of them answered that they prefer to access the result in the system, and almost 30% want to receive the communication of all critical values.

Currently, the laboratory does not have specific standard operational procedure for communication of critical values, but count on a form to register data, hour, test, result and name of who received the communication. The failure to communicate critical results is a problem already reported by other areas of our hospital in a previous study[3] and in other

studies[11,23,24]. As for prolonged TAT, is a systematic non-conformity that has not yet been solved.

This discussion on critical values communication should be deepened among Labtox and users, before implementation, on issues such as what tests and results must be reported, whether outpatients should also be communicated, as well as a definition of different critical values for inpatients and outpatients, and the definition of who should be notified[24]. To improve the efficiency of communicating critical values, technology should be considered an ally[25]. The functionality would increase the adherence of Labtox workers.

Conclusion

The observed TAT met the laboratory's own deadline but not the users' expectations and the one predicted by the UK guideline. In the users' perception, they are not being communicated of critical values. To achieve high efficiency, all laboratory processes must be considered and monitored, from requesting tests to releasing the results and the communication of the critical values. Technological tools must be incorporated into the laboratory system to record all steps, facilitating the routine and automatic monitoring of tests TAT, and the critical values communication.

Although all users reported good satisfaction and reliability on laboratory results, some opportunities for increase the Labtox efficiency were observed, such as reducing the test deadline based on feasible TAT and tests automation, improving the test menu, definition of critical values and way of communication. We also noted the need to strengthen the relationship between CIATox/SC and Labtox, and to conduct regular satisfaction surveys to identify non-conformities, and provide feedback to continuously improve laboratory quality.

Acknowledgments

The authors would like to thank the collaboration of CIATox/SC and the Labtox, especially for all the support of biochemicals Elayne Cristina Rateke and Liana Conrado França. The authors also would like to thank the University Hospital of Federal University of Santa Catarina for enable the execution of the study.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Author Guidelines updated *25.11.2019*