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DESARROLLO DE UN SISTEMA DE ALERTA SOBRE LOS RESULTADOS ANALITICOS EN LABORATORIO COMO NUEVA ESTRATEGIA EN SEGURIDAD DEL PACIENTE

TESIS DOCTORAL

Modalidad de presentación de tesis doctoral con un conjunto de publicaciones

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Possunt quia posse videntur

Pueden los que creen que pueden

They can, because they think they can

Virgilio

A mis padres

A mis hermanos, María y Pablo

A Lucía

AGRADECIMIENTOS

A mis padres, sois los mejores. Por vuestra dedicación e inmenso amor y cariño, por vuestro ejemplo y brillantez, por la educación y los valores que me habéis transmitido. A mis hermanos, María y Pablo, por nuestra gran relación. Me siento infinitamente orgulloso de ser vuestro hermano mayor, cada día. No puedo ser más afortunado de formar parte de una familia como esta, de poder contar con unas personas tan maravillosas, tan cercanas y tan queridas.

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Factor de impacto del conjunto de publicaciones en las que se basa la presente Tesis Doctoral

1. Salinas M, López-Garrigós M, Asencio A, Lugo J, Gutiérrez M, Flors L, Leiva-Salinas C. Alert value reporting: a new strategy for patient safety. Clin Biochem. 2013;46:245-9.

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Índice

Introducción

1. INTRODUCCIÓN

1.1. Patient safety.

In the last years, due to the advances promoted by the universality of the health care system in Spain and the use of increasingly sophisticated diagnostic methods and therapies that are usually progressively more aggressive, there has been a parallel increase in the generation of unwanted adverse effects and also over expenses. Indeed, the cost for health care has gradually and significantly grown over the last years and unfortunately the countries revenues are not increasing at a parallel rhythm. It all make necessary to obtain, in the health care setting, not only the best levels of safety but also the best value for money through diagnosis efficiency.

These facts have created strong interest and concern for patient safety. After the publication of the Institute of Medicine report, To Error Is Human, patient safety is finally a main object of medical attention (1).

Currently, medical errors are one of the major causes of death and co-morbidity. From a global point of view, the patient health procedure is divided into a series of more localized procedures. The overall patient safety will be reached if safety is reached in each one of the steps that constitute the global patient procedure.

1.2. Laboratory safety.

1.2.1. **Laboratory safety:** Introduction.

It is well known that clinical laboratory is involved in more than 70 % of clinical decisions and that its role is even increasing over years (2). Indeed, information provided by the laboratory may stratify populations or patients in order to apply subsequent diagnostic procedures or treatments, and laboratory is considered nowadays as a key process (3, 4). Laboratory progressive automation occurred in recent decades has decreased the errors. However, this decline is in relative terms, since the automation itself has greatly increased the number of laboratory reports and therefore the number of errors in absolute terms. In all, nowadays, the number of laboratory errors in absolute numbers is even greater than in any other time in the history of medicine.

This scenario shows that it is essential to establish strategic lines to reduce and minimize laboratory errors to achieve laboratory safety and hence patient safety (5, 6). As compared with other types of medical errors, however, errors in laboratory medicine received little attention. It is time, then, for the laboratory, and in communication and consensus with every stakeholder that intervenes in laboratory procedure, to set up the necessary strategies for the best contribution to the patient outcome.

Indeed, errors in laboratory medicine are intrinsically obscure as they are difficult to identify and, when found, are less easily understood than other types of medical problems. As compared with adverse events related to surgery or other

therapies that are often clear and obvious, laboratory errors tend to be more insidious and difficult to identify in time and place. The difficulties depend largely because the several steps involved. Indeed, as the overall process of patient care, the laboratory is also a complex procedure divided into a series of sequential steps that begins when the clinician request the tests related to suspicious diagnosis and finishes when interpreting laboratory report. To reach laboratory safety implies to achieve safety in each and every of the steps of the laboratory procedure or total testing process (TTP). The testing process is complex, and consists of numerous steps and stretches across multiple providers. Moreover, only the analytical phase falls under laboratory control, while the pre- and post-analytic phases pertain to different stakeholders other than the laboratory such as the ordering clinician, the nurses, the patient and others involved in patient identification, data entry, specimen collection and transport. In the post-analytic phase there is the possibility of inappropriate response to the receipt, interpretation and utilization of laboratory information (7).

Standardized, well-designed studies, a multidisciplinary approach and teamwork are therefore required for a thorough investigation of TTP. There is therefore an urgent need to evaluate errors in laboratory medicine within the reliable framework of the TTP. From this perspective, any possible defect in TTP should be investigated in order to prevent and obviate any negative impact on patient care, irrespective of the step involved, and of whether the error has been caused by a laboratory professional (e.g. calibration or testing error) or by a non-

laboratory operator (e.g. inappropriate test request, error in patient identification, blood collection and/or result interpretation (8, 9).

1.2.2. **Laboratory safety:** Historical background.

Traditionally, laboratory medicine, as a specialty that had prioritized quality control, has always been at the forefront of error reduction. In terms of quality control and error rates, laboratory medicine has a far better record than most other fields in health care. In fact, some studies indicate that, in the analytic phase, the one under direct control and supervision from laboratory professionals, the average error rate is as low as 0.002% (10).

1.2.3. **Laboratory safety:** Current perspectives.

However until the concept of brain-to-brain loop was developed by Lundberg in 1981, laboratory professionals were not concerned enough about the initial and final TTP steps, namely the appropriateness of test requesting, patient and specimen identification and, respectively, the physician's reaction to the laboratory report, and the interpretation and utilization of laboratory results (11, 12). On exploring the beginning and the end of the loop, it emerges that currently these steps, are more error-prone than others (13, 14). Therefore, the laboratory professional should also focus their attention on those phases of the TTP.

1.3. Laboratory safety and Errors in pre-pre analytical phase

Recent data on errors in the pre-pre analytical phase underline that failures to order appropriate diagnostic tests, including laboratory tests, accounts for approximately 55% of observed incidents of missed and delayed diagnoses in the ambulatory setting (15-17). To get an appropriate use of diagnosis and treatment procedures is one of the main duties of health care workers, and will orient health care organizations to more efficient and safety procedures (18). Test requesting inappropriateness is a major issue for a healthcare system (19) and patient safety. Test under requesting results in misdiagnosis. On the other hand, test over requesting produces unnecessary expenses (20, 21).

Screening is usually performed through a panel of tests. Physicians frequently order batteries of tests that are used to screen for disease. The key point is to what extent this panel should be established (22). At present the value of screening healthy asymptomatic subjects for disease by means of laboratory tests is controversial and may not be cost-effective (23). By leaving the clinicians the option to request the test in an individualized manner instead of as a profile component, we give them the opportunity to think about the convenience of the test according to the patient's individual clinical scenario. As, it was stated more than 100 years ago, "there is a danger that laboratory findings may be allowed to take the place of the keen thinking and the educated senses which our professional ancestors used to such good purpose" (24). In fact, it is important to try and hence

to reduce the test volume for tests that scientific evidence has made as redundant (25).

1.3.1. **Laboratory safety and Errors in pre-pre analytical phase:** Advantages of reducing the rate of inappropriate requests advantages.

There are many advantages regarding an appropriate requesting. First it reduces the economic costs of the laboratory. While the cost of a test may be individually cheap, the request of numerous non-indicated tests can eventually generate high costs (26).

Second, the incidence of false positive results by the fact of being requested in a population with low prevalence of a certain disease could be significantly reduced (27).

Third, it decreases the global request of laboratory tests. Indeed, inappropriate over requesting may have contributed to the considerably increase in the volume of laboratory tests over the last years. This overload causes the laboratory to be commoditized in a way that it is very difficult to pay the necessary attention to really appropriate requested tests, to deliver meaningful clinical laboratory information instead of simply laboratory data. In fact, there is a real danger for the laboratory to become a data-dispensing machine instead of a modern organization issuing personalized, individualized information. Furthermore, unnecessary tests laboratory results can hide or mask the really

clinical important laboratory information, those tests results that are necessary to clinical decision-making, generating a linkage between an appropriate pre-pre-analytical phase and consequently a proper tests result interpretation.

In all, promoting and achieving an appropriate requesting has several and multidimensional advantages.

1.3.2. **Laboratory safety and Errors in pre-pre analytical phase:** Adverse events.

The impact of laboratory errors on the patient's journey regarding further inappropriate investigation, further invasive tests and additional consultations is much higher, and although not necessarily harmful, it creates discomfort to the subject and incurs in higher costs for both patients and the health-care system. Some authors have referred that the availability of serum chemistries for screening both symptomatic and asymptomatic patients has resulted in a clear over requesting, and a marked increase in the number of abnormal chemistry tests, that must be interpreted by physicians (28-37)

Currently, abnormal laboratory tests may be the first indication of sub clinical disease and may thereby guide further diagnostic evaluation (38). The history, physical examination, and the use of more specific disease markers will help to narrow the differential diagnosis (39, 40).

However, facing an asymptomatic patient with abnormal blood tests is a scenario frequently encountered by primary care physicians. In fact, isolated alterations of biochemical markers in an apparently healthy patient may present a daily challenge for the clinician (41). As an example, for instance, a reported 1% to 4% of asymptomatic patients will exhibit abnormal liver tests (42). In that case, the first step will be to repeat the test to confirm the result. A lack of understanding of the nature of the assays and the laboratory assignment of normal versus abnormal often leads to unnecessary diagnostic tests, missed disease or to considerable number of annual consultations to specialized practices.

False positive results generated either by test requesting in a population with low prevalence of the target disease or by the statistical nature of the reference ranges, can produce devastating damage. The anxious patient may undertake a long journey to perform additional diagnostic tests, generally more expensive than the original one, or to attend new medical consultations appointments, to finally, luckily, be diagnosed as healthy, after passing through the cavalry of the "Ulysses syndrome" (43). Another most damaging option would be to continue through the "Imaginary Invalid syndrome" (20) to become "a person with an abnormal laboratory value" (44).

Laboratory tests are a classic example of "little ticket test", each one is very cheap but as they are highly requested they overall generate huge economic costs. Besides the additional costs in reactive and staff, laboratory false positive results generate supplementary expenses, such as further unnecessary diagnostic

tests and referrals, but even physical and psychological patient adverse effects, as widely studied and stated in the prior paragraph. In all, it is necessary to develop strategies in consensus with requesting clinicians for a better requesting (45-48).

It all would suggest that tests over requesting will not only generate high economic costs, but also the typical and potentially devastating adverse effects of false positive results, which could even jeopardize patient safety.

1.4. Laboratory safety and Errors in post-post analytical phase.

One of the most important challenges for laboratory professionals is to assist in the management of patient test results. This assistance requires an expansion of the role of the laboratory. It is no longer enough to send our test results across an interface to an electronic record or call a critical result and assume our work is done. Instead, as previously mentioned, the laboratory should be a source of meaningful clinical information.

Evidence demonstrates that pre-pre and post-post-analytical steps of the TTP are more error-prone than the analytical phase. Most errors are identified in the steps outside of the laboratory. In a patient centered approach to the delivery of health-care services, there is the need to investigate, in the TTP, any possible defect that may have a negative impact on the patient.

1.4.1. **Laboratory safety and Errors in post-post analytical phase:** Reducing the rate of inappropriate requests advantages.

Patient safety is getting the right laboratory result to the right person at the right time in a usable/interpretable format. The electronic health record enables large quantities of data to be sent from the laboratory to a variety of environments and displays. Laboratories should carefully review any physician complaint or patient safety event related to the display of laboratory results.

Post-analytical process occurs to ensure that patients receive an appropriate follow-up of test results. The control of this last TTP step will generate several advantages, mostly the accurate and timely communication of the test result by the laboratory. This step is under the direct and sole control of the laboratory. That results are received by the appropriate or correct provider and interpreted correctly are process steps that require laboratory and clinical processes to be integrated. That test results are reviewed and appropriate follow-up completed can be considered clinical processes into which the laboratory has little input. However, it is necessary from the laboratory to also help and advise the clinician for a right laboratory tests interpretation. Patient safety requires all steps in the new post-analytical process to be completed, as detailed below.

- Communication of result by laboratory

- Result received by correct provider

- Result reviewed

- Result interpreted correctly

- Result follow-up appropriate to patient

1.4.2. **Laboratory safety and Errors in post-post analytical phase:** Adverse events.

As stated before, post-post analytical phase and specially the physician's reaction to the laboratory report, and the interpretation and utilization of laboratory results are the steps more prone to have errors.

1.4.2.1. **Laboratory safety and Errors in post-post analytical phase:** No communication of tests results.

The first type of post-analytical process failure is for the laboratory not to properly communicate the result. This issue might be an accuracy or timeliness issue.

Laboratories are under continuous pressure to supply information as quickly as possible (49); classically, over 80% of laboratories receive complaints about turnaround time (TAT) (50-52). Nowadays, in a changing world with more aggressive and earlier treatments, more informed patients and higher workloads, it is a daily challenge for the clinical laboratory professional to get the appropriate

TAT to every specific clinical situation for a better contribution to patient outcome and requesting clinician satisfaction (53).

A continuous TAT indicator monitoring is necessary to know and improve one's laboratory TAT. However it is also crucial to know what the TAT needs are for every clinician and patient, not only to obtain a better patient management, but to try to do the effort to achieve consensual and customized TAT, as resources are limited especially in this moment of economic constraints.

Laboratories monitor TAT for testing. TAT may be monitored from the point of specimen collection to result reporting or from the receipt of the specimen in the laboratory to result reporting. TAT monitors may be selected for high-volume tests, low-volume tests, or for those tests for which the laboratory has had complaints. A variety of TAT monitors for key clinical services or tests should be selected. TAT goals should be established; if the goal is not being met, action plans should be developed. Benchmarking data for TAT are available for several tests and service areas (54, 55). The timeliness of the critical result notification is a standard post-analytical process quality control, and benchmarking data are available for this process.

Failure to adequately communicate a critical laboratory value is a potential cause of adverse events. Accreditation requirements specify that clinical laboratories must undertake assessments and appropriate measures to improve the timeliness of critical value reporting and prompt receipt by the responsible caregiver. Documentation and communication processes must be regularly

monitored and implemented under ongoing systems for quality monitoring. Critical value reporting is an important phase of the clinical laboratory testing process, and notifications of results outside the target time can indicate ineffectiveness of the process (56).

After first advocated by Lundberg (57) more than 30 years ago, there has been wide agreement on how to define a critical value when a result becomes life-threatening unless some intervention is made by a physician and for which interventions are possible. The development of a critical values policy has become a quality practice in laboratory medicine procedures, and, in some countries such as in the United States, the requirements for reporting critical values are specifically described in the standards of accreditation agencies such as the Joint Commission, formerly the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), and the College of American Pathologists (CAP). Since 2005, the JCAHO has released guidelines in which the reporting of laboratory critical values has become a Patient Safety Goal. At an international level, the most widely accepted standard in the medical laboratory community, ISO EN 15189:2007, includes (in clause 5.8.7) the immediate notification of a critical value as a special requisite (58).

In October 2004, the World Health Organization (WHO) launched the World Alliance for Patient Safety to improve the safety of care and facilitate the development of patient safety policies and practices in all WHO member states. Every year, the Alliance provides a number of programs covering systemic and

technical aspects to improve patient safety worldwide. Recently, the fourth of 23 potential patient safety solution topics, entitled "communicating critical test results," was selected by the WHO International Steering Committee. It is currently under development, and will be released in the near future.

Reporting of critical values is an important phase of the clinical laboratory testing process, and laboratories are responsible for detecting life-threatening results, for reporting them to health care providers, and also for tracking and improving the timeliness of reporting and the receipt of results. To minimize communication errors, accreditation programs require that the critical value must be read back by the health care worker, who should be contacted by phone (59). An indicator of quality of the process may be the critical value reporting rate; the failure to report these values, estimated at 0.1% to 10%, can indicate operational inefficiency of laboratories (60).

The sizable number of critical results, the failure to provide notification within the target time, and the time required for phone calls may be considered tools to measure the quality of critical value reporting.

1.4.2.2. **Laboratory safety and Errors in post-post analytical phase:** Tests results communicated but not received.

In the first article of its kind, Yackel and Embi (61) examined unintended errors in the management of test results in the electronic health record, focusing on the reasons.

1.4.2.3. **Laboratory safety and Errors in post-post analytical phase:** Tests results not reviewed.

Laboratories are not directly responsible for ensuring that all reported test results have been reviewed. In May of 2011, a kidney transplant program in the United States was voluntarily shut down following a failure to follow up on a laboratory test result. The results of a positive hepatitis C test sat in a living kidney donor's medical record for more than 2 months before her kidney was transplanted into a man who did not have the virus (62). But despite several chances to review the test result and possibly stop the transplant due to this potentially lethal hepatitis C virus infecting the donor, none of the doctors or nurses involved in the case did so, according to the Centers for Medicare and Medicaid Services' investigation.

Although not directly responsible, laboratories might participate in the organizational design of systems designed to monitor the reviewing of results, involving automatic or manual tracking systems.

1.4.2.4. **Laboratory safety and Errors in post-post analytical phase:** Results not interpreted correctly.

In the final steps of the laboratory process, the incorrect interpretation of laboratory tests was found to be responsible for a significant percentage of errors in the ambulatory setting. A study showed that failure to inform outpatients of clinically significant abnormal test results or to document that the relevant information was given, appear to be relatively common, occurring in approximately 7% of cases. Examples include patients not being informed of results of total cholesterol as high as 318 mg/dL, a hematocrit level as low as 28.6% and a potassium level as low as 2.6 mmol/L. The overall rate of failure to inform the patient or record/document communication of information was 7.1%, ranging between practices from 0% to 26% (63). Further evidence of errors in reacting to laboratory test results was shown in a study on the prescription of potassium despite the presence of hyperkalemia (64). Another study found that more than 2% of patients with thyrotropin (TSH) results higher than 20mU/mL had no follow-up (65). The same happened in patients with hypercalcemia (46). Finally, an interesting study of hospital inpatients showed almost half of discharged patients had laboratory results pending and that 9% of these results were potentially actionable (66). It is important from laboratory to report information instead of data for a better patient outcome (67-69).

In all, errors in the post-post analytical phase are frequent and may have severe harming consequences for patient safety.

1.5. Processes to reduce errors in laboratory medicine.

Overall, the above data demonstrate that the initial and final steps of the TTP process, in particular test requesting and reaction to laboratory results, not only are more error-prone than all the other steps, but are more important causes of potential adverse outcomes for patients.

As shown, in the last few years, in addition to efforts aiming to reduce analytic errors and improve analytic quality (70), important achievements have been made in addressing errors in laboratory medicine (71, 72). Thanks to the introduction of pre-analytic workstations, a significant reduction has been achieved in pre-analytic errors in the automation of procedures such as specimen preparation, centrifugation, aliquoting, pipetting and sorting (73, 74). The increasing interest in developing guidelines and standard operating procedures for patient identification, blood collection, sample handling and specimen acceptance or rejection (75-78) will surely translate into higher quality standards (79-81). Likewise, significant improvements have been made to the post-analytic phase in data transcription as a result of interfacing analyzers and laboratory information systems. Importantly enough, data transcription is a source of potentially serious errors, particularly if many numbers and results have to be entered into the laboratory computer manually. However, further important achievements in the post analytic phase concern policies and procedures used for reporting critical values as well as initiatives to better understand and improve upon the efficiency

of test report delivery to requesting physicians are needed (82,83). Automatic computerized communication systems have recently been developed to improve the timeliness of notification and avoid potential errors for which accreditation programs require read back of the result. After being validated by laboratory physicians on call, critical values are automatically communicated, in real time, to the clinicians, short message services or alert messages appearing on desktop computers (84). These systems, which improve the likelihood of reaching the physician on call, are even easily adapted to reach patients on their mobile phone or desktop computer, thereby representing an effective means of reducing or indeed eliminating the failure to communicate abnormal outpatient test results to users. Further developments concern the introduction of more effective automated procedures for data validation and reporting as well as the implementation of systems which allows an effective knowledge management to support data interpretation and clinical decision-making (85) because correct interpretation of such results is crucial and requires knowledge of the available laboratory tests, their underlying pathophysiology, and the proper approach to the interpretation of abnormal tests results. Indeed, not every subject with an abnormal test has actually disease, as illustrated previously.

These proactive tools for a proper interpretation of tests results are increasingly, and more readily, used by laboratorians and clinicians and are boosting professional competences through a positive approach to problems by focusing on the examination of the entire testing process, thus anticipating major adverse events and implementing changes to prevent them.

Once again is the responsibility of the laboratory and the laboratory professionals, to be the protagonist in laboratory tests utilization by detecting tests requesting and interpretation inappropriateness and, establishing channels of communication with clinician to design strategies to solve it (86, 87).

Nowadays, achieving an appropriate test requesting and interpretation is not a clinician responsibility. In fact there is a shared responsibility between the laboratory and requesting clinicians. The first step to solve this harmful issue will be to detect the real test inappropriateness and misinterpretation.

It should be the clinical laboratory professional commitment to establish the adequate channels of communication with other stakeholders that take part in clinical decision-making, on the optimal use of laboratory (88). It is imperative to make use of our powerful LIS not only in the phases that occur inside the laboratory walls but also in those occurring outside: to achieve a proper test requesting and tests results clinician awareness. It is important to remember that the goal of laboratory testing is not the data delivering per se but to deliver information and knowledge (89) to improve the outcome for the patient and hence patient safety.

1.6. Introducción al primer artículo en que se basa la presente tesis doctoral

Salinas M, López-Garrigós M, Asencio A, Lugo J, Gutiérrez M, Flors L, et al. Alert value reporting: a new strategy for patient safety. Clin Biochem. 2013;46:245-9.

The concept of critical value refers to a result that may imply a life-threatening situation for a patient unless appropriate therapy is initiated. Every laboratory should have at its disposal a procedure for the notification of critical results. This should include a list of critical limits, either from the literature or reached by consensus with clinicians, and should be evaluated periodically. The usefulness and implementation of critical value reporting is well established. In fact, it is a requirement of quality assurance agencies. In contrast to critical value reporting, alert value reporting concept has not been described in the literature. This term would not allude to a result that may imply a life-threatening situation for a patient, but would rather indicate that an early diagnostic or therapeutic action would greatly improve the patient's quality of life through earlier detection or treatment establishment.

At present, most laboratories receive samples from a variety of clinical settings. As a consequence, it is very difficult to apply universal critical value list for the different types of patients, the distinct laboratory organizations, and the various requesting centers. It seems appropriate to customize the list, as well as the notification procedure, to the type of patient, to the type of laboratory and to

the requester. The same consideration is likely to be expected with alert value reporting.

Alert value reporting could be crucial in primary care. General practitioners (GPs) increasingly monitor specific pathologies traditionally treated by specialists. In this scenario, more unexpected results that require prompt therapeutic actions are likely to be generated. Furthermore, frequently, patients do not immediately return for the follow-up doctor's appointment after the analysis. Many analytical results may, therefore, be ignored until the next consultation, regardless of how quickly they are generated. In these cases, the promptness of the alert value reporting may be fundamental. In addition, new information systems can automate and systematize the daily alert values search, providing a new laboratory service to the primary care physician and patient. In our specific situation, a change in the primary care laboratory reporting process (electronic reports were directly pushed into the electronic medical record, instead of being printed and sent to the primary care centers) changed the GPs habit to review the printed reports that were sent daily, in order to look for test results that might effect when the next patient appointment is scheduled.

1.7. Introducción al segundo artículo en que se basa la presente tesis doctoral

Salinas M, López-Garrigós M, Gutiérrez M, Lugo J, Flors L, Leiva-Salinas C. Should we customise critical value procedure according to patient origin and laboratory turnaround time? J Clin Pathol. 2013;66:269-72.

Laboratory critical values are those values that identify life-threatening conditions requiring prompt medical intervention. The concept has evolved over the years [2, 3] and nowadays accreditation agencies - the most widely accepted standard is ISO EN 15189:2007 - define and require clinical laboratories to list critical limits, formulate notification procedures and document critical results.

Most laboratories attend to a wide variety of patients (inpatients, primary care, emergency outpatients, etc...) and laboratory results that may be critical for some patients may be rather "normal" for others (e.g. intensive care unit, dialysis, oncology, etc…). Furthermore, the improvement in technology and laboratory processes makes possible to produce very short laboratory response times; very often, it is possible for the requesting physician to check for results electronically immediately after they have been verified by the pathologist, when the patient may still be "at hand".

In this scenario, it is becoming increasingly difficult to establish a single critical value list to be used in the different situations that occur daily in a clinical laboratory.[6-9] It seems more appropriate to adapt the test list and thresholds, as

well as the notification procedure, to the type of patient, the laboratory response time, and to the requester, in the interest of efficiency.

Instead of taking into account just the result value, it seems more sensible to also consider other information such as the change in the current test result from previous results, the patient´s characteristics and the ordering provider.

Justificación

La seguridad del paciente depende de la seguridad en cada uno de los procesos que intervienen en el complejo proceso asistencial. Estos procesos se clasifican en clave y de apoyo. El laboratorio es un proceso clave, no solo por su importancia en el diagnóstico, monitorización y la prevención de las enfermedades, sino también porque sus datos intervienen en el 70% de las decisiones clínicas. Sus datos, además, son los que en ocasiones permiten o propician procedimientos diagnósticos más invasivos que los del laboratorio en sí, tratamientos también cada vez más agresivos e incluso decisiones de tipo logístico, pero no por ello menos claves, como la decisión de la alta médica o del ingreso de los pacientes. Por tanto, conseguir la seguridad en el laboratorio es clave para conseguir la seguridad del paciente.

Las consecuencias de los errores de laboratorio pueden ser muy graves, en el 6.4-12% de ellos generan un riesgo en el manejo adecuado del paciente El 26-30% genera problemas de atención paciente como la necesidad de una nueva toma de muestras o un retraso en el resultado. El 30% genera repetición de pruebas de laboratorio, pruebas diagnósticas más invasivas y consultas médicas adicionales que conducen a ansiedad, y gasto económico innecesario. De hecho un error falso positivo de laboratorio puede conducir a innumerables consultas médicas innecesarias. Estos son consecuencia de la solicitud indiscriminada de pruebas en poblaciones de baja prevalencia de la enfermedad a diagnosticar, y de la naturaleza estadística de los valores de referencia poblacionales.

Pero no solo el proceso asistencial de atención al paciente en su conjunto es complejo, sino que el propio proceso del laboratorio es complejo. Se compone de las etapas pre analítica, analítica y postanalitica y la seguridad del laboratorio se conseguirá propiciando la seguridad en cada una de sus fases. En la etapa analítica donde más errores graves se generan. Sin embargo, en la actualidad, es en la etapa pre y postanalítica donde más errores se cometen, dándose cada vez más importancia a dichas fases. Pues es baladí aplicar las más modernas y minuciosas técnicas de calidad analítica a una prueba que nunca debiera haberse solicitado o cuyo resultado nunca vaya a ser observado, consultado, aplicado o correctamente interpretado. De hecho la adecuación en la solicitud de las pruebas es crucial. Una inadecuación por defecto puede propiciar la pérdida de un diagnóstico, pero una inadecuación por exceso no solo produce el aumento del gasto de la prueba en sí, sino también las consecuencias previamente enumeradas de los resultados falsos positivos.

La etapa postanalítica está cobrando cada vez más importancia en la seguridad del laboratorio y en consecuencia en la del paciente. Ya en el año 2005 se describió, mediante una cuidadosa revisión de las historias de los enfermos, que no se tomaba ninguna decisión clínica tras el 15% de la hipercalcemias informadas. Un posterior estudio ha mostrado un porcentaje mayor de resultados elevados de calcio en sangre no visualizados por el médico de atención primaria ni tampoco derivado a la consulta de endocrinología para su estudio. Es clave en dicha etapa no solo que el resultado de la prueba del laboratorio esté accesible para su consulta por el médico solicitante en un tiempo adecuado, sino que

realmente lo visualice, que lo interprete adecuadamente y que tome la decisión diagnóstica o de tratamiento adecuado a la situación clínica del paciente. Todo lo expuesto indica la necesidad no solo de proporcionar desde el laboratorio información y no datos que se consigue aplicando el conocimiento a los datos que emiten los analizadores, sino también "desenmascarando" de entre los resultados de las pruebas del informe del laboratorio aquellos datos de laboratorio con valor clínico y de esta forma propiciar la mayor contribución del laboratorio a la decisión clínica, y en consecuencia a la seguridad del laboratorio y del paciente.

La justificación de una línea de investigación sobre la comunicación de resultados críticos de laboratorio es el mejorar la seguridad del paciente, facilitar la práctica clínica, e integrar la informática y automatización de los potentes servicios informáticos del laboratorio en el marco de la asistencia hospitalaria. Hay pocos estudios sobre este tema. Así pues la realización de esta tesis doctoral es pertinente por su aportación a la promoción de la seguridad del paciente

Hipótesis y Objetivos

3. HIPÓTESIS Y OBJETIVOS

3.1. Hipótesis

Existen pocos datos acerca de cómo se puede mejorar la seguridad del paciente mediante la comunicación de resultados clave de pruebas de laboratorio. Tradicionalmente se ha empleado una lista rígida y arbitraria de pruebas y de valores umbral para comunicar los resultados críticos, aquellos que ponen en riesgo la vida de un paciente. Nuestra primera hipótesis es que el informe de un resultado crítico basado en dicho listado rígido de pruebas y de valores conduce a resultados totalmente diferentes si se aplica a diferentes grupos de pacientes, lo que sugiere que deberíamos adaptar dicha lista a los diferentes escenarios de la atención al paciente y los distintos tipos de pacientes. Nuestra segunda hipótesis es que laa comunicación de aquellos resultados para los que "una acción diagnóstica o terapéutica temprana podría mejorar en mucho el resultado del paciente y su calidad de vida" también puede contribuir a mejorar el bienestar y la seguridad del paciente.

3.2. Objetivo general

El objetivo general de estas Tesis es mejorar la seguridad del paciente mediante la mejora de la seguridad en el laboratorio en la etapa post-post analítica, y en concreto en la comunicación e interpretación del informe de resultados.

3.2.1. Objetivos específicos

El primer objetivo de esta tesis doctoral es demostrar cómo el informe de un resultado crítico basado en un listado rígido de pruebas y umbrales conduce a resultados totalmente diferentes si se aplica a diferentes grupos de pacientes (urgencia o de rutina). Además, queremos proponer un sistema de notificación flexible que se adapte a las características propias del paciente y del servicio que solicita la prueba.

El segundo objetivo de esta tesis doctoral es introducir el término de resultado de alerta, como aquel que "indica que una acción diagnóstica o terapéutica temprana podría mejorar el resultado del paciente y – potencialmente- su calidad de vida", describiendo que lista de pruebas diagnósticas y valores umbrales pueden ser utilizados para maximizar la seguridad del paciente, y como se puede aplicar en nuestro entorno.

3.2.1.1. Objetivo del primer artículo en que se basa esta Tesis Doctoral

Salinas M, López-Garrigós M, Asencio A, Lugo J, Gutiérrez M, Flors L, et al. Alert value reporting: a new strategy for patient safety. Clin Biochem. 2013;46:245-9.

The purposes of this study were: first, to introduce the new "alert value reporting" concept in primary care setting; second, to describe the chemistry and hematology alert parameters and their corresponding threshold values that were chosen for that strategy; and third, to show how alert value notification procedure was designed and established, and agreed upon between primary care physicians and clinical laboratory professionals. Finally, we prospectively evaluated the effectiveness and assessed the physicians' satisfaction with such an intervention.

3.2.1.2. Objetivo del segundo artículo en que se basa esta Tesis Doctoral

Salinas M, López-Garrigós M, Gutiérrez M, Lugo J, Flors L, Leiva-Salinas C. Should we customize critical value procedure according to patient origin and laboratory turnaround time? J Clin Pathol. 2013;66:269-72.

The aim of our study is to show how critical value reporting system using a single list of values and thresholds can result on a completely different results depending on whether the laboratory tests are requested in a stat or routine manner, and to describe a flexible notification system, adapted to the requester and patient clinical situation, that may take into account the variability of the patient population and may overcome this limitation.

Material y métodos

4. MATERIAL Y MÉTODOS

4.1. Material y métodos del primer artículo en que se basa esta Tesis Doctoral

Salinas M, López-Garrigós M, Asencio A, Lugo J, Gutiérrez M, Flors L, et al. Alert value reporting: a new strategy for patient safety. Clin Biochem. 2013;46:245-9.

4.1.1. Setting

The laboratory is located at the University Hospital of San Juan (Alicante, Spain), a 370-bed suburban community hospital that serves a population of 234551 inhabitants including 10 different primary care centers (with a total 115 GPs). It receives samples from inpatients, outpatients and primary care patients. In 2010, and 2011, 87252 and 91603 requests were received from primary care during which 1097668 and 1192735 tests were carried out, respectively.

4.1.2. Description of service

Traditionally, blood samples were transported by couriers from the different primary care centres to our laboratory. Printed laboratory reports were generated and delivered. From December 2010, laboratory requests were made on line and the reports sent out electronically from the laboratory information system (LIS) to the patient's electronic medical record. This change altered the GPs daily habit of manually checking each laboratory report in order to look for test results that might necessitate a re-appointment.

4.1.3. Strategy

To address this potentially problematic situation, the laboratory professionals devised a method that would automatically alert the GP to a result that needed a follow up and alert value reporting concept was established.

In a first stage, 3 meetings were held between the laboratory professionals in order to establish the different alert value tests and limits, and their appropriate notification procedure. The selection of the alert values was based on expert opinion. Initially, a consensus was reached on a potential list of alert values, i.e. which tests should be included, and which limits should be applied. Next, a retrospective 12-month study was made in the LIS to check how many of these alert values would had been communicated in 2010 if this theoretical alert value list and limit values had been applied. Thereafter, a meeting was held between the laboratory staff and the GPs coordinators of primary care centers to inform them about the proposed alert values list and limits, and to comment about the number of notifications that would had been reported using values reported in the previous year. Following discussion and adjustment, definitive alert values list and limits were established and application software for electronic notification designed and tested. The application software for electronic notification was based on a real time consultation of verified patient's test results. The LIS (Omega 3000 3.3, Roche Diagnostics, Spain) works with CACHE2007, a post relational database that allows access to LIS in a friendly environment. The information generated by CACHE2007 is based in HTML and JavaScript.

To assess the intervention effectiveness, we carried out a prospective analysis of every reported alert value during a 6 months period (from July 1st to December 31st 2011) in a single primary care center (with 13 GPs serving 23557 inhabitants), through reviewing primary care patients medical records. To study the requesting physician's satisfaction with the new strategy, we sent a survey including a single question about the interest to continue with alert value reporting strategy (yes/no) to the 10 physicians practicing at the mentioned facility.

4.2. Material y métodos del segundo artículo en que se basa esta Tesis Doctoral

Salinas M, López-Garrigós M, Gutiérrez M, Lugo J, Flors L, Leiva-Salinas C. Should we customize critical value procedure according to patient origin and laboratory turnaround time? J Clin Pathol. 2013;66:269-72.

4.2.1. Description of service

The central laboratory is divided in 2 laboratories: a "Routine" laboratory and a Stat laboratory. The routine laboratory processes samples for the hospital out- and inpatients and for the patients from the different primary care centers that depend on our hospital. The stat laboratory is an independent laboratory that processes requests for inpatients and the hospital emergency department (ED). The rationale behind the Stat laboratory is to offer very short turnaround times. The reports for the inpatients are consulted via intranet except for the Intensive Care Unit (ICU), Oncology Unit and the ED, where the reports are automatically printed locally as soon as they are verified by the pathologist. The stat laboratory is staffed by 3 technicians. As soon as the results are available, they are verified by a pathologist.

The number of requests and tests that were processed by the routine and stat laboratory from 2003 to 2011 are showed in Table 1.

In 2003, our laboratory devised a very simple routine critical value procedure in consensus with the clinicians, according to the published evidence, to report only those critical values that are really life-threatening for the patient if an immediate therapeutic decision is not taken. In our routine Laboratory critical value notification procedure includes a "short list" of six tests values. The laboratory director and the chairmen from the departments of cardiology, rheumatology, endocrinology and haematology defined these values in consensus. They were selected to provide an expert opinion about which abnormal values of the laboratory tests related to their specialty should motivate an immediate treatment/action due to a threatening danger to a patient's life. Table 2 shows the list of tests.

4.2.2. Strategy

The laboratory uses a module in our laboratory information system (LIS) that automatically marks every critical result. Those results are automatically flagged and reviewed by a pathologist that will decide on the need to call the requesting physician.

The rationale behind that approach – the intervention of the pathologist - was to avoid redundant data and the risk for information overload. Instead, the laboratory professional evaluates the results and the previous laboratory data in order to identify other potentially clinically relevant critical values. Since our stat laboratory report is available and printed in the ED, ICU and oncology unit in less than 30 minutes from pneumatic tube laboratory sample arrival, stat laboratory does not use the routine "short list" of values to report critical values. Conversely,

when validating the inpatients requested tests, the pathologist reports a critical value based on the previous laboratory results and on the patient individual medical situation.

For the routine laboratory, we reviewed the number of notifications that were reported annually during the nine years of our program, and calculated the number of notifications that would have been reported based only on the "short list", if nor pathologist intervention would have occurred.

For the stat laboratory, we studied the number of real notifications based on the pathologist criteria and calculated the number of notifications that would have been reported if the routine "short list" would have been used instead. The critical values from the Stat Laboratory for year 2011 were analysed according to the type of patient (ED patients or inpatients). The turnaround time (TAT) for each group was calculated and compared using the Mann-Whitney test. TAT was defined as the time interval between test registration and test validation.

For analysis purposes, we further classified the critical value for the inpatients as "expected", if the new critical value was in agreement with previous laboratory results, or as "unexpected", if there were no previous results or the new value was not coherent with the previous one. We calculated and compared TAT for both expected and unexpected results, using the Mann-Whitney test.

Table 1. Number of laboratory requests and tests ordered in routine and stat laboratory from year 2003 to 2011

Year	Routine laboratory		Stat laboratory	
	Requests	Tests	Requests	Tests
2003	141217	1552534	60055	353339
2004	153890	1696619	61304	375939
2005	155145	1733312	65326	405424
2006	165064	1851537	66351	426434
2007	171635	1951434	71678	497930
2008	174052	2033218	76706	557831
2009	159089	2025598	76231	620511
2010	151523	2034732	75433	652458
2011	155381	2042546	72311	630158

Table 2. The "short list" of laboratory critical values

Test	Critical Value
Glucose	<1.9 mmol/L or >30.6 mmol/L < 35 mg/dL or >550 mg/dL
Sodium	<115 mmol/L or >158 mmol/L
Potassium	<2 mmol/L or >7 mmol/L
Calcium	<1.5 mmol/L or >3.2 mmo/L <6 mg/dL or >13 mg/dL
Hemoglobin	<50 g/L < 5g/dL
Platelet	<10000/mm^3

Resultados

5. RESULTADOS

5.1. Resultados del primer artículo en que se basa esta Tesis Doctoral

Salinas M, López-Garrigós M, Asencio A, Lugo J, Gutiérrez M, Flors L, et al. Alert value reporting: a new strategy for patient safety. Clin Biochem. 2013;46:245-9.

The definitive list of alert values list and limits that were decided in consensus between the laboratory staff and the GPs is shown in Table 1. This table also displays the number of tests requested in 2010 and the total of alert values that would have been communicated. In all, 3490 notifications would have taken place in 2010, entailing 4% of the total requests from primary care centers.

Figure 1 summarizes the procedure that was established at the different primary care centers to perform the alert value reporting intervention.

It is based on a web site LIS informatics consulting. Users access the web site where current date and primary care centre name are requested. Once the web has searched the alert values of the day it finally shows these values in another web. This search provides all the reports containing alert values, classified by the requesting physician. Laboratory reports are printed and placed in the individual requesting physician's message box. Alert reports are printed because they cannot be distributed electronically, and the procedure is assured to be made daily by one

PCC person. It is the GP, who by reviewing the report, will decide upon the advisability of anticipating the patient's appointment.

Regarding the 6 months period prospective analysis in a single primary care center, 4309 requests were received. Among those, there were 154 alert values (3.5%). By reviewing six months 1 primary care center medical records was assessed that 30 of them (19.5%) motivated an anticipation of the patient next appointment. Of the 30 values that encouraged the anticipation of the visit, 7 were related to alanine aminotransferase (ALT), 4 to hemoglobin, 3 to creatinine, potassium and triglycerides (TG), 2 to thyrotropin (TSH) and carcinoembryonic antigen (CEA) and one case related to prostate specific antigen (PSA), glucose, carbohydrate antigen (CA)-125, creatine kinase (CK), CA-19-9 and lipase**.** For the rest 124 alert values (80.5%), the GPs did not consider necessary to bring forward the next patient visit, either because the result was expected, or because the next appointment was early enough. Considering the limitation of the satisfaction survey because only 10 GPS were reviewed, the, 90% of physicians considered alert value reporting as an interesting strategy to be continued.

Figure 1. Processes to design and implement the Alert Value Reporting procedure.

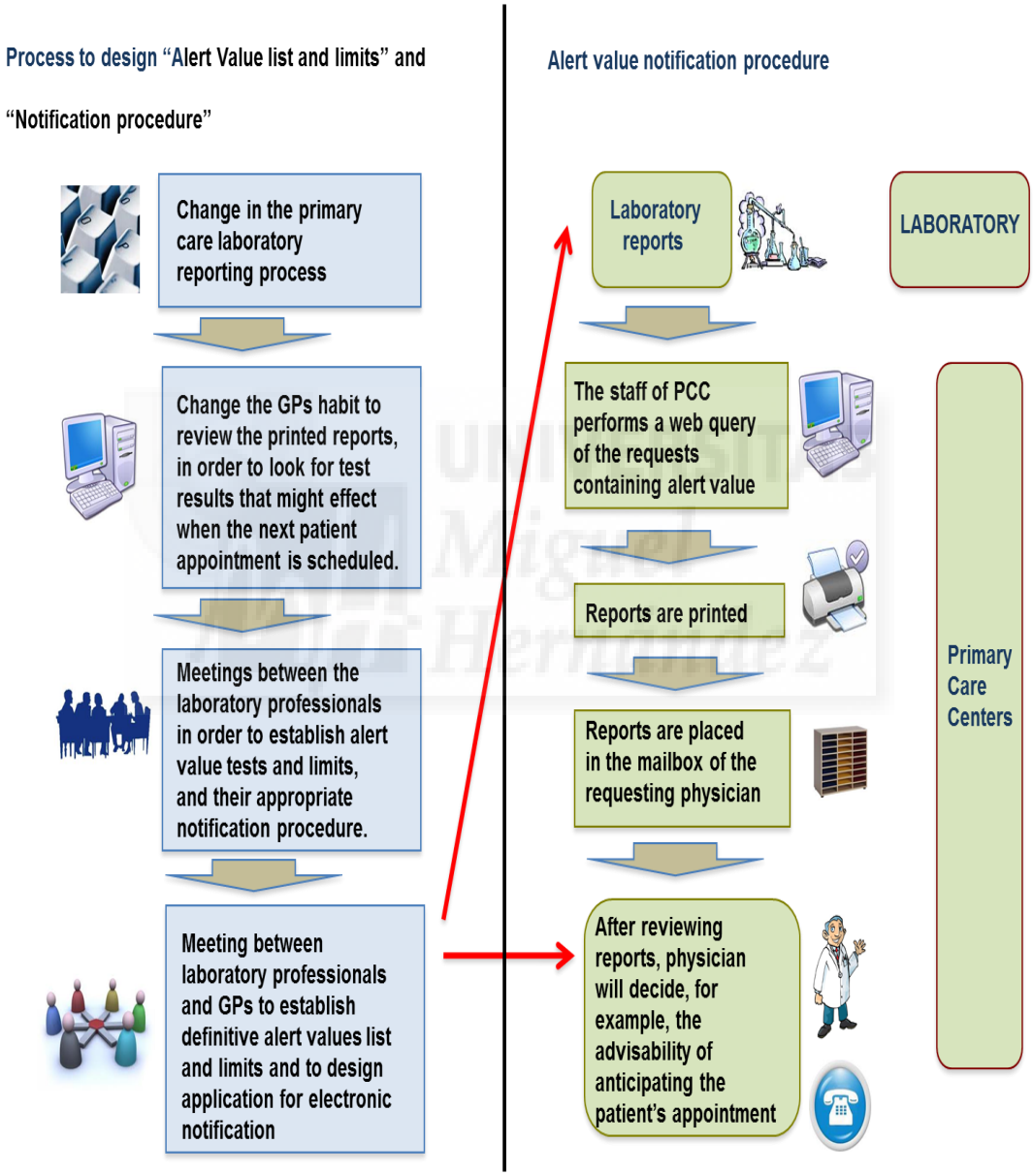

Table 1. Test list and limits of alert values established for primary care patients, total number of tests requested in 2010 and total of alert values that would have been communicated.

Test	Unit (SI)	Low limit	High limit	Tests	Tests with alert result
Alanine aminotransferase	U/L		100	68053	360
Amylase	U/L		200	1356	2
Bilirubin, total	mg/dL (µmol/L)		3 (51.3)	20737	25
CA[a]-125 antigen	U/mL (kU/L)		70 (70)	950	4
CA[a]-19-9 antigen	U/mL (kU/L)		80 (80)	1204	43
Calcium	mg/dL (mmol/L)		11 (2.7)	11822	14
Carcinoembryonic antigen	ng/mL (µg/L)		5 (5)	1186	171
Cholesterol	mg/dL (mmol/L)		400 (10.3)	66056	21
Creatine kinase	U/L		400	4835	52
Creatinine	mg/dL (µmol/L)		2 (176.8)	66538	229
Feces Occult Blood			Positive	761	20
GFR estimate	mL/min/1.73m^2	40		5376	191

Glucose	mg/dL (mmol/L)		300 (16.7)	69316	100
HAV[c] IgM Antibodies			Positive	539	2
HBV[d] IgM Antibodies			Positive	88	2
Hemoglobin	g/dL (g/L)	8 (80)		70850	112
Lipase	U/L		200	96	1
Potassium	mEq/L (mmol/L)	3 (3)	6 (6)	34370	190
Prostate specific antigen	ng/mL (µg/L)		6 (6)	11048	425
Protein, total	g/dL (g/L)	3 (30)	9 (90)	2269	34
Sodium	mEq/L (mmol/L)	125 (125)	150 (150)	33345	71
Thyrotropin	µU/mL (mU/L)	0.35 (0.35)	10 (10)	26146	1026
Triglycerides	mg/dL (mmol/L)		1000 (11.3)	65947	49
Urea	mg/dL (mmol/L)		80 (28.6)	15368	221
Uric Acid	mg/dL (µmol/L)		10 (594.6)	65555	124
Total				643811	3490

[a]CA: Carbohydrate antigen
[b]MDRD: Modification of Diet in Renal Disease equation
[c]HAV: Hepatitis A Virus
[d]HBV: Hepatitis B Virus

5.2. Resultados del segundo artículo en que se basa esta Tesis Doctoral

Salinas M, López-Garrigós M, Gutiérrez M, Lugo J, Flors L, Leiva-Salinas C. Should we customize critical value procedure according to patient origin and laboratory turnaround time? J Clin Pathol. 2013;66:269-72.

The number of routine laboratory notifications based on this "short list" and the final real number of critical value notifications that were performed annually since year 2003 is shown in Table 1. The number of reported critical values was always larger than the one automatically generated by the "short list", since the pathologist usually consider some others, depending on the particular patient situation.

Table 2 shows the number of routine calls for the main individual analytes. Other routine analytes that were prone to be reported as critical were: alanine aminotransferase, carcinoembryonic antigen, estradiol, leukocytes, lipase, lithium, magnesium, phosphate, thyrotropin, triglycerides, urate, urinary catecholamines, as well as qualitative results reporting the existence of immature leukocytes with leukemic expression.

Of all routine reported critical values in 2011, 44 (20.5%) were found in primary care and 170 (79.5%) in hospital patients. Of the ones found in the hospital, 137 (80.5%) were reported to inpatients and 33 (19.5%) to outpatients. 25% were reported to Internal Medicine, 9% to Nephrology and 6% to Oncology. Routine critical values reported to ICU, Haematology, Cardiology,

Gastroenterology and Infectious Diseases were around 5%. Less than 5% of the critical values were reported to other departments such as Gynaecology, Paediatrics, Endocrinology, Pulmonology, Urology and Orthopaedic Surgery.

Table 1 also shows the number of notifications that were made in stat laboratory and the number of notifications that would have been reported if the routine "short list" had been used. Figure 1 shows the "breakdown" of the 627 critical values that would have been reported if the "short list" would have been used in year 2011 in stat laboratory. There were 141 inpatients with unexpected results (37.9%) (120 with a previous result not coherent with the previous one and 21 without previous results).

The median TAT for ED patients was 26 minutes; the median TAT for inpatients was 30 minutes. The TAT for ED patients was significantly shorter that the TAT for inpatients ($p<0.01$). The median TAT for inpatients with "expected" results was 29 minutes; the median TAT for inpatients with "unexpected" results was 31 minutes. The TAT for both groups was not statistically significant ($p=0.532$).

Table 1. Number of routine laboratory notifications based on this "short list" and the final real number of critical value notifications that were performed annually

Year	Routine laboratory		Stat laboratory	
	Reported short list critical values	Total reported critical values	Requests	Tests
2003	142	211	587	154
2004	131	237	467	140
2005	174	181	535	139
2006	176	227	540	152
2007	201	222	649	154
2008	2013	230	679	153
2009	154	249	596	156
2010	154	288	637	159
2011	149	214	627	141

Table 2. Number of routine calls for every listed individual analyte.

	2003	2004	2005	2006	2007	2008	2009	2010	2011
Low glucose	26	25	34	35	40	38	32	23	27
High glucose	10	12	14	12	9	8	9	8	5
Low sodium	7	4	2	5	10	14	7	2	6
High sodium	23	23	28	16	18	18	20	10	29
Low potassium	1	1	2	4	4	4	2	2	2
High potassium	32	28	43	58	55	54	37	30	30
Low calcium	7	7	17	9	21	18	18	23	17
High calcium	6	4	8	5	7	14	7	16	8
Low hemoglobin	12	10	10	13	10	15	11	25	11
Low platelets	18	17	16	19	27	20	11	15	14

Discusión

6. DISCUSIÓN

5.1. Discusión del primer artículo en que se basa esta Tesis Doctoral

Salinas M, López-Garrigós M, Asencio A, Lugo J, Gutiérrez M, Flors L, et al. Alert value reporting: a new strategy for patient safety. Clin Biochem. 2013;46:245-9.

The alert value reporting concept was successfully executed. It is now fully established as a process carried out automatically and systematically at every primary health care center, on a daily basis. At present, alert value reporting allows GPs to acknowledge if tests processed the day before hold any value of interest to which special attention should be paid. As a consequence, if necessary, patient appointments can be anticipated and further diagnostic or therapeutic actions can be quickly performed.

The implementation of the electronic-based laboratory request and report system was crucial to this achievement. Unlike the manual daily visualization of the pile of delivered paper reports, the electronic search is a faster and more efficient process. However, looking in electronic medical record for laboratory reports for every patient phlebotomized the previous day would have been too cumbersome. The proposed alert value notification procedure holds various advantages. First, it is carried out automatically for every laboratory report. Second, it provides information for the entire primary health care center, and does

not depend upon the willingness of every GP. Third, by being computerized, data losses are not expected in contrast to the case if done manually. Furthermore, the tests and limit values are always the same, those agreed upon primary care physicians and laboratory professionals.

Another fundamental pillar for the successful accomplishment of the alert value reporting process was the interdepartmental collaboration. Sharing knowledge between organizations - clinical laboratory and primary care in this case - is crucial for success. The concept was envisioned from 2 different complementary perspectives and the whole process was discussed and agreed on. The implementation was probably successful since all the parts involved in the process took part in its design.

When implementing new technologies, it is crucial not to abandon the execution of processes contributing to organization value, e.g. the daily GP's habit of checking manually each paper laboratory report, to look for tests results that advised a prompt appointment. Conversely, those habits must be maintained and improved by the automation generated by the new technology. Over the years, technological advances have also increased laboratory requests. It has been shown that 37% of laboratory errors in primary care setting occur because an incorrect interpretation of diagnostic test. Reported results have become so numerous that, on occasion, the tests results that provide clinical value may remain hidden by others that do not add any value. As early as 1974, was referred that there is a danger that important findings will be overlooked in the mass of other data which

may prove to be not significant. Millions of orphaned data can be misinterpreted by non-experts in laboratory testing, or may be overlooked when delivered with a huge amount of clinically unimportant data. Therefore, contrary to expectations, the value of laboratory services seems to diminish as test volumes increase. Analytical results may be ignored even more in primary care setting where workload is considerable and very little time is available to attend each patient. Furthermore, primary care is the first step in the health care process, and special attention must be paid to "catch" the pathological values and therefore detect the illness in this first health care step.

Nowadays, the majority of laboratory errors occur in pre-analytical, test requesting, post-analytical and laboratory report interpretation stages i.e. the phases occurring outside the laboratory walls. Various studies demonstrate that inappropriate test requesting and incorrect interpretation account for a large percentage of total errors. Interest in the identification of post-analytic errors related to laboratory report interpretation, physician's reactions, and the actions taken for the patient have increased. Therefore, greater efforts should be made to facilitate the review, interpretation and utilization of test results to improve clinical effectiveness and to provide the best outcome for patients. Improving the post-analytical phase is a task for laboratory professionals as test experts they are, and strategies must be established, agreed upon with the requesting physicians for a correct laboratory report interpretation as this study refers to in alert value reporting. A limitation of the study could be that the tests and alert values were chosen by GPs "expert opinion" probably affected for local influences. Test list

was chosen in a consensual manner but there is not evidence supporting that this test list and the alert values would be helpful in any setting. Another limitation of the study could be that physicians may fail to look at the results and patient as a whole, only responding to flagged values, causing them to miss results that are suggestive of disease in combination. However alert value reporting search and visualization is an additional procedure done before patient is medically attended. Although, alert value reporting is helpful, it does not replace the need to careful and timely (daily) review patient results, during the patient consultation. Another limitation of the study could be that the prospective study was conducted in only 1 primary care center, not all 10 locations. Although it is supposed to have a similar patient case mix, we don't know how this center compare or differ with other locations. However, the major limitation of our work is the absence of any documentation that the new system led to any actual improvement in patient well-being. In any case, the strategy of alert value reporting should encourage other laboratories to adopt its alert value procedure considering their own individual population.

5.2. Discusión del segundo artículo en que se basa esta Tesis Doctoral

Salinas M, López-Garrigós M, Gutiérrez M, Lugo J, Flors L, Leiva-Salinas C. Should we customize critical value procedure according to patient origin and laboratory turnaround time? J Clin Pathol. 2013;66:269-72.

The results show a different critical value reporting behaviour when laboratory tests are requested in a stat or routine manner. The number of notifications for stat laboratory was lower than for routine laboratory; despite the fact that we are dealing with acutely and severely ill patients. In stat laboratory, the number of critical value that would have been reported if using the routine "short list" critical value is approximately four times higher when compared to the number that were indeed reported. Therefore, if we had used the "short list" in the stat laboratory we would have notified too many expected critical values, creating false alarms to the requesting physicians.

The vast majority of the inpatients had a previous laboratory result. Only 37.9% of the inpatients critical values flagged by the "short list" were indeed "unexpected". If there had been no participation of the pathologist, we would have created a significant number of "expected" reports that would have raised a high rate of false alarms. This situation could render our critical value procedure less reliable and less valuable over time. That could be easily solved if our LIS would

allow classifying abnormal results as expected/unexpected, depending on last test values, to avoid calling out expected abnormal results. However, this is not possible with our current LIS.

There are two important differences between stat and routine laboratory: the stat test definition as "those test whose results can imply an immediate change of patient treatment", and the response time. There is an additional third difference; for stat, the requesting clinician is aware that there are high chances to expect a pathologic result, therefore he will quickly visualize the laboratory report and, therefore, virtually no unexpected results are likely.

Every population is different and, probably, the test list and the reporting procedure should be also different. In this scenario it is almost impossible to cover every patient life-threatening clinical situation with a single universal list of laboratory clinical values. As treatments are becoming more and more aggressive, and clinical scenarios are becoming extremely varied, it necessary to trust the pathologist knowledge to take the right critical value reporting decision according to the specific individual clinical context rather than a rigid list. It is of key importance that pathologists evaluate every test result to identify those that can be of a critical value. Doing so, we will meet clinical needs without increasing the risk of information overload (avoiding false positive critical values) and we will also pick up those test results that can sporadically be critical depending on the context they have been requested for.

Our experience indicates that routine laboratory critical values procedure facilitates the systematic communication of only a small number of broad-ranging analytes to the requesting physician. Clinical needs can be met without an increased risk of information overload. As with any other situation, the pathologist will transform laboratory data in laboratory knowledge in order to get the best clinical decision making.

Conclusiones

7. CONCLUSIONES

We have introduced the concept of alert value reporting and proposed a notification procedure designed to improve patient care. Laboratory report interpretation is central to clinical efficiency and effectiveness. By addressing this particular issue, we could greatly enhance patient safety and clinical decision-making, as 19.5% of cases, motivated an anticipation of the patient next appointment. According to physician´s satisfaction, 90% of GPs considered alert value reporting as an interesting strategy to be continued. Further studies are needed to test this hypothesis.

By taking part in the critical value notification, the pathologist can add value to patient management and decision making. It is an important procedure to communicate unexpected and life threatening laboratory results. In stat laboratory, there were 141 inpatients with unexpected results (37.9%). This study shows a different critical value reporting behaviour in routine and stat laboratory and gives some insight about the fact that - in some situations - rather than using a rigid list of laboratory values, customizing the critical value notification by taking into account the requester and patient characteristics seems a better way to improve decision making and system efficiency. In any case, this is a preliminary work, more evidence is needed to confirm the hypothesis that individualisation of call out is preferable. Further prospective studies comparing both approaches will be needed to confirm this initial consideration.

In the meantime, don’t cry wolf. Reporting only really unexpected and life threatening laboratory tests through an individual custom-made critical value reporting procedure will avoid raising false alarms.

Resumen en castellano

8. RESUMEN EN CASTELLANO

Creamos el concepto de valor de alerta en atención primaria como aquel resultado de una prueba de laboratorio que aconseja un adelanto en la consulta del paciente, para mejorar su atención médica y por tanto su seguridad. El personal del laboratorio y los médicos de Atención Primaria decidieron de forma consensuada que pruebas y que rangos se debían incluir. A continuación se diseñó un procedimiento basado en una consulta informática automática vía web, que se utiliza a diario en cada centro de salud. Un programa busca los valores de alerta del día y los muestra a diario a través de una página web. Dichos informes se imprimen y se depositan en el casillero personal del médico solicitante que es el que decide, en vista de los resultados y la historia previa del paciente, si es conveniente adelantar su próxima consulta. Para comprobar la utilidad de dicha estrategia, se realizó un estudio prospectivo durante seis meses en un centro de salud. De las 4309 solicitudes recibidas se encontraron 154 valores de alerta (3.5%) y 30 de ellos (19.5%) motivaron una adelanto en la consulta del paciente. Una encuesta de satisfacción entregada a los médicos de dicho centro mostro que estaban muy interesados en que la estrategia continuara.

En cuanto al resultado crítico, aquel que indica que puede estar en juego la vida del paciente, se abogó por que fuera "customizado" de acuerdo a la situación clínica del paciente pero también el entorno en el que se presenta. Basándonos en una "lista corta" de pruebas con sus valores límite se observó que el número de

resultados críticos informados en un paciente programado fue siempre superior a la automáticamente generada haciendo uso de dicha "lista corta" por considerar en el laboratorio la existencia de otros adicionales, dependiendo de la particular situación clínica del paciente. Sin embargo en los pacientes atendidos en urgencias, aplicando dicha "lista corta" teóricamente se hubieran informado 627 resultados críticos, y sin embargo solo se notificaron 141 ya que, tras comparación con el previo, solo estos eran inesperados.

Tanto el concepto de valor de alerta como el resultado crítico personalizado, han sido diseñados y establecidos con éxito. En la actualidad el informe automático del valor de alerta permite al médico de atención primaria conocer si las pruebas procesadas el día previo muestran algún valor de interés al que dedicar una atención especial y, en consecuencia, si fuera necesario, adelantar la consulta del paciente para mejorar su diagnóstico y tratamiento.

En cuanto al informe del resultado crítico, el comportamiento en el laboratorio es totalmente distinto si la solicitud es programada o urgente. El número de notificaciones fue inferior desde el laboratorio de urgencias a pesar de estar atendiendo a pacientes con patologías más agudas y potencialmente graves. Si desde el laboratorio de urgencias se hubieran notificado de una forma similar al programado, se hubieran informado cuatro veces más, se habrían notificado como resultados críticos muchos valores esperados que hubieran creado una falsa alarma en los médicos que solicitaron la exploración analítica.

Se ha creado, diseñado y establecido el concepto y la estrategia de notificación de valor de alerta en Atención Primaria y de notificación de resultado critico de acuerdo al criterio del laboratorio en función de las características del paciente, y no solo haciendo uso de listas rígidas de pruebas y valores. Ambos procedimientos mejoraran la interpretación del informe de laboratorio que es fundamental para la eficiencia y la efectividad clínica y en consecuencia también para la mejora del manejo del paciente y la decisión clínica.

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ANEXOS

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ANEXO I: CONJUNTO DE PUBLICACIONES EN LAS QUE SE BASA LA PRESENTE TESIS DOCTORAL

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Alert value reporting: A new strategy for patient safety

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ABSTRACT

Objectives: The objectives of this study are to introduce the "alert value reporting" concept in primary care setting, to propose a list of chemistry and hematology alert limit tests that can be chosen for that strategy, to show how this notification procedure can be designed and established, and finally to evaluate the effectiveness and physicians' satisfaction regarding the proposed approach. In contrast to critical value reporting, alert value reporting would not allude to a result that may imply a life-threatening situation, but would indicate that an early diagnostic/therapeutic action would improve the patient's management and quality of life.

Design and methods: A list of chemistry and hematology alert limit tests to be used for the strategy was agreed upon between laboratory professionals and general practitioners. Next, a retrospective 12-month study involving more than 1 million laboratory tests was made to check how many of these alert values would have been communicated if these theoretical alert values had been applied. A prospective analysis of every reported alert value during 6 months was carried out to assess the intervention effectiveness and the requesting physician's satisfaction with the new strategy.

Results: The alert value reporting was successfully executed. 20% of the reported alert values motivated the decision to reschedule the next patient's appointment. 90% of physicians considered alert value reporting as an interesting strategy to be continued.

Conclusions: Alert value reporting strategy motivated changes in patient's management. Further studies are needed to test if this approach can contribute to enhance patient safety and decision-making.

Introduction

The concept of critical value refers to a result that may imply a life-threatening situation for a patient unless appropriate therapy is initiated [1]. Every laboratory should have at its disposal a procedure for the notification of critical results. This should include a list of critical limits, either from the literature or reached by consensus with clinicians, and should be evaluated periodically [2,3]. The usefulness and implementation of critical value reporting is well established [4]. In fact, it is a requirement of quality assurance agencies [5,6].

In contrast to critical value reporting [7,8], alert value reporting concept has not been described in the literature. This term would not allude to a result that may imply a life-threatening situation for a patient, but would rather indicate that an early diagnostic or therapeutic action would greatly improve the patient's quality of life through earlier detection or treatment establishment.

At present, most laboratories receive samples from a variety of clinical settings. As a consequence, it is very difficult to apply universal critical value list for the different types of patients, the distinct laboratory organizations, and the various requesting centers. It seems appropriate to customize the list, as well as the notification procedure, to the type of patient, to the type of laboratory and to the requester [9,10]. The same consideration is likely to be expected with alert value reporting.

Alert value reporting could be crucial in primary care. General practitioners (GPs) increasingly monitor specific pathologies traditionally treated by specialists. In this scenario, more unexpected results that require prompt therapeutic actions are likely to be generated. Furthermore, frequently, patients do not immediately return for the follow-up doctor's appointment after the analysis. Many analytical results may, therefore, be ignored until the next consultation, regardless of how quickly they are generated. In these cases, the promptness of the alert value reporting may be fundamental. In addition, new information

Abbreviations: GPs, general practitioners; LIS, laboratory information system; ALT, alanine aminotransferase; TG, triglycerides; TSH, thyrotropin; CEA, carcinoembryonic antigen; CA, carbohydrate antigen; PSA, prostate specific antigen; CK, creatine kinase.

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systems can automate and systematize the daily alert values search, providing a new laboratory service to the primary care physician and patient.

In our specific situation, a change in the primary care laboratory reporting process (electronic reports were directly pushed into the electronic medical record, instead of being printed and sent to the primary care centers) changed the GPs habit to review the printed reports that were sent daily, in order to look for test results that might effect when the next patient appointment is scheduled.

The purposes of this study were: first, to introduce the new "alert value reporting" concept in primary care setting; second, to describe the chemistry and hematology alert parameters and their corresponding threshold values that were chosen for that strategy; and third, to show how alert value notification procedure was designed and established, and agreed upon between primary care physicians and clinical laboratory professionals. Finally, we prospectively evaluated the effectiveness and assessed the physicians' satisfaction with such an intervention.

Material and methods

Setting

The laboratory is located at the University Hospital of San Juan (Alicante, Spain), a 370-bed suburban community hospital that serves a population of 234551 inhabitants including 10 different primary care centers (with a total 115 GPs). It receives samples from inpatients, outpatients and primary care patients. In 2010, and 2011, 87252 and 91603 requests were received from primary care during which 1097668 and 1192735 tests were carried out, respectively.

Description of service

Traditionally, blood samples were transported by couriers from the different primary care centers to our laboratory. Printed laboratory reports were generated and delivered.

From December 2010, laboratory requests were made online and the reports sent out electronically from the laboratory information system (LIS) to the patient's electronic medical record. This change altered the GPs daily habit of manually checking each laboratory report in order to look for test results that might necessitate a re-appointment.

This change did not affect our critical value notification procedure, which still includes a "short list" of six test values that are automatically called out [10].

Strategy

To address this potentially problematic situation, the laboratory professionals devised a method that would automatically alert the GP to a result that needed a follow-up and alert value reporting concept was established.

In a first stage, 3 meetings were held between the laboratory professionals in order to establish the different alert value tests and limits, and their appropriate notification procedure. The selection of the alert values was based on expert opinion. Initially, a consensus was reached on a potential list of alert values, i.e. which tests should be included, and which limits should be applied. Next, a retrospective 12-month study was made in the LIS to check how many of these alert values would have been communicated in 2010 if this theoretical alert value list and limit values had been applied. Thereafter, a meeting was held between the laboratory staff and the GPs' coordinators of primary care centers to inform them about the proposed alert value list and limits, and to comment about the number of notifications that would have been reported using values reported in the previous year. Following discussion and adjustment, definitive alert value list and limits were established and application software for electronic notification was designed and tested. The application software for electronic notification was based on a real time consultation of verified patient's test results. The LIS (Omega 3000 3.3, Roche Diagnostics, Spain) works with CACHE2007, a post relational database that allows access to LIS in a friendly environment. The information generated by CACHE2007 is based in HTML and JavaScript.

To assess the intervention effectiveness, we carried out a prospective analysis of every reported alert value during a 6 month period (from July 1st to December 31st 2011) in a single primary care center (with 13 GPs serving 23557 inhabitants), through the review of the patients' medical records. The center was selected as it was the closest to the hospital. To study the requesting physician's satisfaction with the new strategy, we sent a survey including a single question about the interest to continue with alert value reporting strategy (yes/no) to the 10 physicians that were practicing at the mentioned facility at the time of the study.

Results

The definitive list of alert values and limits that were decided in consensus between the laboratory staff and the GPs is shown in Table 1.

This table also displays the number of tests requested in 2010 and the total of alert values that would have been communicated. In all, 3490 notifications would have taken place in 2010, entailing 4% of the total requests from primary care centers.

Fig. 1 summarizes the procedure that was established at the different primary care centers to perform the alert value reporting intervention.

It is based on a web site LIS informatics consulting. Users access the web site where current date and primary care center name are requested. Once the web has searched the alert values of the day it finally shows these values in another web. The administrative assistants of the different primary care centers consult that web site, print the result, and classify them in the respective requesting physician's pigeonholes. Laboratory reports are printed and placed in the individual requesting physician's message box. Alert reports are printed because, at present, they cannot be distributed electronically to the GP. It is the GP, who by reviewing the report, will decide upon the advisability of rescheduling the patient's appointment.

Regarding the 6 month period prospective analysis in a single primary care center, 4309 requests were received. Among those, there were 154 alert values (3.5%). 30 of them (19.5%) motivated an anticipation of the patient's next appointment. Of the 30 values that encouraged the anticipation of the visit, 7 were related to alanine aminotransferase (ALT), 4 to hemoglobin, 3 to creatinine, potassium and triglycerides (TG), 2 to thyrotropin (TSH) and carcinoembryonic antigen (CEA) and one case related to prostate specific antigen (PSA), glucose, carbohydrate antigen (CA)-125, creatine kinase (CK), CA-19-9 and lipase. For the remaining 124 alert values (80.5%), the GPs did not consider it necessary to bring forward the next patient visit, either because the result was expected, or because the next appointment was early enough. Considering the limitation of the satisfaction survey due to the fact that a single question was asked to just 10 GPs, 90% of physicians considered alert value reporting as an interesting strategy to be continued.

Discussion

The alert value reporting concept was successfully executed. It is now fully established as a process carried out automatically and systematically at every primary health care center, on a daily basis. At present, alert value reporting allows GPs to acknowledge if tests processed the day before hold any value of interest to which special attention should be paid. As a consequence, if necessary, patient

Table 1
Test list and limits of alert values established for primary care patients, total number of tests requested in 2010 and total of alert values that would have been communicated.

Test	Unit (SI)	Low alert limit	High alert limit	Number of tests performed	Number of tests with alert result
Alanine aminotransferase	U/L		100	68053	360
Amylase	U/L		200	1356	2
Bilirubin, total	mg/dL (μmol/L)		3 (51.3)	20737	25
CA[a]-125 antigen	U/mL (kU/L)		70 (70)	950	4
CA[a]-19-9 antigen	U/mL (kU/L)		80 (80)	1204	43
Calcium	mg/dL (mmol/L)		11 (2.7)	11822	14
Carcinoembryonic antigen	ng/mL (μg/L)		5 (5)	1186	171
Cholesterol	mg/dL (mmol/L)		400 (10.3)	66056	21
Creatine kinase	U/L		400	4835	52
Creatinine	mg/dL (μmol/L)		2 (176.8)	66538	229
Feces occult blood			Positive	761	20
GFR estimate (MDRD[b]-4)	mL/min/1.73 m^2	40		5376	191
Glucose	mg/dL (mmol/L)		300 (16.7)	69316	100
HAV[c] IgM antibodies			Positive	539	2
HBV[d] IgM antibodies			Positive	88	2
Hemoglobin	g/dL (g/L)	8 (80)		70850	112
Lipase	U/L		200	96	1
Potassium	mEq/L (mmol/L)	3 (3)	6 (6)	34370	190
Prostate specific antigen	ng/mL (μg/L)		6 (6)	11048	425
Protein, total	g/dL (g/L)	3 (30)	9 (90)	2269	34
Sodium	mEq/L (mmol/L)	125 (125)	150 (150)	33345	71
Thyrotropin	μU/mL (mU/L)	0.35 (0.35)	10 (10)	26146	1026
Triglycerides	mg/dL (mmol/L)		1000 (11.3)	65947	49
Urea	mg/dL (mmol/L)		80 (28.6)	15368	221
Uric acid	mg/dL (μmol/L)		10 (594.6)	65555	124
TOTAL				643811	3490

[a] CA: Carbohydrate antigen.
[b] MDRD: Modification of Diet in Renal Disease equation.
[c] HAV: Hepatitis A virus.
[d] HBV: Hepatitis B virus.

appointments can be anticipated and further diagnostic or therapeutic actions can be quickly performed.

The implementation of the electronic-based laboratory request and report system was crucial to this achievement. Unlike the manual daily visualization of the pile of delivered paper reports, the electronic search is a faster and more efficient process. However, looking into the electronic medical record for laboratory reports for every patient phlebotomized the previous day would have been too cumbersome. The proposed alert value notification procedure holds various advantages. First, it is carried out automatically for every laboratory report. Second, it provides information for the entire primary health care center, and does not depend upon the willingness of every GP. Third, by being computerized, data losses are not expected in contrast to the case if done manually. Furthermore, the tests and limit values are always the same, those agreed upon between primary care physicians and laboratory professionals.

Another fundamental pillar for the successful accomplishment of the alert value reporting process was the interdepartmental collaboration. Sharing knowledge between organizations – clinical laboratory and primary care in this case – is crucial for success. The concept was envisioned from 2 different complementary perspectives and the whole process was discussed and agreed on. The implementation was probably successful since all the parts involved in the process took part in its design.

When implementing new technologies, it is crucial not to abandon the execution of processes contributing to organization value, e.g. the daily GP's habit of checking manually each paper laboratory report, to look for test results that advised a prompt appointment. Conversely, those habits must be maintained and improved by the automation generated by the new technology. Over the years, technological advances have also increased laboratory requests [11]. It has been shown that 37% of laboratory errors in primary care setting occur because of an incorrect interpretation of diagnostic tests [12]. Reported results have become so numerous that, on occasion, the test results that provide clinical value may remain hidden by others that do not add any value. As early as 1974, it was referred that there is a danger that important findings will be overlooked in the mass of other data which may prove to be not significant [13,14]. Millions of orphaned data can be misinterpreted by non-experts in laboratory testing, or may be overlooked when delivered with a huge amount of not clinically significant data [15]. Therefore, contrary to expectations, the value of laboratory services seems to diminish as test volumes increase [16]. Analytical results may be ignored even more in primary care setting where workload is considerable and very little time is available to attend each patient. Furthermore, primary care is the first step in the health care process, and special attention must be paid to "catch" the pathological values and therefore detect the illness in this first health care step.

Nowadays, the majority of laboratory errors occur in pre-analytical, test requesting, post-analytical and laboratory report interpretation stages [17–19] i.e. the phases occurring outside the laboratory walls. Various studies demonstrate that inappropriate test requesting and incorrect interpretation account for a large percentage of total errors [20]. Interest in the identification of post-analytic errors related to laboratory report interpretation [21], physician's reactions, and the actions taken for the patient has increased. Therefore, greater efforts should be made to facilitate the review, interpretation and utilization of test results [22] to improve clinical effectiveness and to provide the best outcome for patients [23]. Improving the post-analytical phase is a task for laboratory professionals [19] as test experts they are, and strategies must be established, agreed upon with the requesting physicians for a correct laboratory report interpretation as this study refers to in alert value reporting.

A potential limitation of our approach could be that physicians may fail to look at the results and the patient as a whole, only responding to flagged values, causing them to miss results that are suggestive of disease in combination. However alert value reporting search and visualization is an additional procedure done before a

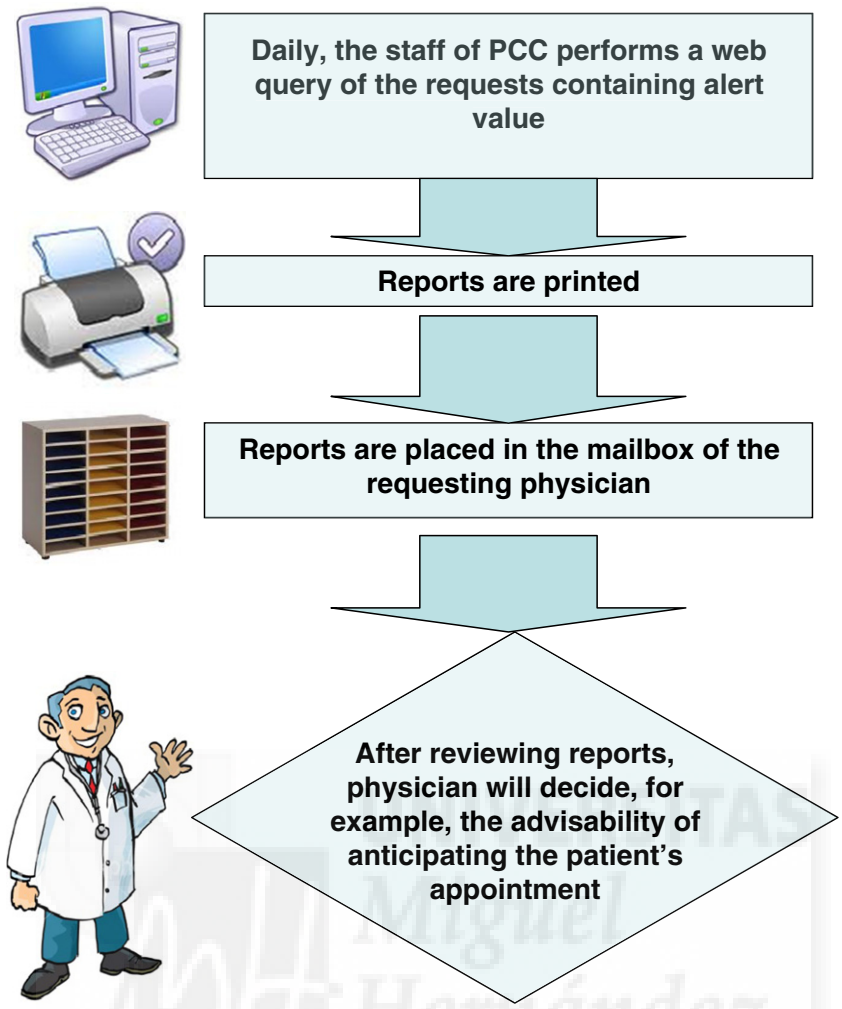

Fig. 1. The figure shows the procedure established at the different primary care centers to perform the alert value reporting intervention.

patient is medically attended. Although, alert value reporting may be helpful, it does not replace the need to carefully and timely review patient results.

One limitation of our study is that the tests and alert values were chosen by the GPs "expert opinion" and the selection was probably affected by local influences. The test list was chosen in a consensual manner but there is no evidence supporting that it would be helpful in any setting. Another limitation could be that the prospective study was conducted in only 1 primary care center, not all the 10 locations. Although it is supposed to have a similar patient case mix, we cannot ascertain how this center compares to the others.

Furthermore, the major limitation of our work is the absence of any documentation that the new system led to any actual improvement in the patient care. In any case, the strategy of alert value reporting may encourage other laboratories to adopt its alert value procedure considering their own individual characteristics.

Conclusions

As a summary, we have introduced the concept of alert value reporting and proposed a notification procedure designed to improve patient care. Laboratory report interpretation is central to clinical efficiency and effectiveness. By addressing this particular issue, we could greatly enhance patient safety and clinical decision-making. Further studies are needed to test this hypothesis.

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Should we customise critical value procedure according to patient origin and laboratory turnaround time?

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ABSTRACT

Introduction Our routine laboratory critical value notification procedure is based on a short list of six fundamental critical values. The report system for our Stat laboratory is not based on this 'short list'; instead, critical values are always reported according to the patient clinical context and the previous laboratory results. The aim of our work is to show how a critical value notification procedure based on a rigid list of values and thresholds can result in completely different results depending on whether the tests are requested in a stat or a routine manner.

Material and methods We reviewed the number of critical value notifications based on the short list for the routine laboratory. For the stat laboratory, we studied the number of real notifications based on the pathologist validation of the individualised situation of the patient and calculated the number of notifications that would have been reported if the routine short list would have been used instead.

Results The number of critical values that would have been reported if using the routine short list in stat laboratory was high when compared with the number of critical values that were really reported.

Conclusions Using a rigid list of laboratory values to notify critical values resulted in completely different results depending on whether the tests were requested in stat or routine. Reporting only really unexpected values through an individual custom-made reporting procedure may avoid the wasting of time and resources and raising false alarms among referring physicians and patients.

INTRODUCTION

Laboratory critical values are those values that identify life threatening conditions requiring prompt medical intervention.[1] The concept has evolved over the years[2 3] and nowadays accreditation agencies—the most widely accepted standard is ISO EN 15189:2007—define and require clinical laboratories to list critical limits, formulate notification procedures and document critical results.[4] Most laboratories attend to a wide variety of patients (inpatients, primary care, emergency outpatients, etc) and laboratory results that may be critical for some patients may be rather 'normal' for others (eg, intensive care unit (ICU), dialysis, oncology). Furthermore, the improvement in technology and laboratory processes makes possible to produce very short laboratory response times;[5] very often, it is possible for the requesting physician to check for results electronically immediately after they have been verified by the pathologist, when the patient may still be 'at hand'. In this scenario, it is becoming increasingly difficult to establish a single critical value list to be used in the different situations that occur daily in a clinical laboratory.[6–9] It seems more appropriate to adapt the test list and thresholds, as well as the notification procedure, to the type of patient, the laboratory response time and to the requester, in the interest of efficiency.[2] Instead of taking into account just the result value, it seems more sensible to also consider other information such as the change in the current test result from previous results, the patient´s characteristics and the ordering provider.

The aim of our study is to show how a critical value reporting system using a single list of values and thresholds can result in completely different results depending on whether the laboratory tests are requested in a stat or routine manner, and to describe a flexible notification system, adapted to the requester and patient clinical situation, which may take into account the variability of the patient population and may overcome this limitation.

MATERIAL AND METHODS

The laboratory is located at the University Hospital of San Juan (Alicante, Spain), a 370-bed suburban community hospital that serves a population of 234 551 inhabitants. It is certified to ISO 9001 standard since 2004.

The central laboratory is divided into two laboratories: a 'Routine' laboratory and a Stat laboratory. The routine laboratory processes samples for the hospital outpatients and inpatients and for the patients from the different primary care centres who depend on our hospital. The stat laboratory is an independent laboratory that processes requests for inpatients and the hospital emergency department (ED). The rationale behind the stat laboratory is to offer very short turnaround times (TATs). The reports for the inpatients are consulted via intranet except for the ICU, Oncology Unit and the ED, where the reports are automatically printed locally as soon as they are verified by the pathologist. The stat laboratory is staffed by three technicians. As soon as the results are available, they are verified by a pathologist. The number of requests and tests that were processed by the routine and stat laboratories from 2003 to 2011 are shown in table 1.

In 2003, our laboratory devised a very simple routine critical value procedure in consensus with the clinicians, according to the published evidence,[10] to report only those critical values that are

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Table 1 Number of laboratory requests and tests ordered in routine and stat laboratories from the year 2003 to 2011

	2003	2004	2005	2006	2007	2008	2009	2010	2011
Routine laboratory									
Requests	141 217	153 890	155 145	165 064	171 635	174 052	159 089	151 523	155 381
Tests	1 552 534	1 696 619	1 733 312	1 851 537	1 951 434	2 033 218	2 025 598	2 034 732	2 042 546
Stat laboratory									
Requests	60 055	61 304	65 326	66 351	71 678	76 706	76 231	75 433	72 311
Tests	353 339	375 939	405 424	426 434	497 930	557 841	620 511	652 458	630 158

really life threatening for the patient if an immediate therapeutic decision is not taken. Our routine laboratory critical value notification procedure includes a 'short list' of six tests values. The laboratory director and the chairpersons from the Departments of Cardiology, Rheumatology, Endocrinology and Haematology defined these values in consensus. They were selected to provide an expert opinion about which abnormal values of the laboratory tests related to their specialty should motivate an immediate treatment/action due to a threatening danger to a patient's life. Table 2 shows the list of tests.

The laboratory uses a module in our laboratory information system (LIS) that automatically marks every critical result. Those results are automatically flagged and reviewed by a pathologist who will decide on the need to call the requesting physician.

The rationale behind this approach—the intervention of the pathologist—was to avoid redundant data and the risk for information overload. Instead, the laboratory professional evaluates the results and the previous laboratory data in order to identify other potentially clinically relevant critical values. Since our stat laboratory report is available and printed in the ED, ICU and oncology unit in less than 30 min from pneumatic tube laboratory sample arrival,[11] stat laboratory does not use the routine short list of values to report critical values. Conversely, when validating the inpatients requested tests, the pathologist reports a critical value based on the previous laboratory results and on the patient's individual medical situation.

For the routine laboratory, we reviewed the number of notifications that were reported annually during the 9 years of our programme, and calculated the number of notifications that would have been reported based only on the short list, if nor pathologist intervention would have occurred. For the stat laboratory, we studied the number of real notifications based on the pathologist criteria and calculated the number of notifications that would have been reported if the routine short list would have been used instead. The critical values from the stat Laboratory for year 2011 were analysed according to the type of patient (ED patients or inpatients). The TAT for each group was calculated and compared using the Mann–Whitney test. TAT was defined as the time interval between test registration and test validation.

Table 2 The 'short list' of laboratory critical values

Test	Critical value
Glucose	<1.9 or >30.6 mmol/l <35 or >550 mg/dl
Sodium	<115 or >158 mmol/l
Potassium	<2 or >7 mmol/l
Calcium	<1.5 or >3.2 mmol/l <6 or >13 mg/dl
Haemoglobin	<50 g/l <5 g/dl
Platelets	<10 000/mm^3

For analysis purposes, we further classified the critical value for the inpatients as 'expected', if the new critical value was in agreement with previous laboratory results, or as 'unexpected', if there were no previous results or the new value was not coherent with the previous one. We calculated and compared TAT for both expected and unexpected results, using the Mann–Whitney test.

RESULTS

The number of routine laboratory notifications based on this short list and the final real number of critical value notifications that were performed annually since year 2003 are shown in table 3. The number of reported critical values was always larger than the one automatically generated by the short list, since the pathologist usually consider some others, depending on the particular patient situation.

Table 4 shows the number of routine calls for the main individual analytes. Other routine analytes that were prone to be reported as critical were: alanine aminotransferase, carcinoembryonic antigen, oestradiol, leukocytes, lipase, lithium, magnesium, phosphate, thyrotropin, triglycerides, urate, urinary catecholamines, as well as qualitative results reporting the existence of immature leukocytes with leukaemic expression.

Of all routine reported critical values in 2011, 44 (20.5%) were found in primary care and 170 (79.5%) in hospital patients. Of the ones found in the hospital, 137 (80.5%) were reported to inpatients and 33 (19.5%) to outpatients; 25% were reported to Internal Medicine, 9% to Nephrology and 6% to Oncology. Routine critical values reported to ICU, Haematology, Cardiology, Gastroenterology and Infectious Diseases were around 5%. Less than 5% of the critical values were reported to other departments such as Gynaecology, Paediatrics, Endocrinology, Pulmonology, Urology and Orthopaedic Surgery.

Table 3 also shows the number of notifications that were made in stat laboratory and the number of notifications that would have been reported if the routine short list had been used. Figure 1 shows the 'breakdown' of the 627 critical values that would have been reported if the short list would have been used in year 2011 in stat laboratory. There were 141 inpatients with unexpected results (37.9%) (120 with a previous result not coherent with the previous one and 21 without previous results).

The median TAT for ED patients was 26 min; the median TAT for inpatients was 30 min. The TAT for ED patients was significantly shorter that the TAT for inpatients ($p<0.01$). The median TAT for inpatients with expected results was 29 min, and the median TAT for inpatients with unexpected results was

Table 3 Number of routine laboratory notifications based on this 'short list' and the final real number of critical value notifications that were performed annually

	2003	2004	2005	2006	2007	2008	2009	2010	2011
Routine laboratory									
Reported 'short list' critical value	142	131	174	176	201	203	154	154	149
Total reported critical value	211	237	181	227	222	230	249	288	214
Stat laboratory									
Theoretically 'short list' critical value	587	467	535	540	649	679	596	637	627
Reported critical value	154	140	139	152	154	153	156	159	146

31 min. The TAT for both groups was not statistically significant (p=0.532).

DISCUSSION

The results show a different critical value reporting behaviour when laboratory tests are requested in a stat or routine manner. The number of notifications for stat laboratory was lower than for routine laboratory despite the fact that we are dealing with acutely and severely ill patients. In stat laboratory, the number of critical values that would have been reported if using the routine short list critical value is approximately four times higher when compared with the number that were indeed reported. Therefore, if we had used the short list in the stat laboratory we would have notified too many expected critical values, creating false alarms to the requesting physicians.

The most common abnormalities flagged in the routine laboratory, as shown in table 4, were tests related to water–electrolyte imbalance, hypernatraemia and hyperkalaemia. Those were probably related to hypertonic dehydration. In our region, summers are very hot and hypertonic dehydration is frequently observed, especially in elderly patients. Restoring electrolyte balance in these patients is fundamental to minimise the risk of hypovolaemic shock. The second most frequently flagged abnormality was hypoglycaemia, which is commonly associated with diabetes therapy. The prevalence of type 2 diabetes mellitus in the Autonomous Community of Valencia among adult patients is 13.3%.[12] Immediate treatment of hypoglycaemia is crucial to avoid diabetic coma.

The vast majority of the inpatients had a previous laboratory result. Only 37.9% of the inpatients critical values flagged by the short list were indeed unexpected. If there had been no participation of the pathologist, we would have created a significant number of expected reports that would have raised a high rate of false alarms. This situation could render our critical value procedure less reliable and less valuable over time. That could be easily solved if our LIS would allow classifying abnormal results as expected/unexpected, depending on last test values, to avoid calling out expected abnormal results. However, this is not possible with our current LIS.

There are two important differences between stat and routine laboratories: the stat test definition as 'those test whose results can imply an immediate change of patient treatment' and the response time. There is an additional third difference: for stat, the requesting clinician is aware that there are high chances to expect a pathological result; therefore, he or she will quickly visualise the laboratory report and, therefore, virtually no unexpected results are likely.

Every population is different and, probably, the test list and the reporting procedure should be also different. In this scenario, it is almost impossible to cover every patient life threatening clinical situation with a single universal list of laboratory clinical values. As treatments are becoming more and more aggressive, and clinical scenarios are becoming extremely varied, it necessary to trust the pathologist knowledge to take the right critical value reporting decision according to the specific individual clinical context rather than a rigid list. It is of key importance that pathologists evaluate every test result to identify those that can be of a critical value. Doing so, we will meet clinical needs without increasing the risk of information overload (avoiding false positive critical values) and we will also pick up those test results that can sporadically be critical depending on the context they have been requested for.

Our experience indicates that routine laboratory critical value procedure facilitates the systematic communication of only a small number of broad-ranging analytes to the requesting physician. Clinical needs can be met without an increased risk of information overload. As with any other situation, the pathologist will transform laboratory data in laboratory knowledge in order to get the best clinical decision making.[13]

Table 4 Number of routine calls for every listed individual analyte

	2003	2004	2005	2006	2007	2008	2009	2010	2011
Glucose <1.9 mmol/l (<35 mg/dl)	26	25	34	35	40	38	32	23	27
Glucose >30.6 mmol/l (>550 mg/dl)	10	12	14	12	9	8	9	8	5
Sodium <115 mmol/l	7	4	2	5	10	14	7	2	6
Sodium >158 mmol/l	23	23	28	16	18	18	20	10	29
Potassium <2 mmol/l	1	1	2	4	4	4	2	2	2
Potassium >7 mmol/l	32	28	43	58	55	54	37	30	30
Calcium <1.5 mmol/l (<6 mg/dl)	7	7	17	9	21	18	18	23	17
Calcium >3.2 mmol/l (>13 mg/dl)	6	4	8	5	7	14	7	16	8
Haemoglobin <50 g/l (<5 g/dl)	12	10	10	13	10	15	11	25	11
Platelets <10 000/mm^3	18	17	16	19	27	20	11	15	14

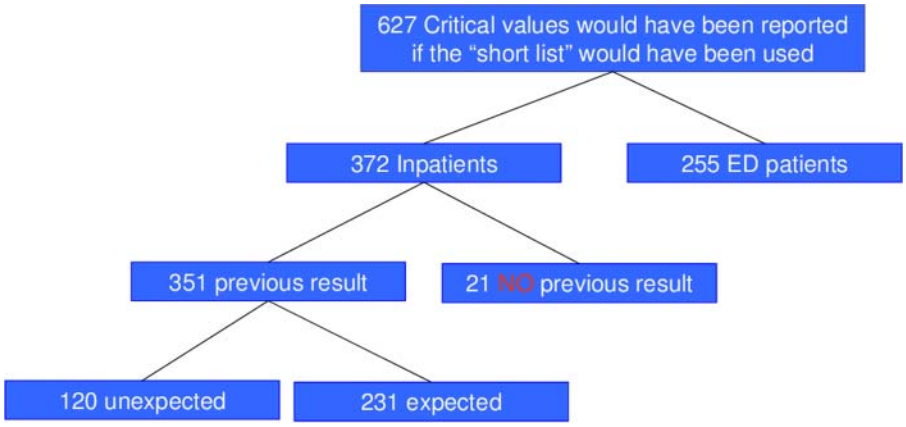

Figure 1 The 'breakdown' of the 627 critical values that would have been reported if the 'short list' would have been used in year 2011 in stat laboratory.

CONCLUSIONS

By taking part in the critical value notification, the pathologist can add value to patient management and decision making. It is an important procedure to communicate unexpected and life threatening laboratory results. This study shows a different critical value reporting behaviour in routine and stat laboratories and gives some insight about the fact that—in some situations—rather than using a rigid list of laboratory values, customising the critical value notification by taking into account the requester and patient characteristics seems a better way to improve decision making and system efficiency. In any case, this is a preliminary work, and more evidence is needed to confirm the hypothesis that individualisation of call out is preferable. Further prospective studies comparing both approaches will be needed to confirm this initial consideration.

In the meantime, do not cry wolf. Reporting only really unexpected and life threatening laboratory tests through an individual custom-made critical value reporting procedure will avoid raising false alarms.

Take-home messages

- Routine laboratory critical value procedure facilitates the systematic communication of only a small number of broad-ranging analytes to the requesting physician.
- Only a small test list critical value results will be automatically reported. Other critical values will be reported according to the medical problem, response time and patient origin.
- Do not cry wolf: reporting only really unexpected and life threatening laboratory tests through an individual custom-made critical value reporting procedure will avoid raising false alarms.

What this paper adds

- Customising critical value report through adaptation to the requester characteristics and patient situation could be a better way to improve system efficiency and, ultimately, decision making.
- Rather than using a rigid list of laboratory values, reporting only really unexpected and life threatening results through an individual custom-made critical value reporting procedure may avoid raising false alarms.

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