Informatics of Newborn Screening for Congenital Hypothyroidism in Alberta 2005-08: Flow of Information From Birth to Treatment

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ABSTRACT

Objectives: Alberta maintains a universal screening program for congenital hypothyroidism, a condition which, when treated promptly prevents neurological impairment. Because the program relies on multiple stakeholders working in different areas, it is not known how effective the overall process is in achieving timely treatment initiation. Our objective was to analyze and describe the informatics of this program.

Methods: Data were collected from the Newborn Metabolic Screening Program and physician offices for hypothyroidism screen positive infants born between January 1, 2005 and May 31, 2008. Where data were available, times were determined for each interval: birth to sample collection, collection to receipt in central laboratory, receipt to report to the primary clinician, report to confirmatory test, and finally confirmation to thyroxine treatment.

Results: Complete information was found on the stages up until report generation. Although subsequent intervals had less complete data, all but 5 of the 57 newborns were followed to the endpoint of treatment initiation or diagnosis exclusion. The program was consistent and efficient in collecting, analyzing and reporting results to the primary physician by a median of 8 days (range 4-14 days). Subsequent steps resulted in a median time from birth to treatment of 11 days. There were 4 cases for which delays in clinician follow-up led to treatment initiation at 27, 34, 56 and 70 days.

Conclusion: Newborn screening for congenital hypothyroidism in Alberta is efficient and consistent up until responsibility shifts to the community. Quality improvement work is needed to reduce potential delays.

Key words: Newborn screening; congenital hypothyroidism; health informatics

La traduction du résumé se trouve à la fin de l'article.

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Congenital hypothyroidism (CH) is the state of inadequate thyroid hormone production in the newborn. Thyroid hormone is critical for central nervous system development.¹ Newborns with CH may demonstrate few findings on initial examination, leading to a falsely reassuring newborn assessment and discharge. Left untreated, a host of features develop including poor growth and developmental delay.²

Approximately 1 in 3-4,000 infants are born with CH.³ Alberta data describe an incidence of 1 in 3,500 live births.⁴

Early initiation of thyroid hormone replacement is essential to achieving normal intellectual outcomes. The European Society for Paediatric Endocrinology, the American Pediatric Society, the American Thyroid Association, and US Preventative Task Force have all published recommendations that treatment should be initiated by 14-15 days of age.⁵⁻⁷

In Alberta, samples are collected by front-line nurses, conveyed first to local laboratories and then shipped to the central screening laboratory in Edmonton. Technicians test the samples under the supervision of laboratory scientists and final results are promptly faxed to the primary doctor listed on the screening collection card. Health information analysis is an important part of newborn screening because of the complexity of a system that includes birth registries, systematic sample collection and transport, results sharing and coordination between multiple stakeholders from the bedside nurse to the laboratory staff to the involved physicians, nurses and guardians.

There are no national standards for newborn screening in Canada. Alberta Health and Wellness (AHW) is responsible for the Newborn Metabolic Screening (NMS) Program, setting policies and

standards and providing funding.⁸ Within the program, responsibility is divided among a variety of stakeholders. Individual health zones are responsible for timely collection and transportation of samples to the NMS laboratory (Edmonton). The laboratory is responsible for receiving, analyzing and reporting screen results. Finally, local primary care providers are responsible for acting on the reports.

The objective of this study was to analyze the efficiency and completeness of newborn screening for CH in Alberta.

METHODS

The design was a retrospective description of the flow of information and, ultimately, action towards the goal of timely treatment of CH. Cases were defined as ones in which the infant was born in Alberta between January 1, 2005 and May 31, 2008, and found to have a newborn screening TSH >50 mU/L. A timeframe was selected that was considered recent and practical.

Cases were identified from the NMS database. Data accompanying each child's positive screen included health number, birth date,

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and the name of a responsible physician. The database was queried for dates of sample collection, receipt at NMS laboratory, and report to primary care physician's office.

A master fax-out was sent to each physician listed on the screening card, requesting information on the dates of the confirmatory test and initiation of therapy. In some cases, the physician reported that management was taken over by a specific specialist. In these instances, a fax was sent to the identified specialist.

Notably, this study did not attempt a reconciliation of births with samples. Spady et al. performed such a study in Alberta in 1992 and confirmed that coverage was 98%.⁹ Furthermore, more recent 2002-2005 data confirm that coverage is greater than 99%.⁴

Statistical analysis

Statistical analysis was done using Microsoft Excel and SPSS 14.0 software. The statistical analysis was carried out by calculating median times and interquartile distances for each segment of the screening process.

Ethical considerations

Ethics approvals were obtained from the Universities of Alberta and Calgary. Permission was secured from AHW.

RESULTS

Results of collection effort

Some infants were diagnosed clinically, meaning that data on dates of confirmation and treatment were not indicative of screening informatics. For these patients, only the intervals from birth to generation of confirmatory test reports were analyzed. Similarly, several newborns were found not to have CH, but their data were analyzed up until the time of confirmatory testing. Unfortunately, the receipt of sample date for 10 cases was unavailable at the time of this study. Figure 1 shows the results of the data collection effort.

Initially, 57 newborns were identified from the NMS database. For this case list, all dates of sample collection were found. NMS laboratory records provided dates of sample receipt for 47 cases (82.4%); 55 newborns (96.5%) had complete information on date of report to primary care physician. Involved physicians fax reported that 5 cases were diagnosed and treated early based on clinical features or family history. Excluding these 5 cases, the target case list for the latter two steps in the screening process included 52 infants. Dates of confirmatory tests were found in 48 instances. The fax response rate was 96.5%.

Of the 52 infants, 6 did not have CH and were excluded from the confirmation to treatment analysis. Of the 46 infants identified exclusively by screening and requiring therapy, treatment dates were found for all but 5.

Results for steps from screening to treatment

Birth to Collection

As shown in Figure 2, the median time was 2 days (range 0-7 days) with an interquartile distance of only 1 day, suggesting that this step was carried out consistently.

Collection to Receipt

For the 47 cases with available data, the median time for this interval was 2 days (range 1-8 days). The interquartile distance was small

Figure 1. Results of data collection effort for all CH screen positive Alberta newborns, January 1, 2005 to May 31, 2008

at 1.75 days, suggesting a consistent transportation procedure. The 2 samples that went beyond the threshold set by provincial standards took 7 and 8 days respectively to reach the NMS laboratory.

Receipt to Report

For the 47 cases with dates of receipt *and* report, the median duration was 3 days (range 1-8 days) with an interquartile distance of 4 days.

Birth to Report

Before April 2007, the screening goal was result availability by 13 days of age (maximum 7 working days for collection, 4 for transportation and 2 for laboratory analysis). In April 2007, the screening goal became result availability by 10 days of age. It is helpful to combine the intervals to determine the *birth to report* statistic. For this, the median time was 8 days (range 4-14 days). There was only 1 case, taking 14 days, that exceeded the 13-day threshold. This occurred because of the additive effect of slightly longer transportation and laboratory analysis intervals.

Report to Confirmation

The median time between report and confirmation test was 1 day (range 0-64 days). Consistent with the wide range, the interquartile distance was 5 days, longer than any other step.

Confirmation Test to Treatment Initiation

The median time was 0 days (range 0-42 days) with an interquartile distance of 1 day, suggesting reasonably prompt practice in ini-

Figure 2. Box and whisker plot for time, in days, for each interval in the newborn screening process for CH screen positive Alberta newborns, January 1, 2005 to May 31, 2008

tiating thyroxin replacement. Except for one 42-day measure, the remaining values were all in the range of 0-9 days.

Birth to Treatment in Newborns Identified as a Result of NBS

For the 41 infants with confirmed treatment initiation, the median time from birth to treatment was 11 days (range 5-70 days) with an interquartile distance of 9 days; 9 patients were treated by 21 days, leaving 4 patients who went until 27, 34, 56 and 70 days before treatment initiation. For the latter four cases, the delays all occurred in the final stages, report receipt to confirmation or confirmation to treatment.

None of the authors, all of whom practice out of Alberta's main pediatric tertiary care centres, are aware of any missed cases of CH during the target period.

Other results

In the 3.3-year period analyzed, no non-specialist had more than one patient reported to them. Three pediatricians were the primary care physician for 2-3 cases. CH is an uncommon disorder for any generalist physician to encounter.

DISCUSSION

The results of this analysis of the flow of information and action show mixed success in achieving timely treatment of CH. AHW Standards and Policy articulate that the birth to collection interval should not exceed 7 days.⁸ Our data show that these goals were achieved in 100% of cases, which compares favourably with other reports. Simpson et al. audited the screening program results for the Bath area of England, 1994-1996.¹⁰ Ray et al. conducted a similar audit of Scotland, 1979-93.¹¹ The Bath data showed that 1.2-1.35% of samples were collected past 10 days while the Scottish series found that 10.5% of screens were collected past 10 days.^{10,11}

Prior to 2007, AHW standards for newborn screening stated that the collection to receipt (at the lab) interval should not exceed 4 days; after April 2007, this was changed to 3 days. Our data demonstrated that this was met in 91.5% of cases. In the 4 delayed cases, the longest period was 8 days.

For the interval from sample receipt to report to physician, the median time was 6 days, within which 25% of cases had a laboratory turnaround that exceeded 7 days. This is longer than the AHW goal of 3 days. However, these delays compare favourably given the fact that many of the literature-reported missed CH diagnoses were because of collection or analytic errors. Leger, reviewing 1978-87 data from France, found 27 missed cases due to collection or laboratory processing errors.¹² Holtzmann et al., reporting on the largest series of missed diagnoses, found that 14% were due to collection errors and 45% to laboratory procedure errors.¹³

The greatest variation took place in the steps following report to the physician. While the median time to confirmation was only 1 day, there were 5 instances (10.9%) in which it took two weeks or longer for the confirmation test to be performed. Whereas the scope of this study prevented us from scrutinizing physicians for the causes, one could reasonably attribute them to misfiling, office miscommunication or misunderstanding about the necessity for haste.

While the median 0-day time from confirmation to treatment is reassuring, it makes more striking the three instances in which it took a week or more to act upon the confirmatory test.

Regarding the most important outcome, *the total time from birth to treatment*, the median result of 11 days is well within the 14- to 15-day American and European standard. While 13 cases (31.7%) took more than 15 days to treatment, 9 of these still met the 21-day goal set for the United Kingdom.¹⁴ This left 4 cases (9.8%) that exceeded the 21-day threshold. Grant and Smith, investigating England, Wales and Ireland for the period 1982-84, found a median age of treatment of 17 days.¹⁵ Other median times reported are 18 days (The Netherlands) and 6 days (Finland).^{16,17}

Clearly, median age of treatment does not tell the whole story when there are concerning outliers. Pharoah and Madden reported that 10% of a 1983-89 CH cohort were treated after 21 days.¹⁸ Hopfner and colleagues, reviewing 1988-92 German data, found that 2.3% of patients were treated after 4 weeks of age.¹⁹ Our series included 4 instances in which treatment did not commence until 27, 34, 56 and 70 days, despite the NMS Laboratory having reported to the physician at 6, 7, 12 and 11 days of age, respectively.

Impact of bias

Despite the dependence on questionnaires, the final data were relatively complete. Non-responding physicians may have been reluctant to publicize delayed care, meaning that our results may appear slightly better.

CONCLUSION

This study demonstrates that, while efficiency and consistency were the norm for steps leading up to the NMS report, sporadic delays occurred during clinical follow-up. The flow of information represented a transition from the large, regulated segment of the program to the scattered and heterogeneous domain of physician offices and families. One quality improvement effort, since implemented in Alberta, would be to have a coordinator provide phone support to physicians and monitor each case until a positive screen has resolved in definitive treatment or exclusion. Another approach could be to include supporting information emphasizing the importance of the result and providing detailed steps to follow. While new procedures may be more labour- and cost-intensive, it is important to acknowledge the screening maxim – “if it is important enough to screen for, it is important enough to follow-up”.²⁰

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RÉSUMÉ

Objectifs : L'Alberta administre un programme de dépistage universel de l'hypothyroïdie congénitale, une affection qui peut entraîner des déficiences neurologiques si elle n'est pas traitée promptement. Comme le programme fait appel à de nombreux intervenants qui travaillent dans différents secteurs, on ignore si le processus est efficace, dans l'ensemble, pour amorcer des traitements en temps utile. Nos objectifs étaient d'analyser et de décrire les données informatiques de ce programme.

Méthode : Les données provenaient du programme de dépistage métabolique néonatal de l'Alberta et des rapports des cabinets de médecins sur les nourrissons atteints d'hypothyroïdie nés entre le 1^{er} janvier 2005 et le 31 mai 2008. Lorsqu'il était possible de le faire, nous avons déterminé les dates de chacun des intervalles suivants : de la naissance à la cueillette de l'échantillon; de la cueillette à la réception au laboratoire central; de la réception à la communication du résultat au clinicien de premier recours; de la communication au test confirmatoire; et enfin de la confirmation au traitement par thyroxine.

Résultats : Nos renseignements étaient complets à tous les stades jusqu'à celui de la communication du résultat. Pour les intervalles suivants, nos données étaient moins complètes, mais seuls 5 des 57 nouveau-nés n'ont pas été suivis jusqu'au stade final (amorce du traitement ou diagnostic d'exclusion). Le programme était cohérent et efficace pour ce qui est de la collecte, de l'analyse et de la communication des résultats aux médecins de premier recours en 8 jours environ (valeur médiane), l'intervalle étant de 4 à 14 jours. En incluant toutes les étapes, le temps médian de la naissance au traitement était de 11 jours. Dans quatre cas, des retards dans le suivi par le clinicien ont reporté l'amorce du traitement, qui a eu lieu après 27, 34, 56 et 70 jours, respectivement.

Conclusion : Le dépistage néonatal de l'hypothyroïdie congénitale en Alberta est efficace et cohérent jusqu'au stade où la responsabilité du programme revient à la communauté. Il faudrait apporter des améliorations qualitatives pour réduire les retards possibles.

Mots clés : dépistage néonatal; hypothyroïdie congénitale; informatique médicale