The Digi-NewB project for preterm infant sepsis risk and maturity analysis

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Abstract

It is known from the literature that the careful analysis of the heart rate variability of a preterm infant can be used as a predictor of sepsis. The Digi-NewB project aims at collecting a database of at least 750 preterm infants including physiological signals, video and clinical observations. These data are used to design a decision support system for the early detection of sepsis and for the evaluation of the infant maturity. The preparation of the data for the exploratory analysis has turned out to be time-consuming. 190 infants have been recorded by March 2018 and of these, the R-R interval analysis of the ECG signals has been completed of 136 infants. The results of the project are still preliminary but seven heart rate variability parameters have been found to be different in preterm and full-term infants with a P value less than 0.01. The video analysis algorithm detecting the presence of personnel or relatives reached 96.8% of sensitivity and 95.1% of specificity.

Keywords: decision support system, artificial intelligence, preterm infant, sepsis risk, infant maturity, health informatics

Introduction

Evaluation of the risk of sepsis and evaluation of maturity of the preterm infants are both central in the decision-making in neonatology. One of the most dangerous complications of preterm infants in the neonatal intensive care units (NICUs) is bacterial sepsis. Around 15-25 % of preterm infants hospitalized in NICUs suffer from this complication which can lead to death or significant morbidity. In order to release the infants at the right time from the NICU, it would be important to know if the regulatory systems of the infant are mature enough to survive well outside the NICU.

The infants are being monitored in NICUs with medical devices which record physiological signals but the obtained data are not yet fully exploited. There are reports that the signs of sepsis can be observed from the recorded variables already before the clinical signs of sepsis are recognized [1]. Additionally, the maturity of the infant could be estimated from the recorded physiological signals by comparing their characteristics with a data set of healthy newborns in a known state of maturity.

Artificial intelligence has been recently applied to many fields in the society with great success. Artificial intelligence and expert systems in medicine are not very new; a survey of them was made already in 1988 [2]. However, due to the life-criticality of the field, such systems are not in so wide use as one could expect. Even the recent draft guidance from the FDA in USA suggests that clinical decision support systems which analyze signals from the patients remain to be classified as medical devices, requiring a normal medical device approval process, including validation, before taking into use [3]. Therefore the Digi-NewB approaches the development of such a system for the early sepsis detection and the maturity evaluation with great care.

Starting points and objectives for the project

Sullivan and Fairchild state that the C-reactive protein (CRP) is the most widely used acute phase reactant to indicate sepsis [4] but they comment also that this laboratory value is not always available and it may indicate sepsis too late in some cases. They report that the heart rate characteristics monitoring reduced sepsis-associated mortality in preterm infants by 40% in a randomized clinical trial. They conclude also that adding new vital sign and hemodynamic metrics and integrating laboratory values, biomarkers, and clinical information could lead to even better algorithms for early sepsis detection.

This project aims at designing a clinical decision support system for the early warning of preterm infant sepsis and for the infant maturity estimation. The objective is to improve the state-of-the-art by including more variables to the analysis, adding parameters such as clinical signs, breathing, movements, video etc. to the heart rate variability analysis. The objective of the project is to collect so much patient material that the methods can be clinically validated which supports the commercialization of the system and thus its rapid availability to NICUs all over the world to decrease preterm infant mortality.

Implementation and results

The Digi-NewB project organization consists of a consortium of pediatric clinics, university departments with skills in physiological signal processing, pattern recognition and usability and SMEs with experience in medical device development. The role of the clinics, located in North-Western France, is to use the developed system prototype to collect signal, video and sound information of the preterm infants in the ICUs for the development and validation of the analysis algorithms to be developed in the project. The target number of inclusions is 750 infants. In addition to the measurements, the observations of the nurses are also included as inputs to the system. When the prototype develops further, the clinics will also evaluate its suitability for the purpose and its usability.

The system prototype, developed in Voxygen Health, Rennes, France integrates the collection of physiological signals, video and sound into a single package. The signal and video processing algorithms to be developed in the University of Rennes, University of Porto and Tampere University of Technology convert the input data into calculated features, typically in five minute segments. These features are inputs to a decision support system which predicts the risk of sepsis of the infant. The results are presented in an easily understandable form and it will be possible to obtain more detailed information about the situation by navigating deeper into the user interface.

The approach in developing the decision support system is explorative. This means that a large number of input variables will initially be considered as inputs to the system. Statistical analyses will reveal which input variables have the most significance and the best reliability in predicting sepsis and estimating the maturity of the newborn. Information from the literature, such as the meaning of the baby's cry in assessing maturity [5] will naturally be considered as an input variable but the exploratory study may reveal that some other variables are even more useful.

Although 190 infants have already been recorded, the data set is not yet sufficient to make conclusions about the parameters to choose for the final implementation. It has been noticed that the preparation of the collected data to the format suitable as input to the explorative analysis takes considerable effort. The reason for this is the necessity to guarantee the high quality of the input data so that the decision making modules base their decision on facts and not on artefacts. Effort has been spent to detect the presence of the relatives of the care personnel near the infant because they may introduce artefacts to the input data [6]. Similarly, the quality of the heart rate data needs to be confirmed as the input training material to the exploratory analysis. However, the final system needs to cope with the artefacts automatically because their manual labeling would require an unacceptable amount of work from the personnel.

Once the input data has been cleaned, it is relatively straightforward for the developers to apply different machine learning methods for the data. The experiences from other fields have indicated that these methods can learn patterns which are not recognizable by human experts even after various visualization techniques. The relative performance of the various machine learning algorithms can be compared with receiver operating characteristics (ROC) analysis [7].

Some first results have already been obtained. The video analysis algorithm detecting the presence of personnel or relatives reached 96.8% of sensitivity and 95.1% of specificity [6]. Another infant maturity related study could identify seven heart rate variability parameters which are different in preterm and full-term infants with a P value less than 0.01 [8].

Discussion

Artificial intelligence has potential in detecting sepsis from preterm newborns but these hopes need to be confirmed with a sufficient amount of clinically confirmed sepsis cases and normal controls. Although good initial results have been obtained, it would be too early to publish results of the sepsis detection parameter set, the method and its performance yet. The prediction of the maturity of the infant shows promise at this stage, as well. Here, too, the results are still preliminary.

All the potential variables have not yet been included in the exploratory analysis. When they become available, the order of importance of the variables in predicting sepsis and assessing maturity may change. The inclusion of more variables may also make the analysis method more robust in case a part of the variables is not available all the time.

Our initial results, which still need confirmation with a larger data set, suggest that it is possible to predict sepsis from the data earlier than medication had been started to the infant. If the system were in use, the medication could be started earlier and the worsening of the patient’s state could be prevented. This would improve the outcomes and shorten the stays in NICUs thus reducing costs.

It is currently debated whether the European Union General Data Protection Regulation (GDPR) guarantees a “right to explanation” about how the system made the decision in an individual case [9]. Even without the GDPR, it would improve the acceptability of the system in the clinic if the system could explain its suggestions. For this reason the preference in the development is in such methods which can provide a human understandable explanation of the machine decision.

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Conflict of interest statement

The authors are researchers in the project that is described here but they have no conflicts of interests with the producers of the equipment or producers of the data used in this study.

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