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

Alpo Värri¹, Dr.Tech., Antti Kallonen¹, M.Sc., Elina Helander¹, Dr.Tech., Andres Ledesma¹, M.Sc., Patrick Pladys², M.D.

¹ Tampere University of Technology, Finland; ² Rennes University Hospital, Rennes, France

Alpo Värri, Dr.Tech. Faculty of Biomedical Sciences and Engineering Tampere University of Technology P.O. Box 553, FI-33101 Tampere, FINLAND. Email: Alpo.Varri@tut.fi

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 de-
tection 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 indi-
cate 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 integrat-
ing laboratory values, biomarkers, and clinical infor-
mation 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 vari-
ables 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 commer-
cialization 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 con-
sortium of pediatric clinics, university departments with
skills in physiological signal processing, pattern recogni-
tion 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 infor-
mation of the preterm infants in the ICUs for the devel-
opment and validation of the analysis algorithms to be
developed in the project. The target number of inclu-
sions 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 sup-
port system which predicts the risk of sepsis of the
infant. The results are presented in an easily under-
standable 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 sys-
tem 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 reli-
bility 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 collect-
ed data to the format suitable as input to the explora-
tive 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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