LETTER TO THE EDITOR

Predictors for the quantity not sufficient sweat collection for ionic conductivity in newborns and young infants

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KEY WORDS: cystic fibrosis, sweat conductivity, quantity not sufficient, newborn, infant.

RUNNING HEAD: quantity not sufficient of sweat for conductivity assays

ABSTRACT

Background: Sweat conductivity (SC) is a semi-automated method widely used as a screening test for Cystic Fibrosis. Quantity not sufficient (QNS) is defined when collecting a volume lower than 15 µl of sweat during 30 minutes.

Objective: To verify the rate and factors related to QNS for SC in newborns and young infants.

Methods: Newborns and infants aged less than three months that had undergone sweat conductivity after two abnormal immunoreactive trypsinogen results, were recruited prospectively and consecutively. Statistical analysis included descriptive statistics, univariate and multivariate logistic regression.

Results: A total of 1020 individuals were included. Among them, the rate of QNS was 8.9%. Subjects with gestational age <37 weeks (OR=5.0), birth weight <2.000g (OR=3.5), and daily weight gain <25g/day (OR=3.4) were more likely to produce an insufficient quantity of sweat.

Conclusion: Our results suggest that QNS rates for SC could successfully fulfill the Cystic Fibrosis Foundation standards in newborns and young infants. In cases of QNS, SC should be scheduled as early as possible when the infant is older than 37 weeks (corrected age).

Sweat conductivity (SC) is a semi-automated method that does not require specially trained technicians.[1] Sweat sample induction, collection, and analysis are performed through Pilogel® discs, Macroduct® coils, and Sweat-Chek analyser® (Wescor Inc., USA), which allows direct reading of the results with a small amount of sweat.[1] These characteristics are suitable for low-middle income settings with few Cystic Fibrosis (CF) reference centers where classical coulometry is available.

For SC assays, the Cystic Fibrosis Foundation (CFF) defines quantity not sufficient (QNS) as a volume lower than 15 µl of sweat collected during 30 minutes.[2,3] CFF accepts a QNS rate lower than 10% in infants younger than three months.[4,5] Higher QNS rates can reveal problems in sweat collection, and in that situation, a new attempt must be scheduled.[2]

Our literature search found no study reporting rates and predictors of QNS for SC analysis in newborns and young infants. Identifying predictors of QNS results may be helpful for clinicians and technicians to optimize the timing of SC. Therefore, the present study aimed to verify SC's QNS rate in infants younger than three months of age and assess its related predictors.

This study recruited prospectively and consecutively 1020 clinically stable young infants enrolled in the statewide newborn screening program with two previous positive immunoreactive trypsinogen results (IRT).

Exclusion criteria were clinically unstable infants older than 90 days of life. Sweat samples were collected and analyzed according to the manufacturer’s recommendations using the Macroduct system® and then, Sweat-Chek analyzer® (Wescor Inc., USA). [1]

SC assays were performed in the single accredited Reference Center for the Statewide Newborn Screening and Genetic Diagnosis, located in the city of Belo Horizonte, Brazil.

Explanatory variables were dichotomized to analyze their potential role as predictors of QNS, as follows, age, gender, gestational age (< 37 weeks or ≥ 37 weeks), birthweight (< 2.500 g or ≥ 2.500 g), weight at the day of SC (< 2.000 g or ≥ 2.000 g), and daily weight gain from birth to the date of sweat collection (< 25g/day or ≥ 25g/day).

Multivariate logistic regression was used to identify predictors of insufficient sweat volume. All predictors were initially included in the baseline model, and backward elimination with the inclusion criterion of P < .20 was used to select the final model. Statistical analysis refers only to the first individual appointment. Analyses were performed through SPSS software, version 23.0 (SPSS Inc., Chicago, Illinois). The research protocol was approved by the Research Ethics Committee of Federal University of Minas Gerais, under number CAAE 21958014.1.0000.5149.

The mean and median age were respectively 48 days (SD 47.3-49.7) and 43 days (range 15-90 days) of life; among them 150 (14.7%) were newborns. Almost 54% were female. A rate of 8.9% of QNS was found (91 out of 1020 babies). About 56% of the studied individuals were preterm**,** and 59.1% of them with a birth weight lower than 2.500g. On the day of SC, 46.2% were younger than 44 days of life, 1.2% weight less than 2kg, while 75.3% had a weight gain lower than 25g/day.

Table 1 displays the multivariate analysis final model. As shown, o*dds ratios* for QNS for gestational age, birth weight, and daily weight gain were 5.0

(95% CI: 2.47 – 10.1), 3.5 (95% CI: 1.8 – 6.9), and 3.4 (95% CI: 2.0 – 5.9) respectively.

Insert Table 1

There is no previous work studying the rate and factors related to QNS exclusively for SC in newborns and young infants to the best of our knowledge. Therefore, the unavailability of previous studies hinders comparisons with our results.

In conclusion, our findings suggest that QNS rates for SC could successfully fulfill the Cystic Fibrosis Foundation requirements in newborns and young infants. In cases of QNS, SC should be scheduled as early as possible when the infant is older than 37 weeks (corrected age).

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CONFLICT OF INTERESTS

The funding organizations played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

AUTHOR CONTRIBUTIONS

RMB contributed to the manuscript conception, writing, revision, and editing. CGA contributed to the manuscript conception, writing, editing, and critical revision of the manuscript. OGS contributed to data collection, interpretation, and analysis. DN supervised and/or performed SC assays. JVAJ and FHP contributed to data collection, analysis, validation, and interpretation, and writing of the manuscript. PC conceived the study, and the study design; investigation, methodology, project administration, validation; manuscript conception, writing, editing, and revising the manuscript.

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ETHICAL APPROVAL

All relevant ethical guidelines have been followed for data collection and reporting.

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Table 1 Multivariate final model for explanatory variables and QNS sweat conductivity results.

	OR	95% CI	P value
Gestational age <37 weeks	5.0	2.5 - 10.1	0.001
Birth weight <2000 g	3.5	1.8 - 6.9	0.001
Daily weight gain <25 g	3.4	2.0 - 5.9	0.001

Hosmer e Lemeshow test 0.715 , R^2 0.28