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Title: Reference values for offline exhaled and nasal nitric oxide in healthy children

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Body: Exhaled and nasal Nitric Oxide (eNO and nNO) are valuables markers in respiratory diseases such as asthma and primary ciliary dyskinesia (PCD). The possibility to collect gas samples from the upper and lower airways in an offline manner offers the advantage to improve the screening and follow-up of respiratory diseases, but reference values from healthy children remains sparse. Objectives: To identify normal values for offline eNO and nNO in healthy children of school age. Methods: Offline eNO was measured in 88 healthy children of school age and nNO in 31 of them using an offline collection kit. We performed offline eNO measurements in 30 children with naive asthma and/or respiratory allergy. The eNO samples were obtained using the FeNO offline collection kit from ECO MEDICS, and the offline nNO samples were collected at 300 ml/min aspiration flow rate through a nasal olive during a 20 seconds apnea. All measurements were obtained using the NIOX Flex analyzer. Results: Offline eNO value was determined after multiple regression analysis by the following equation -8.206 + 0.176*Height. The ULN was 27.4 ppb. In children, pre-teens and adolescents, the mean offline eNO was 13.6 ± 4.7 ppb, 16.3 ± 13.7 ppb and 20.0 ± 7.2 ppb respectively. The sensitivity and specificity of offline eNO value to predict asthma or respiratory allergies were 77% and 91% respectively at the cut-off value of 23.3 ppb. Mean offline nNO was determined at 660 ± 232 ppb and the LLN was 197 ppb. Conclusion: Offline eNO and nNO reference values in healthy children are provided. The measure of eNO and nNO should help and favour the widespread screening of respiratory diseases for clinical practice in a paediatric population.