Correlation between FLACC Pain Score and Salivary Alpha-Amylase Level (A Review on Children with Down Syndrome)

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Abstract

Face, leg, activity, cry, and consolability (FLACC) pain scores are commonly used to assess pain intensity in children with developmental disorders. Salivary alpha-amylase (SAA) is an enzyme found in saliva that is used as a reliable biomarker for anxiety because it increases sympatho adrenal medullary (SAM) system activity. The aim of this study was to analyze the correlation between FLACC pain scores and SAA levels, during dental treatment, in children with Down syndrome. Purposive sampling was used to select the population for this study. Pain was assessed during the children's treatments to obtain FLACC pain scores. Salivary alpha-amylase levels were measured with a nipro cocoro meter shortly after local anesthetic injection. A significant correlation was found between FLACC pain scores and SAA levels. Since SAM system activity and the hypothalamic-pituitary-adrenal axis increased with painful stimuli, SAA levels may reflect pain related stress and may be used as non-invasive pain biomarkers. Further studies are required to confirm whether SAA levels can be used as pain biomarkers for other types of special needs children.

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Introduction

Children with intellectual disabilities may have limited communication skills.[1] Thus, dental practices encouraging children with intellectual disabilities to cooperate with dentist's instruction can be a major challenge. In 2001, the American Association of Pediatrics (AAP) stated that pain assessment for children with developmental impairments may be particularly difficult and that careful and thorough assessments are necessary.[1] Recent studies showed that there are some instruments, based on behavioral observation, can be used to assess pain in children with cognitive impairment.[1,2] However, more studies are needed to evaluate pain perception in children with intellectual disabilities. Down syndrome (DS) is a disorder consist of multiple, common congenital abnormalities that arise from the presence of an extra chromosome 21.[3] Based on Local Community Research in 2013, the number of babies born with DS increased about 13% over one year.

Mental handicap is the most prominent symptom, with levels of mental retardation ranging from mild to profound. Children with DS usually have difficulties in understanding words and communicating with their caregivers.[3] Despite these limitations, many studies have shown that children with DS have the same sensitivity to pain as normal children.[4] Moreover, children with DS showed more positive emotion compared to children with other types of cognitive impairments.[3,4]

The Face, Leg, Activity, Cry, and Consolability (FLACC) pain scale is an instrument to assess pain, which has been adapted for children with cognitive impairment.[5] To obtain a pain score, a clinician is required to observe the behavior of children, providing a simple and consistent method to identify and evaluate pain in children with cognitive impairment.[5] Each category of the FLACC (face, leg, activity, cry, and consolability) pain scale has a potential score ranging from 0 to 2, with the

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entire scale having a potential maximum score of 10.[5]

Salivary Alpha-Amylase is a protein enzyme that hydrolyzes polysaccharides, such as glycogen, to glucose and maltose. Salivary alpha-amylase levels reduce significantly within 60 minutes after waking up and steadily increase during the day.[6]

A correlation between anxiety and Salivary Alpha-Amylase (SAA) levels has been studied significantly and is well-documented in the literature.[6] Earlier studies have stated that there is a small correlation between levels of SAA and pain intensity.[7]

Specifically, one study found that there was a positive relationship between a decrease in SAA levels and Visual Analogue Scale (VAS) pain scores after participants received an epidural block.[8]

Two primary systems in our body that responded to psychological stress are the Hypothalamus-Pituitary-drenocortical Axis (HPA) and Sympathoadrenal Medullary (SAM) system. Activation of the HPA causes an increase of cortisol secretion in the adrenal cortex. Activation of SAM system causes an increase of Salivary Alpha-Amylase.[9]

Body responses similarly to pain stimuli as to those of psychological stress, which both activated the SAM system. Previous studies have shown that when pain stimuli occur, SAM system activity increases.[10] In the present study, whether SAA levels can be used as a pain biomarker was assessed.

Method

All protocols and informed consent forms were approved by the Ethics Committee of Faculty of Dentistry, Universitas Indonesia. After obtaining approval from four special needs schools and written informed consent from parents, 25 children with DS, ages 6-11, were selected as subjects.

After gathering parents' anamnesis about medical and drug history, subjects were seated in a dental chair unit and received an intraoral examination. Children with a definitive negative Frankl score and those who needed restraint treatment were excluded. Also, since a previous study demonstrated that some diseases including diabetes, renal diseases and chronic pancreatitis can increase SAA levels, those who had systemic diseases were excluded from the present study.[11]

Topical anesthetic was used in the mucobuccal area of the tooth to be extracted. A local anesthetic injection was performed on a point of the mucobuccal area with a Morita Disposable Dental Needle (0.3x16mm) containing Septocaine 1.7ml.

A FLACC pain score (0 [comfortable and no pain] – 10 [severe pain]) was obtained during the injection. Sublingual saliva was collected with a disposable Cocoro strip, for 30 seconds, shortly after the injection.

The strip was inserted into a portable SAA monitor (Nipro Cocoro Meter, Japan) consist of a salivary transcription device and an optical analyzer. The strip contained α-2-Chloro-4-Nitrophenyl-Galactopyranoside (Gal-G2-CNP) that was hydrolyzed by SAA, resulting in 2-Chloro-4-Nitrophenol (CNP).

The level of CNP was analyzed by optical analyzer and a number, representing level of SAA, appeared on the monitor. Data were presented as means ± standard deviations (SDs). Obtained data were analyzed with Spearman Correlation Coefficient tests. The significance level was set at $p \leq 0.05$.

Results

There was a significant correlation between FLACC pain scores and SAA levels ($p < 0.01$, $r = 0.867$, Fig. 1). The mean of FLACC pain scores during local anesthetic injections in children with Down syndrome was 2.08, with a minimum score of 1 and a maximum score of 3.

The mean of SAA levels during local anesthetic injections in children with Down syndrome was 60.96 u/ml, with a minimum level of 29 u/ml and a maximum level of 95 u/ml (Table 1).

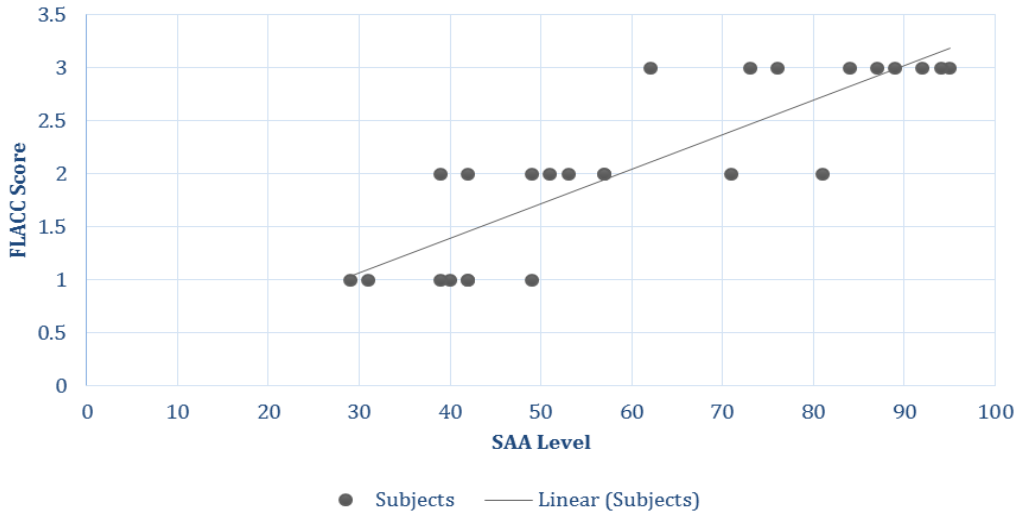

Figure 1. Correlation between FLACC pain score and SAA level ($r = 0.867$, $p < 0.01$)

Variable	N	Mean ± SD (u/ml)	Min – Max (u/ml)
FLACC Score	25	2.08 ± 0.81	1 – 3
SAA Level		60.96 ± 21.37	29 – 95

Table 1. Mean level of Salivary Alpha-Amylase (SAA) and pain score during local injection.

Discussion

A self-report pain assessment is currently a recommended method to assess pain intensity in both adults and children. However, children with cognitive impairment often do not have the ability to understand and communicate how they feel. Thus, a self-report pain assessment cannot be performed in children with cognitive impairment.[12] Another way to assess pain is through the measurement of biomarkers. There are several pain biomarkers in the blood, such as cardiac troponin T, troponin I and myoglobin, but extracting them would be painful for children.[13]

There are also some proteins in cerebrospinal fluid (CSF) that can be measured and used as pain biomarkers. In the present study, measuring SAA was chosen to assess pain levels. The SAA level of subjects during local anesthetic injections was found to have a wide range, 29 to 95 u/ml. The results showed that SAA levels correlated with FLACC pain scores.

FLACC pain scale can be used to assess pain in children with communication limitation.[5] Thus FLACC can represent pain level. The results of this study agree with previous literature. One such study showed that there were positive significant correlations between Visual Analogue Scale (VAS) pain scores and SAA levels.[8] An increase of SAA levels, along with VAS pain scores, was documented in patients with symptomatic irreversible pulpitis.[14]

In another study, SAA levels were used as an instrument to assess the severity of pain in mice and a significant correlation was found.[15] Other studies have shown that there is an association between SAA levels and pain scores in epileptic children.[11]

Also similar to this study, a study related to anxiety in patients with global developmental delays, showed that SAA levels increased during dental treatment.[16] Another study revealed that psychological stress can increase cortisol and SAA levels in saliva.[10] Yet another study revealed that SAA levels can be used as anxiety biomarkers since psychological stress activates the SAM system.[12]

Previous studies have shown that when both pain stimuli and anxiety occured, SAM

system activity increased.[8] When pain stimuli occurs, it will be detected by nociceptors, transmitted by C fibers, through the reticular formation, reaching the intralaminar nuclei of the thalamus which then increase the activity of SAM system. Both the reticular formation and intralaminar thalamus nuclei are components of the Reticular Activating System (RAS). The RAS is composed of a set of connected nuclei that are responsible for transmitting signals to all parts of the brain, especially the thalamus and the basal region of the brain around the thalamus, including the hypothalamus.[17] Thus, pain stimuli can activate SAM system which then increase SAA levels.

Conclusion

In conclusion, based on the correlation between FLACC pain scores and SAA levels, our study suggest that SAA levels can be used as pain biomarkers. This correlation may be because both pain stimuli and anxiety can activate SAM system thus increase SAA levels. However, further studies are required to confirm whether SAA levels can be used as pain biomarkers for other types of special needs children.

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