Induction and emergence behavior of children undergoing general anesthesia correlates with maternal salivary amylase activity before the anesthesia

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Background: The parents of the children who undergo surgery experience stress during the pre-anesthetic period. Such stress influences the mental status of their children, thereby inducing their pre-anesthetic anxiety and problematic behavior at emergence. Recently, measurement of salivary biomarkers was evaluated as stress biomarkers. Especially, α-amylase is utilized as an excellent index for psychological stress. In the present study, we tested whether salivary amylase activity of mothers before the surgery of their children correlates with the peri-operative children’s behaviors.

Methods: A total of 22 pairs of mothers and children were analyzed. Maternal salivary amylase activity was evaluated at the entrance of the operation room. The children underwent minor plastic surgery under general anesthesia, and induction and emergence behaviors were assessed.

Results: The higher the maternal salivary amylase activity, the severer the children’s induction anxiety ($r_s = -0.667$, $n = 22$, $P < 0.0001$), and the higher the maternal amylase activity, the severer the children’s emergence agitation ($r_s = 0.705$, $n = 22$, $P < 0.0001$).

Conclusion: Induction and emergence behaviors of children undergoing general anesthesia significantly correlated with their respective maternal salivary amylase activity during the pre-anesthetic period.

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Key words: Maternal stress; pre-anesthetic child’s anxiety; emergence behavior; salivary amylase.

It is well known that the parents of the children who undergo surgery experience stress during the pre-anesthetic period (1, 2). Such stress of the parents influences the mental status of their children, thereby inducing their pre-anesthetic anxiety (1–3). The pre-anesthetic anxiety influences their peri-operative behaviors such as distress at induction and emergence from general anesthesia (4–7).

Evaluation of psychological stress has been relying on subjective assessment tools such as the State-Trait Anxiety Inventory Score or Visual Analog Scale (8–10). However, if subjects fail to report reliably, these subjective evaluation tools are not reliable (10). Several investigators have sought objective assessment tools. Recently, measurement of salivary biomarkers, which are sampled non-invasively, was evaluated as stress biomarkers (10–12). Especially, salivary α-amylase is associated with changes in plasma noradrenaline and is utilized as an excellent index for psychological stress (13, 14). We thus hypothesized that parental salivary amylase would be a useful indicator of parental mental stress and that amylase activity of parents before the surgery of their children would correlate with peri-operative behaviors of their children. In the present study, we tested whether salivary amylase activity of mothers before the surgery of their children correlates with the children’s behaviors at induction and emergence from general anesthesia.

Methods
The study population of the present blind trial consisted of mothers and their children. The children were aged 1–3, ASA and scheduled for minor plastic surgery; removal of medium congenital nevi, under general anesthesia. Children who had a history of chronic illness or developmental delay,
or central nervous system or cardiovascular system dysfunction and mothers who had a history of psychological illness, or central nervous system or cardiovascular system dysfunction were not invited to participate in the present study. A history of previous surgery excluded patients from participation in the present study. After obtaining approval from the Ethics Committee of Aichi Medical University and written informed parental consent, we studied 24 pairs of mothers and children.

We used a hand-held monitor (COCORO meter, Nipro, Osaka, Japan) to measure amylase activity in a batch type, using a reagent paper containing 2-chloro-4-nitrophenyl-4-α-β-D-galactopyranosylmalto side (Gal-G2-CNP, Toyobo Co. Ltd, Osaka, Japan) which is hydrolyzed by amylase (14). The hydrolyzing reaction continues until the substrates are completely consumed. The monitor quantifies amylase activity by assessment of the reaction time. The hand-held monitor consists of a disposable test strip and a monitor. The test strip consists of a collecting paper and a reagent paper for amylase.

All patients were fasted for 5 h before surgery, but encouraged to take clear fluids until 2 h before induction. Forty-five minutes before induction, midazolam (Dorumicum, Astellas Pharma Inc., Tokyo, Japan) 0.5 mg/kg was given orally by the mothers. Children who refused to take the whole dose were excluded. At the entrance of the operating room at 08:15 hours, the collecting paper of a disposable test strip was directly inserted into the oral cavity of the mother, approximately 20–30 μl of whole saliva was collected from under the tongue in 30–60 s and then the test strip was set into the monitor for assessment of maternal salivary amylase activity. After collection of maternal saliva and separation at the entrance of the operating room, children were laid on a table alone. When anesthesia was induced with 7% sevoflurane (Maruishi Pharmaceutical Co. Ltd, Osaka, Japan) in 100% oxygen, anxiety was assessed by an observer, blinded to the aim of the present study and how the child behaved at induction. After induction, the lengths of the surgical procedure and anesthesia were recorded. A minimum sample size of 20 was needed to detect the specific person correlation coefficient (r), for an expected correlation coefficient of 0.6 with a power of 80% (β = 0.20) and a significant level of 0.05 (α = 0.05). Data are presented as median (range). Spearman’s rank correlation coefficient (r_s) was applied to analyze the possible relationship between maternal salivary amylase activity and induction or emergence behavior of children. A P value of <0.05 was considered significant. Furthermore, the cut-off values of maternal salivary amylase activity to induction anxiety and emergence agitation were investigated using receiver–operating characteristic (ROC) curve methodology. To construct the ROC curve for the analysis of the area under the curve (AUC) and the cut-off values, we split each behavior scale into two [1 and 2 (distressed) vs. 3 and 4 (calm)] during induction and 1–3 (calm) vs. 4 and 5 (agitated) during emergence.}

**Results**

A total of 24 pairs of children and mothers participated in the present study, but two pairs were
excluded because the children refused midazolam. Nine boys and 13 girls were included: median (range) of age, 2 (1–3) years; weight, 13 (9–16) kg; operation time, 54 (41–84) min; anesthetic time, 110 (82–129) min. Mothers enrolled in the present study were aged 33 (24–39) years.

The higher the maternal salivary amylase activity, the severer the children’s induction anxiety ($r_s = -0.667; n = 22; P < 0.0001$; Spearman’s rank correlation coefficient). The higher the maternal salivary amylase activity, the severer the children’s emergence agitation ($r_s = 0.705; n = 22; P < 0.0001$; Spearman’s rank correlation coefficient).

The scores of the induction anxiety or emergence behavior did not correlate with the duration of anesthesia. None of the children complained of pain when we visited 2 h after the emergence or used rescue analgesia in the immediate post-operative period. The AUCs generated from induction anxiety and emergence agitation data were 0.868 and 0.953, respectively. The cut-off values of induction anxiety and emergence agitation were 46 and 44, respectively (Figs 3 and 4).

**Discussion**

The present study showed that the induction and emergence behaviors of children undergoing general anesthesia significantly correlated with their respective maternal salivary amylase activity during the pre-anesthetic period, and the higher the maternal salivary amylase activity during the pre-operative period, the severer the induction anxiety and emergence agitation of their children undergoing general anesthesia.

In the present study, several mothers showed an increased activity of salivary amylase before the surgery of their children and their children showed induction anxiety and problematic behavior at emergence from general anesthesia. Thus, we speculated that these mothers would have been...
under greater stress during the period, thereby inducing induction anxiety and emergence problematic behavior of their children undergoing general anesthesia.

We studied children aged < 4 years old, because more than half of the children aged more than 3 years in this institution had already experienced nevus removal surgery under general anesthesia, and we speculated that the experience might influence children’s behaviors during induction and emergence (19).

In conclusion, the induction and emergence behaviors of children undergoing general anesthesia significantly correlated with their respective maternal salivary amylase activity during the pre-anesthetic period.

References

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