Medworld –asia International Publishers
Applied Physiology and Anatomy Digest [P ISSN: 2456 – 4095]
June 2019 (4) 01 , 43 - 48

Original article:

Study of antinociceptive effect of sucrose to cold pressor test in human adults

Smita J Mokal[1], Amol Bhalerao[2*], Kalyani Ghodeswar[3], Muktpal Bhalerao[4]

[1]M.D (Physiology), Assistant Professor, Dept. of Physiology, Rural Medical College, Loni, Maharashtra, India.

[2*]M.D (Anesthesiology), Assistant professor, Dept. of Anesthesiology, Rural Medical College, Loni, Maharashtra, India.

[3] M.D (Physiology), Senior Resident, Dept. of Physiology, Indira Gandhi Government of Medical college, Nagpur, Maharashtra, India.

[4]M.D (Physiology), Assistant Professor, Dept. of Physiology, Rural Medical College, Loni, Maharashtra, India.

[*]Corresponding author- Dr Amol Bhalerao, Dept. of Anaesthesiology, Rural Medical College, Loni, Maharashtra, India.

Abstract:

Background: Sucrose-induced analgesia (SIA) has been known as non-pharmacological intervention for pain relief in both rat pups and infants. The mechanism underlying SIA is suggested to be mediated by the endogenous opioids system. This effect is produced by the sweet sensation rather than by the absorption of sucrose. The SIA has been frequently investigated for the pain relief in infants but less so for SIA in adults.

Aim: The aim of study was to explore the effect of sucrose on the pain tolerance time in adults.

Objective: To study the effect of oral sucrose solution on pain tolerance time in human adult.

Method: The study includes 40 participants of age group 20-40years. The pain was induced in the participants by cold stimuli using cold pressor test while holding mouthful of plain water (control) and sucrose solution (30%) and the pain tolerance time (sec) of the participants was noted for each plain water and sucrose solution.

Results: The results showed an increase in the pain tolerance time to cold pressor test on holding mouthful of sucrose solution in respect to plain water.

Conclusion: These data clearly indicate that the sweet stimulus of sucrose induces antinociception in adults, suggesting sweet substance–induced analgesia can be applied to human adults.

Keywords: Sucrose induced analgesia (SIA), sucrose, cold pressor test, pain tolerance time, antinociceptive.

INTRODUCTION

Pain is an unpleasant sensation induced by noxious stimuli which is detected by the peripheral afferent nociceptors. Most pain resolves once the painful stimulus is removed or the body has healed but sometimes pain persists despite removal of the stimulus and apparent healing of the body. Psychological factors such as social support, stress, excitement or distraction can significantly modulate pain intensity or unpleasantness. Studies in animals have shown tasting a sweet solution increases their ability to tolerate pain [1] A systematic review and meta-analysis of 13 studies have shown that the administration of sucrose is the most commonly used non pharmacological intervention for relief of procedural pain in neonates [2] Few hospitals in western countries use oral sucrose as safe and an effective method for the management of painful procedure in neonates and infants.

Some studies have shown that pleasant taste of sucrose in infants triggers the release of endogenous endorphins that could create an analgesic effect [3]. Evidence of this opioid mechanism of sweet is shown by a study in which analgesic effect of sucrose is not seen in neonates born to methadone dependent mother [4]. Studies in rodents have shown tasting a sweet solution increases their ability to tolerate pain [5]. This analgesic effect is thought to be involved in activation of the central regulating systems mainly opioid related descending inhibitory network. In fact, consume of sucrose solution increases beta–endorphin levels in rat brain indicating that sucrose activates the endogenous opioid system [5, 6]. Several studies have revealed that the sucrose induced analgesia (SIA) is involved in opioid related neurotransmitters, including serotonine (5HT) and noradrenaline (NA) in the central regulating system [7, 8]. Thus it was found in the study that SIA may involve the endogenous opioid related the descending inhibitory system rather than distraction. Very few studies in western countries have shown the analgesic effect of sweets like sucrose and glucose in adults [9]. An Indian study had shown gender specificity of sucrose induced analgesia by using nociceptive flexion reflex [10]. This study was carried out on a sample of 12 adults. The purpose of the present study was to find the analgesic effect of sucrose in adults so as to reduce minor procedural pain and also to reduce the side effects of some of the medication which is used to reduce pain during the minor surgical procedures.

Materials & Methods:

The study was an interventional. The study was carried out in 40 adult residents and staff of a tertiary hospital of age of 20-40 years. Written informed consent was obtained from the participants and ethical committee approval was taken before the start of the study. Individuals willing to participate were enrolled in the study. All the participants was administered the Cohen perceived stress for measuring stress levels for consideration for inclusion. The participant with normal to mild perceived stress scale was included in the study. Individual with history of smoking, acute illness during past one month, diabetes, hypertension, autoimmune disorder, pain syndromes, vascular disorders, thyroid disorder, spondylitis, rheumatoid arthritis, neuritis and migraine, consuming medicines like tricycle antidepressants, serotonin reuptake inhibitor like duloxetine, antiinflamatory drugs was excluded from the study. The participants were instructed to get well hydrated before the cold pressor test to avoid syncopal attack and also to refrain from food and drinks 2 hours prior to the test. In female participants test was carried on the second day after their last day of menses so as to avoid the influence of hormonal variation of the menstrual cycle on pain tolerance time. The study was conducted on the participants under two conditions in a single day. The pain tolerance time using cold pressor test was noted, first while holding a mouthful of plain water in the oral cavity and then 30% sucrose solution, maintaining an interval of 15 min between the two sessions. 30% sucrose solution was prepared by mixing 30 grams of sucrose in 100 ml of water. The participants was asked to hold the water in the mouth till they were able to tolerate pain and after noting the readings the participants was allowed to swallow or throw the water out of their mouth depending on their own wish.

Method of hand cold pressor test-

A container filled with cold water, maintained at 4^0 Celsius was used. Its temperature was recorded immediately before performing the test. A water circulator was used to prevent the warming of the water near the

participant's hand. At the onset of the test, subjects were instructed to immerse their right hand completely up to the wrist joint and to remain still. Subject was instructed to indicate when they were no longer able to or willing to tolerate the pain (pain tolerance) or feels dizzy by raising his or her hand. A maximum time limit of 4 minute was imposed, though subjects were not informed of this limit.

Statistical analysis:

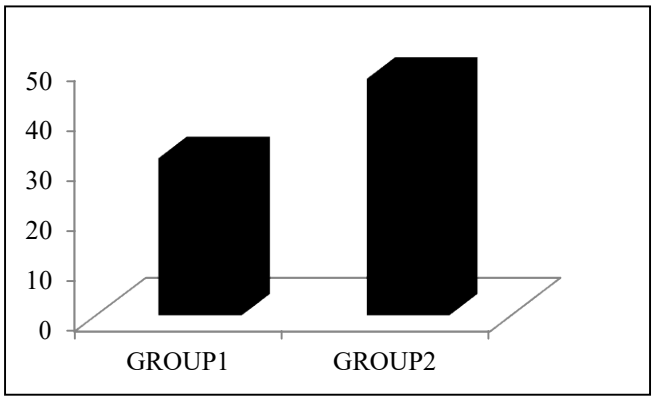
The analgesic effect of sucrose in adults i.e. the pain tolerance time in adults while holding plain water and then sucrose solution was analysed using Unpaired T-test. P value < 0.05 was considered significant.

Observation and results:

The data of 40 adults with mean age 26.517 was analyzed using unpaired t-test. The mean for pain tolerance time with water is 31.413 and the mean for the pain tolerance time with sucrose is 47.206 seconds. The standard deviation and p-value for pain tolerance time with water and sucrose is given in table.1

Table.1:

	Pain tolerance time with water(seconds)	Pain tolerance time with sucrose(seconds)
Standard deviation	24.019	46.214
Standard error of mean	4.460	8.582
p-value	>0.10	<0.0001



Graph.1: Graph showing mean of pain tolerance time with water (Group1) and mean of pain tolerance time with sucrose (Group2).

Discussion:

In the present study there was a significant difference in the pain tolerance time with sucrose solution in respect to water. This finding is consistent with the previous studies showing the analgesic effect of sweet taste. One study of adults reported increased tolerance to mechanical pain in women immediately following 10 min of consumption of highly palatable sweet food (Mercer and Holder, 1997) [9]. As in that study, tolerance was the only pain measure to show an analgesic effect of sweet taste. In the current study, pre-absorptive effects of sucrose were examined since participants did not swallow the solutions while recording the pain tolerance time

and has been found to reduce pain sensitivity in human adults. These data clearly indicate that sucrose stimulus induced antinociception or sweet substance induced analgesia can be applied to human adults. The administration of sweet taste solution in the present study was therefore comparable with the study done in infants (Barr et al., 1994; Blass and Hoffmeyer, 1991) [11, 12] and children (Miller et al; 1994). Conversely, Pepino et al[14] had showed that sweet stimulus from sucrose solution does not induce analgesia on CPT in female adults. However, that study did not consider the menstrual cycle among female subject, a factor that is known to influence pain perception. This variable might have contributed to the conflicting results found in the present study. A study done by Weid and Verbaten [15] had reported similar pain tolerance specific effects of various analgesic manipulations such as mood induction and distraction. In the study they found that sweet taste only modified pain tolerance, a measure of the motivational-affective dimension of pain, but did not affect threshold, a measure of the sensory-discriminative dimension of pain. Previous studies demonstrated that nursing or intraoral infusion of certain components of mother's milk (e.g. sugars and fats) produces calming and opiate receptor-dependent analgesia in newborn rats and humans. Sucrose also elicited Fos expression in several brainstem areas associated with centrally mediated analgesia, including the periaqueductal gray and the nucleus raphe magnus. Taken together, these findings demonstrate that analgesia elicited by intraoral sucrose does not require involvement of the forebrain. Intraoral sucrose activates neurons in the periaqueductal gray and nucleus raphe magnus [8], two key brainstem sites critically involved in descending pain modulation. Although the analgesic mechanisms of sucrose in human adults still remains unclear.

Conclusion

In conclusion, this study demonstrated that sweet stimulus of sucrose induces antinociceptive effects on pain tolerance in adults. The pleasant taste of sucrose might modify pain sensation by affecting the affective dimension of pain in adults. Thus administration of sucrose may have clinical implications as an adjunct to pain in adults. Accordingly, more clinical trials need to be performed before sweet substance– induced analgesia is used for adults for pain.

Limitation

The study had a small sample size so further study needs to be done with a larger sample size. Very little is also known about the analgesic mechanism in human adults so further studies need to be carried out for the same.

References:

1. Blass EM, Shide DJ. Some comparisons among the calming and pain relieving effects of sucrose, glucose, fructose, and lactose in infant rats. Chem Senses.1994; Jun;19 (3): 239-49.
2. Stevens B, Taddio A, Ohlsson A, Einarson T:The efficacy of sucrose for relieving procedural pain in neonates--a systematic review and meta-analysis, Acta Paediatr.1997;Aug 86(8):837-42.
3. Blass EM, Ciaramitaro V. A new look at some old mechanisms in human newborns: taste and tactile determinants of state, affect, and action. Monogr Soc Res Child Dev.1994; 59:1–80.
4. Segato F, Castro-Souza C, Segato E. Sucrose ingestion causes opioid analgesia. Braz J Med Biol Res.1997; Volume 30(8) 981-984.
5. Dum J, Gramsch C, Herz A. Activation of hypothalamic beta endorphin pools by reward induced by high palatable

food, Pharmacol. Biochem. Behav.1983; 58: 443- 447.

6. Yamamoto N, Sako S, Maeda S. Effects of taste stimulation on β-endorphin levels in rat cerebrospinalfluid and plasma. Physiol. Behav.2000; 69: 345-350.
7. Reboucas E, Segato E, Kishi R, Freitas R, Savoldi M, Morato S, Coimbra N.Effect of the blockade of mu1-opioid and 5HT2A-serotonergic/ alpha1-noradrenergic receptors on sweet-substance induced analgesia. Psychopharmacology.2005; 179: 349-55.
8. Miyase CI, Kishi R, de Freitas RL, Paz DA, Coimbra NC. Involvement of pre- and post-synaptic serotonergic receptors of dorsal raphe nucleus neural network in the control of the sweet-substance-induced analgesia in adult Rattus norvegicus (Rodentia, Muridae). Neurosci. Lett.2005; 379:169-173.
9. Mercer ME, Holder MD. Antinociceptive effects of palatable sweet ingesta on human responsivity to pressure pain. Physiol Behav 1997; 61(2): 311–8.
10. Bhattacharjee M, Bhatia R, Mathur R. Gender specificity of sucrose induced analgesia in human adults. Indian J Physiol Pharmacol. 2007; 51(4): 410-414.
11. R. G. Barr, M. S. Pantel, S. N. Young, J. H. Wright, L. A. Hendricks and R. Gravel, The Response of Crying New- borns to Sucrose: Is It a 'Sweetness' Effect?". Physiology and Behavior.1999; Vol. 66(3):409-417.
12. E. M. Blass and L. B. Hoffmeyer, "Sucrose as an Analgesic for Newborn Infants". Pediatrics.1991; Vol. 87(2):215-218.
13. Miller A, Barr RG, Young SN. The cold pressor test in children: methodological aspects and the analgesic effect of intraoral sucrose. Pain.1994; 56:175–83.
14. Pepino, MY, Mennella JA. Sucrose-induced analgesia is related to sweet preferences in children but not adults. Pain.2005; 119: 210-218.
15. Weid M, Verbaten M. Affective pictures processing, attention and pain tolerance. Pain. 2001; Vol 90(1-2):163-72.
16. T. Kakeda, T. Ishikawa. "Gender Differences in Pain Modulation by a Sweet Stimulus in Adults: A Randomized Study." Nursing and Health Sciences.2011;Vol. 13(1): 36-40.
17. T. Kakeda. "Potential of Sucrose-Induced Analgesia to Relieve Pain in Male Adults: A Preliminary Study." Japan Journal of Nursing Science.2010; Vol (2):169-173.
18. T. Kakeda, M. Ito, T. Matsui, T. Ishikawa, "The Evidence for Sweet Substance- induced Analgesia in Adult Human." Pain Research. 2008. Vol. 23(3):159- 166.
19. Anseloni VC, Ren K, Dubner R, Ennis M.A brainstem substrate for analgesia by intraoral sucrose. Neuroscience. 2005; 133(1):231-43.
20. Lewkowski, MD, Ditto B, Roussos M, Young SN. Sweet taste and blood pressure- related analgesia. Pain.2003; 106:181-186.
21. Kanarek RB, Carrington C.Sucrose consumption enhances the analgesic effects of cigarette smoking in male and female smokers. Psychopharmacology.2004; 173:57-63
22. Anseloni VC, Ren K, Dubner R, Ennis M. A brainstem substrate for analgesia elicited by intraoral sucrose. Neuroscience.2005; 133:231-243.
23. Acharya AB, Annamali S, Taub NA, Field D. Oral sucrose analgesia for preterm infant venepuncture. Arch. Dis. Child. Fetal. Neonatal Ed.2004; 89:17-18.
24. Anseloni VC, Weng HR, Terayama R, Letizia D, Davis BJ, Ren K, Dubner R, Enis MAge dependency of analgesia elicited by intraoral sucrose in acute and persistent pain models. Pain.2002; 97: 93-103.

25. Fantino M, Hosotte J, Apfelbaum M. An opioid antagonist, naltrexone, reduces reference for sucrose in humans. Am. J. Physiol.1986; 251:91-96.

26. Drewnowski A, Krahn DD, Demitrack MA, Nairn K, Gosnell BA. Naloxone, an opiate blocker, reduces the consumption of sweet high-fat foods in obese and lean female binge eaters.Am. J. Clin. Nutr.1995; 61:1206-1212.