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## Alleviating Pain in Neonates – What is The Best?

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Newborns are often exposed to minor invasive procedures such as venepuncture. Current evidence suggests that neonates are able to perceive pain. Studies have documented that babies born at less than 32 weeks of gestation are exposed to 10-15 painful procedures each day during the first few weeks of life, and in almost 80%, no treatment for pain relief is offered [1]. Pain in neonates is known to cause adverse short and long-term effects. Prolonged or repeated pain also increases the response elicited by future painful stimuli (hyperalgesia) and even by usually non-painful stimuli (allodynia). The consequences include altered pain sensitivity (which may last into adolescence) and permanent neuro-anatomical, behavioral, emotional and learning disabilities [2].

Healthcare providers are constantly on the lookout for a safe and effective pharmacological or non-pharmacological method to alleviate pain in neonates. Orally administered sweet solutions such as glucose and sucrose have been shown to be effective in reducing procedural pain in neonates. One Cochrane review examined 44 randomized trials enrolling 3496 infants for efficacy, effect of dose and safety of sucrose for relieving procedural pain in neonates [3]. Despite significant clinical heterogeneity in the dose of sucrose and tools used to measure effect of pain, there was significant reduction in total cry time and composite pain scores during heel lancing. Expressed breast milk (EBM) which contains 7% lactose is a good physiological alternative [4]. Studies have reported the analgesic effect of breastfeeding before, during and after venepuncture [5].

Despite convincing evidence, routine measurement of indicators of pain and use of pain-relieving measures is

limited. Non-availability of sucrose in India and aversion of many neonatologists to administering anything other than breast milk to neonates may be contributing factors. In this issue, Sahoo, *et al.* [6] report reduced cry duration and pain score on using EBM or 25% dextrose before venepuncture. Their study shows 25% dextrose was more effective; EBM also significantly reduced the cry duration and pain score. Although, this is a well-conducted randomized controlled trial, exclusion of eligible subjects after obtaining consent and allocation of study group is undesirable. Probability of selection bias in such a scenario defeats the purpose of randomization. Administration of high concentration of dextrose can potentially cause hyperglycemia, rebound hypoglycemia and difficulty in subsequent breastfeeding. It is not clear whether investigators looked for these side effects.

There are inherent difficulties in conducting studies on neonatal pain. Standardization of dose of exposure (amount of pain) is difficult. Amount of pain inflicted is dependent on who conducted venepuncture, with what type/brand of needle and how the prick was given. Another concern with studies evaluating measures to reduce pain in neonates is about choice of a valid measure to detect and quantify pain. A recent study has suggested that although sucrose decreases clinical observation scores, there is no reduction in nociceptive brain activity and magnitude or latency of the spinal nociceptive reflex withdrawal response [7]. Whether the ability of sucrose to reduce the pain score or the duration of cry can be interpreted as reduced pain is not clear. Further studies are needed to evaluate the effect of sucrose, breast milk or other non-pharmacological measures in high-risk groups like extreme premature neonates exposed to repeated

painful stimuli. Future studies should aim to report effect of these measures on long-term cognitive and behavioral outcomes.

*Competing interests:* None stated; *Funding:* Nil

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## Probiotics and Allergic Rhinitis

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Allergy is a hypersensitivity reaction initiated by immunological mechanisms to substances that, in the majority of people, cause no symptoms and clinically manifests as atopic eczema, rhino-sinusitis, conjunctivitis or asthma. During the current era, there has been an increase in prevalence of allergic disorders which is attributed to changes in environmental-host factors. The so-called “hygiene hypothesis” (Microbial deprivation syndrome) suggests that a lack of exposure to microbial stimulus early in childhood is a major factor involved in this trend. This provides a rationale for using probiotics to modify the gut microbial flora, thereby altering the immune response of the host (from Th2 to Th1) and reducing the symptoms of allergy.

There is a recent surge in studies on the effect of probiotics on the clinical symptoms and medication use among children with established allergic diseases. Probiotics are products or preparations containing viable numbers of microorganisms that are able to modify the host’s microflora, thereby producing beneficial health effects [1]. Lactobacilli are considered to induce reactions involving Th1 cells and to improve allergic diseases. In the article published in this issue of the

journal [2], it has been concluded that *Lactobacillus salivarius* treatment reduces rhinitis symptoms and drug usage in children with allergic rhinitis. A meta-analysis of the published randomized controlled trials studying the effect of probiotics on allergic disorders revealed nine of the 12 RCTs showing an improvement due to the use of probiotics. All the RCTs that studied perennial allergic rhinitis showed lower symptom scoring and medication use with the use of probiotics compared with placebo [3]. There is also evidence from animal models and *in vitro* studies that gut micro biota modulate immune programming, promote oral tolerance, and are important inhibiting the development of the allergic phenotype.

However, the therapeutic effect of prebiotics or probiotics may be reduced once colonization and the allergic phenotype are established compared with treatment at younger ages when there is greater plasticity. It has also been studied that probiotics have some beneficial role in reducing the allergic disorders in the children when given to their mother during the third trimester of pregnancy and also in the newborn period before colonization occurs [4]. After a decade of research in the field of allergy and probiotics, no general recommendations for their use can be given [5]. There are