Development of Tearing in Preterm and Term Neonates

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Background: Although term and preterm infants have the capacity to secrete tears, the relative contribution of basal and reflex secretion of tears has not been previously assessed together in a prospective study. This information potentially has practical clinical importance.

Objectives: To measure basal and reflex tear secretion in preterm (30-37 weeks after conception) and term (38-42 weeks) newborns and to determine the developmental pattern of tear production.

Methods: Tear secretion was evaluated by applying Schirmer tear test strips to the inferior fornix for 5 minutes before (reflex plus basal secretion) and after (basal secretion) applying a topical anesthetic agent.

Results: Seventy infants (36 preterm and 34 term) were tested. Mean (± SD) basal tear secretion was 6.2 (± 4.5) mm in preterm and 9.2 (± 4.3) mm in term infants and increased progressively with increasing weight ($P<.001$) for all newborns. Mean (± SD) reflex tear secretion was 7.4 (± 4.8) mm in preterm and 13.2 (± 6.5) mm in term infants and also increased with increasing weight ($P<.001$) for all newborns.

Conclusions: Preterm infants have reduced reflex and basal tear secretion. This may mask the diagnosis of a nasolacrimal duct obstruction, concentrate topically applied medications, and allow corneas to quickly become dry during ophthalmological examination and treatment. By term, tear production in newborns is similar to that in adults.


AFTER YEARS of disagreement, studies by Apt and Cullen and others established that full-term newborns produce tears normally and that preterm infants also have the function to secrete tears. Studies have not been conducted, however, to differentiate between basal and reflex tear secretion. This differentiation may help in the early diagnosis of tear deficiency diseases such as familial dysautonomia or congenital absence of the lacrimal gland.

This differentiation also has a number of practical applications if newborns are found to have little reflex secretion. Topical medication may not be adequately diluted by reflex tear production, allowing the medication to remain more concentrated. This could lead to systemic toxic effects, as has been seen with phenylephrine and other medications.

Also during ophthalmological examination or the treatment of intraocular structures, corneal clarity may quickly decrease because of insufficient basal or reflex tear production, thus requiring more than the usual supplemental lubrication. Without sufficient tearing, nasolacrimal duct obstruction may go unnoticed because of the lack of overflowing tears.

We, therefore, wanted to evaluate tear production prospectively in preterm and term neonates and to differentiate basal and reflex secretion.

RESULTS

The 36 preterm infants had a mean post-conceptional age of 30.7 (± 3.3) weeks with a range of 25.4 to 37.0 weeks and a mean weight of 1495 (± 569) g with a range of 583 to 2700 g. Their mean basal tear secretion was 6.2 (± 4.5) mm, and mean reflex secretion was 7.4 (± 4.8) mm. Correlation analysis of basal secretion with either weight or postconceptional age was significant ($P<.004$). Correlation analysis of reflex secretion in preterm infants with weight or postconceptional age was not significant ($P>.27$).

The 34 term infants had a mean weight of 3402 (± 429) g. Their mean basal tear secretion was 9.2 (± 4.3) mm, and mean reflex secretion was 13.2 (± 6.5) mm. In this group, reflex tear secretion sig-
PATIENTS AND METHODS

Seventy infants were examined. Of these, 34 infants were term (born 38-42 weeks after conception) and 36 were preterm (postconceptional age <38 weeks). The mean (± SD) postconceptional age of the preterm newborns at the time of investigation was 33.3 (± 2.3) weeks (range, 30-38 weeks). The term newborns were studied at a mean (± SD) of 39.1 (± 29.4) hours after birth (range, 3-100 hours). All infants were born and studied at the Harbor–University of California–Los Angeles Medical Center, Torrance, when medically stable. Infants with any ocular abnormality, such as conjunctivitis or retinopathy of prematurity, were excluded. Before the study, informed consent was obtained from each infant’s mother in accordance with the Human Subjects Committee of the Harbor–University of California–Los Angeles Medical Center.

Testing was done at various times during the day with the infants supine. All examinations were conducted in moderate room lighting. Both eyes were tested consecutively. First, the external eye structures were inspected to rule out any abnormalities. Excess moisture on the eyelid margin was dried with a sterile cotton tip applicator. A prepackaged standardized sterile Schirmer tear test strip (Alcon Laboratories Inc, Fort Worth, Tex) was bent at the notch, and the rounded wick end was placed over the lower eyelid margin in the inferotemporal area. Care was taken to avoid contact between the cornea and the filter strip. The eyes were allowed to close around the strip. After 5 minutes, wetting of the strips was measured and recorded in millimeters as “reflex plus basal secretion.”

To measure basal tear secretion, a drop of topical anesthetic agent (0.5% proparacaine hydrochloride) was instilled in each eye. Excess moisture on the eyelid margin was dried with a sterile cotton tip applicator. After waiting 3 minutes, a standardized sterile Schirmer tear test strip was placed in the inferotemporal area of the lower eyelid margin. After 5 minutes, wetting was measured and recorded in millimeters as “basal secretion.” The amount of reflex secretion was calculated from the difference between the measurement of basal secretion and reflex plus basal secretion.

The measurements of basal and reflex tear secretion were statistically evaluated using correlation analysis and the unpaired 2-tailed t test. Because the measurements for each parameter were not statistically different when comparing right and left eyes, the mean value for the 2 eyes of each infant was used.

Results are presented as means (± SDs).

Significantly correlated with weight (P=.05), whereas basal secretion did not.

The mean values of both basal and reflex secretion were significantly greater in the term than the preterm infants by an unpaired 2-tailed t test (P=.006 and .001, respectively).

For all 70 infants, basal secretion, reflex secretion, and total tear production correlated with weight (P=.001 for all). These relationships are depicted in Figure 1, Figure 2, and Figure 3. There was no significant correlation between the basal secretion and reflex secretion measurements in individual infants (P=.82). No statistical differences were found between females and males and among infants of different racial origins.

COMMENT

Controversy has existed regarding the ability of newborns to produce tears. Mutch thought that infants do not produce tears until a few weeks after birth. Sjogren measured tear production after irritation to the nose with a pencil and reported that 13% of term newborns produced no tears, whereas 65% had a subnormal level. In premature infants, he found that even with nasal irritation, 37% had no tear production, whereas 93% had a subnormal value. Sjogren thought that tear secretion increased with maturity. McEwen thought that reflex secretion expressed after ocular irritation was decreased in newborns and did not develop fully until 1 to 7 weeks after birth. Apt and Cullen found that 82% of their non-crying full-term infants had normal tearing (defined as

Figure 1. The relationship between basal secretion of tears and weight in neonates.

Figure 2. The relationship between reflex secretion of tears and weight in neonates.
at least 15 mm of wetting of the tear test strip in 5 minutes) at 1 day of age, with the number increasing to 93% by the end of the first week of life. They also found that the incidence of normal tear secretion in the group of non-crying preterm infants was proportional to body weight. Of infants weighing less than 1500 g, 14% had normal lacrimation; of infants weighing 1500 to 2000 g, 44% had normal tear secretion; and of infants weighing 2000 to 2500 g, 63% had normal lacrimation.

Similarly, Patrick\(^8\) reported that 84% of 212 term infants in Australia displayed normal tearing (>15 mm of wetting of the tear test strip) without ocular or nasal irritation. The tearing of the 10 premature neonates in the study by Patrick (34-36 weeks after conception), however, was reported not to differ from that in the term neonates. More recently, Spiegler and Mayer\(^9\) investigated only basal secretion (after administering a topical anesthetic eyedrop) in 50 term and preterm infants in Germany. They reported that mean (± SD) basal tear production measured 5 (± 3) mm in 5 minutes and “was independent of the absolute age of the babies, of birth weight, [and] of the degree of maturity.”

Not all investigators agree on the distinction between reflex and basal secretion.\(^10\) Some think that nearly all tearing is reflex, although some tearing is produced when no stimulation occurs. Reflex secretion may not be totally eliminated by topical anesthesia because stimulation of the eyelid margin and lashes may still lead to tearing. During testing of the infants, the tear test strips were left in place to minimally irritate the eyelids.

It is helpful, however, to consider total tear production as the relative sum of basal and reflex secretion. In neonates with very low birth weights, both basal and reflex tearing were decreased relative to older infants, but the reflex secretion did not increase significantly over the preterm weeks of development. Thus, although there is a small amount of tear production, these very small newborns will not secrete much additional tears in response to the irritation generated by an eyedrop, eyelid speculum, or cryoprobe.

The topical application of medications may have an increased local effect on preterm infants. The low level of basal tear secretion and reduced reflex tear secretion in response to irritation will limit the dilution of topical medication, allowing medication in the tear film to become more concentrated than in older children and adults. This concept may explain, at least partially, the exaggerated effects that some medications have in preterm infants. Isenberg and Everett\(^2\) demonstrated that commercially available concentrations of phenylephrine hydrochloride as low as 2.5% can raise the blood pressure in low-weight neonates by more than 50%. Isenberg et al\(^3\) reported that applying cyclopentolate hydrochloride eyedrops in the 0.5% concentration can affect gastric acid volume and secretion in preterm neonates.

Other mechanisms also contribute to the exaggerated systemic response to topical medications in neonates. Obviously, the overall smaller body mass of an infant will respond more to the volume of a single drop of medication compared with an adult. The thin keratin layer of infantile skin and the thin skin of the eyelids will more readily permit absorption of topical medications spilling out of the eye onto the eyelids.

The retina of a preterm infant often is examined to rule out retinopathy of prematurity. During this examination, the cornea is fully exposed by the use of an eyelid speculum and may become dry and somewhat opaque. Based on the data in this study, examiners should anticipate that the cornea of preterm infants will dry faster than that in more mature infants because of a relative lack of tear production. They should, therefore, be prepared early in the examination to provide adequate lubrication to the cornea.

The diagnosis of nasolacrimal system obstruction disorders in preterm infants may be obscured by their decreased tearing function. With decreased tearing, overflow tears may then not appear. This circumstance explains why a preterm infant with a congenital mucocele (dacryocele or amniocele) of the lacrimal sac may not have excessive tearing or a conjunctival discharge. A frequent presenting symptom is an expanding mass.\(^11\)

In considering the diagnosis of certain diseases in infants, it may also be helpful to differentiate basal and reflex secretion. One of the characteristics of familial dysautonomia is a lack of both basal and reflex secretion.\(^12\) Congenital absence of the lacrimal gland, however, affects reflex more than basal secretion.\(^13\) Hereditary congenital alacrima is a rare disorder in which both basal and reflex tearing is markedly reduced.\(^14\) The data provided by this study may permit earlier diagnosis of these disorders.

By term, an infant appears to have a level of tear production comparable to that in adults. In the term infants, using a tear test strip for 5 minutes, we found a mean basal tearing of 9.2 mm, reflex tearing of 13.2 mm, and total tearing of 22.4 mm. Using similar methods, Henderson and Prough\(^15\) found the total tearing in 27 subjects between 16 and 25 years old to measure 18.0 mm for the men and 22.1 mm for the women. Wright and Meger\(^16\) reported total tearing in 98 eyes of persons between 10 and 39 years old of 17.5 mm. Lamberts et al\(^17\) reported basal tearing of 7.7 mm and reflex tearing of 11.9 mm in 86 adult eyes.

In newborns, basal and reflex tear secretion are at low levels in preterm infants and increase substantially
as they grow and mature. In the preterm period, basal tearing increases more than reflex tearing, whereas the opposite is true for the term period (38-42 weeks after conception). By term, basal and reflex tear production is similar to adult levels. Compared with older children, the low level of tears evident in early preterm newborns may allow topical eye medications to remain more concentrated, cause the cornea to become dry and opacified faster during ocular examination and treatment, and mask nasolacrimal system obstruction disorders.

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REFERENCES


A look at the past . . .

Theses findings, together with the exophthalmus, indicated plainly a tumor deep in the orbit. All evidence of an inflammatory process, fever, pain, redness, and swelling, was wanting, and orbital aneurism could be excluded by the absence of pulsation and bruit. Taking the age of the child into consideration, the first thought would be of a tumor of the optic nerve.