

Anesthesia for Neonatal Circumcision: Who Benefits?

Author: Howe, Robert S Van, MD, FAAP

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Full Text: Headnote ABSTRACT: As the medical myths used to justify the practice of neonatal circumcision have each been disproven, the latest "myth" used by circumcisers to perpetuate the surgery is that the use of topical and local anesthetics "eliminates" the pain of neonatal circumcision. While some interventions have reduced the amount of crying during the surgery, it is not clear whether topical or local anesthetics reduce pain substantially. Their impact on the stress of the surgery appears to be minimal. If these attempts at pain relief are not very beneficial for the infant, are they employed to make the circumciser and the parents feel better about what they are doing to the newborn? If these methods are not effective, why is there currently a call for their routine use? INTRODUCTION For most of this century, physicians have been performing procedures and surgeries on newborns without anesthesia with the mistaken notion that newborns were not neurologically complex enough to experience pain. Although this myth has been dispelled[1] the most common surgery in the newborn period, circumcision, continues to be performed, in the majority of cases, without any attempt at pain relief. In 1994, only 4% of obstetricians under 34 years of age used anesthetic for circumcisions. Overall the rate of anesthetic use was 14% among obstetricians with 20% of the female obstetricians using anesthetic.[2] As routine circumcision comes under attack, the most recent backlash against the anti-circumcision crusade is advocating local and topical anesthesia. Like most information used to perpetuate neonatal circumcision, it is a mixture of well-collected data and hyperbole. This article will review the medical research regarding topical and local anesthesia for neonatal circumcision and what information should be given regarding its effectiveness. CIRCUMCISION HURTS-A LOT! If there is a bright side to this topic, performing this extremely painful procedure without anesthetic has allowed researchers to study the parameters of extreme pain in experiments that would not have been allowed on laboratory animals.[3] The most evident expression of pain and stress in the newborn is crying. The amount of crying and pitch of the cry can give an indication of the degree of pain and stress.[4] Facial expressions have also been found to be a reliable measure of distress. Electrophysiological measurement of cardiac activity assesses the reactivity and regulation of the autonomic nervous system. This direct measure of vagal tone is a very sensitive measure of stress.[5] Vital signs, such as heart rate, blood pressure, and oxygenation levels all change with pain and stress and are easily measured. Cortisol levels assess the hypothalamic-pituitary-adrenocortical response to pain and stress. A recent development has been measuring salivary cortisol levels, so the stress and pain of drawing blood are no longer confounding factors.[5] Omitting any of these parameters will give a less than complete picture of neonatal stress reactivity.[5] Cortisol may be the consistently studied parameter. A positive correlation has been demonstrated between the average behavioral state and crying during circumcision and increase in serum cortisol levels.[6-7] Cortisol may also effect the type of sleep babies experience. Quiet sleep, which investigators call a shallow, restless sleep, was negatively correlated with cortisol levels prior to circumcision. Quiet sleep increased significantly following circumcision, with the greatest increase in quiet sleep corresponding to the period of the most rapid drops in cortisol levels.[8] Vagal tone is significantly reduced during the severe stress of circumcision. These reductions were paralleled by significant increases in the pitch of the infant's cries. In addition, individual differences in vagal tone measured prior to circumcision surgery are predictive of the physiological and acoustic reactivity to subsequent stress. For example, those with the highest vagal tone prior to circumcision experienced the greatest drop in vagal tone. Those with a low vagal tone before circumcision had little or no drop in vagal tone (they stayed low).[4] Crying duration, as opposed to cry acoustics, may not be as reliable a measure of stress

and pain as vagal tone and cortisol levels. While cry acoustics and vagal tone are correlated, cry duration is not significantly correlated with vagal tone.[4] Similarly, when the effect of pacifier use during circumcision was investigated, cry duration was decreased, but it had no effect on cortisol levels. While previous studies had shown a correlation between crying duration and cortisol levels, this correlation could not be demonstrated with use of a pacifier. While studies without a pacifier found cry duration was predictive of behavioral state following circumcision, the pacifier study did not find this correlation.[7] During the circumcision, a baby's blood oxygen level drops.[9] His heart rate, respiratory rate, blood pressure, and cortisol level (a measure of stress) shoot up.[5-8,10] His cry takes on a surprisingly high-pitched character seen only when a baby experiences excruciating pain.[4,11] He may completely dissociate, a response that is similar to severe post-traumatic stress disorder,[12] and become quiet-giving up because no one has rescued him. How could a circumciser watch this drama unfold in front of him and believe the baby was not experiencing pain? The standard excuse was that the baby was not feeling pain from the surgery, but rather he was crying from being strapped into the circumcision restraint. Experimental evidence does not support his contention. Infants strapped in a circumcision restraint for 20 minutes showed no appreciable change from baseline plasma cortisol levels 30 minutes later.[13] The same study found drawing blood from the baby's heel significantly increased plasma cortisol levels. A boy's sleep pattern is altered following circumcision. The average sleep state demonstrates a shift with light sleep increasing and deep sleep decreasing in the post-circumcision period.[6-7,14-15] Infants who are circumcised have been observed to suck harder, faster, and more vigorously at their bottles, making them less available to their surroundings, and less able to interact with their mother.[16-17] In babies who breastfeed, feeding deteriorates following circumcision.[18] When circumcised males were compared to intact boys and girls, they show less active sleep time, more time awake and agitated (active awake and crying awake), a greater drop in heart rate, and longer latencies to sleep.[19] Monitoring heart rate, salivary cortisol levels, and behavioral states before and after a mildly stressful behavioral assessment procedure, males were found to have increased cortisol levels following the assessment compared to the females. There were no sexual differences on the behavioral assessment with the exception that females had better motor performance than males. The increase in heart rate following the assessment was significantly higher in boys who had been circumcised prior to the assessment. The circumcised boys also had a lower mean heart rate prior to the assessment, suggesting a higher vagal tone.[20] Boys circumcised using anesthesia had a significantly lower vagal tone during a heelstick more than 24 hours after the circumcision than intact boys.[5] Nonoptimal birth conditions in otherwise healthy full-term infants have been demonstrated to persist for at least the first six months of life.[21] In a study in Toronto, circumcised boys were found to cry longer and louder when receiving their immunizations at 4 to 6 months of age than those left genitally intact.[22] When the study was repeated, the results were similar.[23] The authors stated, "Because memory of pain is believed to be important in subsequent pain perception, and the main structures for memory are functional in the neonatal period, it is conceivable that pain from circumcision may have long-lasting effects on pain response and/or perception." [22] PAIN RELIEF In an effort to alleviate the pain of circumcision, a number of interventions have been assessed. These include comforting measures, sucrose nipple, acetaminophen, dorsal penile nerve block, topical anesthesia, injection of local anesthesia, alternative restraints, and different circumcision methods. Schoen and Fischell suggest that, "Any method to relieve pain in newborn circumcision must be almost risk-free to be acceptable." [24] COMFORT MEASURES Marchette's group looked at non-medical nursing interventions to alleviate the pain associated with circumcision. Unfortunately, in the first study the two interventions looked at were unable to offset the effects of circumcision pain.[25] Similarly, in the second study the comforting measures of classical music, intrauterine sounds, pacifier, music and pacifier, intrauterine sounds and pacifier had little or no impact on changes in heart rate, rhythm, dysrhythmias, blood pressure, transcutaneous oxygen, rate pressure product, or behavioral state.[26] SUCROSE NIPPLE Blass and Hoffmeyer discovered that ten control infants who underwent a standard circumcision procedure without intervention cried 67% of the time while a water-moistened pacifier

reduced crying to 49% in ten others, and crying was reduced further to 31% in the last group of ten infants by providing infants with a sucrose-flavored pacifier to suck.[27] As mentioned earlier, cry duration is probably the least reliable of the pain and stress indicators in newborns. Gunnar et al. found that while nonnutritive sucking effectively reduced behavioral distress during neonatal circumcision and time spent crying, it was not associated with a reduction in the adrenocortical response.[6,28] In a study looking at the effectiveness of sucrose as an analgesic agent during routine immunizations it was ineffective after two weeks of age. Sterile water worked equally well as sucrose in the two-week olds.[29] The small number of patients in Blass and Hoffmeyer's study, and relying on the least reliable parameter of pain and stress, make their results suspect. Speculation that sucrose releases endorphins has no scientific basis, but has been promoted by circumcisers.[30] If sucrose releases endorphins, why doesn't it work in older infants? ACETAMINOPHEN A prospective, randomized, double-blind, placebo-controlled, clinical trial of acetaminophen analgesia prior to Gomco circumcision demonstrated that acetaminophen produced no clinically significant differences between those treated and those not treated. Postoperative comfort scores showed no significant differences between the groups until the 360-minute postoperative assessment, when the acetaminophen group showed improved scores.[18] Although acetaminophen was not effective in ameliorating either the intraoperative or the immediate postoperative pain of circumcision, circumcisers still recommend its routine use.[31] DORSAL PENILE NERVE BLOCK Dorsal penile nerve block is a nerve block of the dorsal penile nerves at the base of the phallus with local anesthesia. It was introduced by Kirya and Werthmann in 1978.[32] The positive effects of this intervention were quickly replicated by other investigators.[17,33-34] In controlled studies blinded surgeons could usually identify which boys had been anesthetized.[17,34] When compared to controls, boys who received a dorsal penile nerve block had smaller drops in oxygen saturation, and smaller increases in blood pressure and heart rate, but even with a dorsal penile nerve block the oxygen saturation, blood pressure, and heart rate changed significantly from baseline values.[34-38] Crying time is also lowered by dorsal penile nerve block.[35-37] One study comparing circumcision without anesthesia, circumcision with dorsal penile nerve block, and calcaneal heel puncture found no difference in observational pain scores using a modified Gronigen Distress Scale and the Children's Hospital of Eastern Ontario Pain Scale.[39] The effect of dorsal penile nerve block on cortisol levels has been inconsistent. A study of 11 boys given dorsal penile nerve block and 13 given no anesthesia found both had a significant rise in cortisol levels 30 minutes after the surgery. When compared to six boys not circumcised, both groups had significant increases in their cortisol levels.[40] Another study of 10 boys receiving dorsal penile nerve block and 10 receiving no anesthetic found no difference in 30 minute cortisol levels.[41] In another study of 20 boys given a dorsal penile nerve block and 20 boys given normal saline, treated boys had 30 and 90 minute cortisol levels below those of the saline treated boys.[42] While dorsal penile nerve block blunted the cortisol response to circumcision, those who underwent the procedure still had a significant rise in their cortisol levels when compared with baseline levels. This group of investigators had previously shown that the injection itself did not increase stress reactions and did not offset the beneficial effects of anesthesia. COMPLICATIONS FROM DORSAL PENILE NERVE BLOCK A retrospective chart review of 1022 cases of circumcision where dorsal penile nerve block was used revealed 12 complications (1.2%). Eleven boys had small ecchymoses at injection sites and one had excessive bleeding from the needle stick. No cases of lidocaine toxicity, voiding delay, or vascular compromise were noted. There was a trend toward an increased incidence of injection-site hematomas with the Plastibell as compared with the Gomco technique.[43] In a prospective study of 491 boys who received dorsal penile nerve block, 11% had bruising at the injection site while 2.6% had a bruise of greater than 1 centimeter and 0.2% had a hematoma.[44] Three reports of complications from dorsal penile nerve block have been found in the literature. In the first, two boys, aged 13 months and 3 years received bupivacaine to induce a dorsal penile nerve block to supplement general anesthesia. Both boys developed gangrene of the skin of the glans penis.[45] The second report involved blanching of the phallus when lidocaine with epinephrine was inadvertently used. [46] Finally, Mandel reported a case of methemoglobinemia following a circumcision in

which prilocaine was used to perform a dorsal penile nerve block.[47] The choice of prilocaine, rather than the dorsal penile nerve block was most likely the reason for this complication. WHY IS DORSAL PENILE NERVE BLOCK INEFFECTIVE? A survey of family physicians found that they felt dorsal penile nerve block was effective only 70% of the time.[48] The dorsal penile nerve supplies the dorsal surface of the penis with sensation. In most, but not all males, it provides sensation to the ventral surface of the penis along with the pudendal nerve. A significant number of males have sensation of ventral surface of the penis provided by only the pudendal nerve.[49] As a result, the ventral surface, which includes the frenulum, the most densely innervated portion of the penis,[50] may not be anesthetized by a dorsal penile nerve block. This is supported by the observation that local (distal) anesthetic was more effective than dorsal penile nerve block in the portions of procedure that involved the ventral surface of the penis.[41] TOPICAL ANESTHESIA Topical anesthesia involves applying anesthetic agent over the end of the penis prior to amputating the foreskin. Most of the experience has been with a eutectic mixture of local anesthetics (EMLA), but lidocaine cream has also been used. A double blind trial of 20 treated boys and 24 placebo controls found that 4% lidocaine cream lowered the increase in heart rate but had no effect on increases in respiratory rate or decreases in oxygen saturation. Crying time was decreased. When compared to baseline levels, heart rate, respiratory rate, and crying time were all increased whether or not anesthetic was used. Oxygen saturation dropped significantly from baseline levels as well.[51] A study of 15 boys given 30% lidocaine cream and 15 boys given placebo showed stress related behaviors were greater in the placebo group. Serum beta-endorphin concentrations increased postoperatively in 11 of 15 subjects receiving placebo, but decreased or remained unchanged in 10 of 15 subjects receiving lidocaine. Reporting the beta-endorphin data in this fashion may have been a bit disingenuous as the change in beta-endorphins was not significantly different for either the treated or placebo groups, and actually rose in the treated group.[52] In a study using EMLA on 14 full-term males and 14 placebo controls, all boys showed significant increases in heart rate crying, facial activity, and decreased oxygen saturation. When the two groups are compared, EMLA blunted the change in heart rate, oxygen saturation, facial activity, and crying. None of the interventions eliminated the distress of the procedure.[53] A review article addressing the question of whether EMLA should be used prior to circumcision in newborn infants concluded that, "There are insufficient data to support the use of EMLA cream for circumcision in newborn infants at this time. There are no studies that adequately address safety or efficacy. Before efficacy studies can be evaluated, pharmacodynamic studies need to be completed." [54] In a study financially supported by Astra Pharma, the company that manufactures EMLA, Taddio et al. compared 38 boys who received EMLA prior to circumcision to 30 boys who had placebo applied. This study recorded crying time, heart rate, blood pressure and facial activity. There was no difference noted in changes in systolic or diastolic pressure. Heart rate increases and cry duration were greater in those treated with placebo. When facial activity score was assessed during the 13 stages of the surgery, no difference between EMLA and placebo was demonstrated during 69% of the stages. During the stages where EMLA performed better than placebo, the facial-activity scores were significantly above baseline.[55] In spite of these findings, the authors concluded that EMLA cream was "efficacious and safe," which reflects the source of their funding more than the data. WHY IS EMLA INEFFECTIVE? The anatomy may explain the poor results. To be effective, the EMLA would have to penetrate the outer epidermis, dermis, dartos fascia, mucosal lamina propria, and fused inner prepuce mucosa/glands penis mucosa to anesthetize the free nerve endings of the glans penis.[56] In Taddio's study, the four steps of the surgery where EMLA was more effective than placebo were those in which only the prepuce was involved.[55] Any steps that involved the glans, or the fused preputial/glanular mucosa, EMLA was no more effective than placebo. This suggests that EMLA, at the dose and duration used by Taddio, did not achieve adequate penetration. IS EMLA SAFE FOR NEONATAL CIRCUMCISION? EMLA is not approved by the FDA for use in children under one month of age. One of the ingredients in EMLA, prilocaine, has been linked with methemoglobinemia.[47,57-58] Applying EMLA to piglet penes showed no significant increase in methemoglobin levels.[59] In infants less than three months of

age, applying two grams of EMLA for eight hours resulted in methemoglobin levels of 2.24% (range 0.95%-3.37%, above 1% is considered abnormal).[60] Methemoglobinemia has been reported in a full-term newborn boy who had EMLA applied prior to circumcision. His methemoglobin level was 16%. He had received only 40% more than the recommended dose.[61] While the Taddio study found EMLA was not toxic in their patients, it was not very effective. On the basis of on the literature published to date, the doses of EMLA used in neonatal circumcision have been safe but ineffective. Larger doses of EMLA may be needed to provide pain relief, but even a 40% increase in the dose has been demonstrated to be toxic.

LOCAL ANESTHESIA One study compared the effectiveness of differing sites for injecting lidocaine and found that dorsal penile nerve block at the nerve root had better results than when injected at the suprapubic space or the distal branches. The differences were only minor when heart rate and oxygen saturation changes were looked at. The biggest difference was in the percentage of infants crying. Cortisol levels and vagal tone were not assessed.[62] In a study comparing dorsal penile nerve block, local (distal) injection of lidocaine, and no anesthetic, dorsal penile nerve block and local anesthesia demonstrated smaller changes in heart rate, oxygen saturation and crying than no anesthetic. The changes were smaller with local anesthesia than with dorsal penile nerve block. Cortisol levels 30 minutes after circumcision were lower in the local anesthetic group than in those receiving dorsal penile nerve block or no anesthetic.[41] While local anesthetic has been reported to cause gangrene of the penis[63] and impotence[64] in older males, there have been no adverse effects reported using this technique in newborns.

ALTERNATIVE RESTRAINTS A pediatrician from Ashland, Wisconsin, who routinely uses dorsal penile nerve block, found that when the babies she circumcises are swaddled in a blanket, they cry less than those restrained on a circumcision restraint board. [65] Similarly, an abstract published in Pediatrics found that when a specially designed physiological circumcision restraint chair or a 24% sucrose solution were used in conjunction with dorsal penile nerve block, behavioral distress scores were lowered but there was no effect on 30 minute cortisol levels.[66]

CIRCUMCISION METHOD While no difference was found between the Plastibell and the Gomco clamps in their aversiveness or stressfulness to the newborn,[8] a modified Gomco procedure, where the prepuce is removed as soon as the clamp is secured, resulted in higher cortisol levels than when a standard Gomco procedure, where the clamp is left in place for 5-6 minutes before amputating the prepuce. The modified procedure was also associated with more behavioral arousal.[7] The modified Gomco procedure was adopted to shorten an already short procedure, to lessen the time spent by the physician performing it. A couple of mohels have promoted the traditional Jewish bris as "the fastest most humane method" for performing circumcision, which usually takes less than 10 seconds.[67-68] They offer no references for their claims, and the 10 seconds does not include the lysis of fused preputial/glanular mucosa. In the literature that accompanies the Mogen clamp, it is claimed to be "The least painful method of circumcision." [69] There are no published studies to support this claim. In a poster presentation, use of the Mogen clamp during circumcision in conjunction with dorsal penile nerve block showed less of a heart rate increase and less crying time than using the Gomco clamp in conjunction with dorsal penile nerve block. Procedure time was shorter with the Mogen clamp and lasted an average of 90 seconds.[70]

DISCUSSION With the medical justifications for neonatal circumcision crumbling in succession,[71-75] circumcisers need to erect a new barrier so the public is shielded from the barbarity of removing the most neurologically complex portion of the penis.[50] Now that neonates do feel pain, and may actually feel more pain from a given stimulus than older infants,[1] circumcision advocates such as Wiswell are finally admitting that, "The current method of performing the procedure [circumcision] is still all too often barbaric." [31] But as the previous circumcision myths fade away, they need to be replaced with new myths for circumcision to continue. The new myth is that topical and local anesthetic make the surgery "painless." In the same editorial, Wiswell praises the Taddio EMLA study as "the best of approximately 20 studies." [31] Some investigators have stated that dorsal penile nerve block "eliminates" the pain of neonatal circumcision,[62] when it is clear from the medical literature that the pain is not "eliminated." [76] When it was demonstrated that circumcision adversely affected pain-response months later, it was speculated that

anesthetics might make a difference.[22] The study was repeated to see if anesthetic altered the outcome. Anesthetic use at the time of circumcision did little or nothing to change circumcision's effect on later pain-response.[23] Despite this disturbing after-effect and lack of effectiveness of topical anesthesia, the authors of the study advocate more pain relief measures. They missed the more obvious solution: don't perform neonatal circumcisions.[77-79] Too much consideration has been given to cry duration. While crying makes the procedure more burdensome for the circumciser, it is not clear that methods that decrease crying relieve pain. Cortisol levels, an accurate measure of stress, are unaffected when measures that decrease crying are employed. It may be safe to say that swaddling and sucrose nipples are used for the benefit of the circumciser rather than the newborn. The transition from one set of unsubstantiated myths to another is a slow process, and even some of circumcision's strongest advocates have been reluctant to get on board.[80-81] In a 1990 survey of family practitioners, 29% believed that the pain response in circumcision was insignificant.[48] In a 1993 survey, a questionnaire mailed to physicians found that only 24% of physicians used any form of analgesia, the most common being oral ethanol (20%). Of those responding 12% believed that neonates do not feel pain, and 35% believed that neonates do not remember pain.[82] The circumcisers need to get these physicians "up to speed." With the old myths gone and the anesthetic myth not firmly rooted and widely disseminated, the American public may figure out that circumcision is unnecessary painful surgery performed on infants against their will. Although the interventions mentioned throughout this paper have been documented to be inadequate in relieving the pain and sequelae of neonatal circumcision, physicians offer these remedies, often giving the parents the reassurance that everything possible has been done for their baby. Again, the parents may obtain more relief from these measures than their baby. When parents are told that an anesthetic will be used during a circumcision, they often incorrectly assume that the anesthetic will completely remove the pain of the surgery. If an adult was offered topical therapy for genital surgery with the accurate information that it was effective during only 31% of the procedure, very few would volunteer. Most, if not all, would insist on general anesthesia. This lack of effectiveness of topical and local anesthesia has prompted the Australasian Association of Paediatric Surgeons to recommend delaying the procedure until 6 months of age when an experienced surgeon and a pediatric anesthesiologist are available.[83] While some would argue that some relief from an anesthetic is better than no anesthetic at all,[84] in an elective case that can wait until better (general) anesthesia can be employed, it is difficult to justify. Do we use ineffective anesthesia, that would not be acceptable to older children and adults, on newborns because of cost savings, or simply because we can get away with it? The 12th century rabbi and physician Moses Maimonides insightfully noted that ritual Jewish circumcisions are performed on the eighth day before adequate maternal-infant bonding can take place. Waiting longer would allow the stronger bonding between the baby and the mother to develop. With this bond in place, it would be unlikely that a mother would subject her son to circumcision.[85] In order to be fully informed, parents need to be told that the currently available pain relief techniques may blunt the pain, but, even with these techniques, neonatal circumcision is extremely painful and stressful. CONCLUSION These studies make it absolutely clear that newborns experience excruciating pain while undergoing circumcision. The use of local anesthesia may lessen the pain, but it does not make it go away completely. While interventions such as dorsal penile nerve block, EMLA cream, and sucrose flavored pacifiers appear to ameliorate the physiological parameters associated with pain, none of these studies compare these changes to boys, who, instead of being circumcised, were at their mother's breast nursing or sleeping. When compared to these infants, even the treated infants still showed physiologic changes consistent with extreme pain. Clearly, avoiding the procedure is less painful than any of the above interventions. While the immediate impact of the surgery may be somehow softened with anesthetics, the procedure's primordial barbarism cannot be completely concealed. The level of pain these neonates experience is definitely higher than those who have the procedure performed later under general anesthesia.[1] The major difference is that older boys and men can articulate the level of pain they experience. REFERENCES REFERENCES 1. Anand KJS, Hickey PR. Pain and its effects in the human neonate and fetus. N Engl J Med 1987; 317: 1321-9 2. Garry

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