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Pediatric Pain from Hypodermic Needles: History, Causes and Increasing the Efficacy of Pain Mitigation

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Venous access is one of the most innovative and effective medical technologies developed. It provides the ability to deliver medications that are distributed quickly throughout the body, while blood analysis is one of the primary diagnostic tools used by physicians. Hypodermic venipuncture is as vital as it is commonplace, but is a procedure of a particularly distressing nature for young patients. An inability to accurately track developing pediatric anatomy and the incomplete neurological development of younger patients results in a challenging environment for the clinicians and an often traumatic and painful one for the young patients. Although there have been methods suggested to mitigate these challenges, a safe and reliably effective solution has not been found or established as a patient standard of care. This review will cover the evolution and purpose of the procedure, considerations for pediatric physiological variations and current pain reduction methods. Finally, a high efficacy mitigation technique will be proposed, utilizing current neurological understanding based on primary literature sources.

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Venipuncture/Subdermal Access

Origin

The most obvious initial human understanding of blood flow likely came from stopping bleeding from an injury by recognizing and assisting the natural clotting process. Eventually, the concept developed that bleeding itself could be a treatment for illness. This forced and theoretically beneficial loss of the body's blood though a cut with a sharp instrument made in a vein of the arm, leg or other region was widely practiced from ancient Egypt to the late 19th century [1]. The bloodletting practice eventually overlapped with the concept of using the blood to distribute medication quickly and efficiently throughout the body. In 1656, Sir Christopher Wren used a goosequill and bladder apparatus to inject opium into the leg veins of dogs to study the effects of its intravenous introduction [2]. He found that it resulted in anesthesia and that the dogs recovered afterwards, in one of the first well-documented instances of medical delivery of a substance through the blood of a patient. Gradually, the usefulness of intravenous delivery became more developed. In Ireland, Dr. Francis Rynd is credited with the invention of the first hollow metal "needle," what we would call in today's medical terms a trocar [3]. This large tube with a beveled end was inserted transdermally, and (usually opioids) were allowed to flow by gravity alone into the patient. For obvious reasons, this device did not provide access to the circulatory system as even the lower pressure of veins would cause blood to flow out of the trocar, and for bleeding and blood quality inspection, a lancet was less traumatic. However, 1853 brought two versions of a pressurized column attached to a hollow metal tube, one in Scotland, introduced by Alexander Wood with a glass column and another all metal version in France by Charles Gabriel Pravaz [3]. The plunger pressurized chamber allowed not only for the injection of material subdermal and intravenously, but also new medical procedures such as the removal of fluids, allowing for the drainage of cysts, less invasive methods of small tissue sample collection, as well as the withdrawal of blood samples. The design of a hollow metal needle, cylinder and plunger of the popular model invented by Wood is still the basis for syringes today. In 1956, the veterinarian Colin Murdoch of New Zealand patented a plastic disposable syringe [4]. Initially, the plastic syringe was viewed with skepticism and the New Zealand Department of Health called the device too futuristic [4]. Today, the metal needle and clear graduated plastic syringe is found in almost every medical treatment setting.

Current Hypodermic Devices

Although there have been some design modifications, such as retracting needles to prevent inadvertent needle sticks, the overall hypodermic needle design remains extremely similar to Murdock’s 1956 model [5]. Further developments attempt to address pain, including a reduction of needle size to the size of microns distributed across an eluting gel to deliver medication through the skin without activating surface nociceptors, as well as new systems which can analyze other bodily fluids such as saliva to detect analytes normally found in withdrawn blood [6,7]. These are promising technologies, however hollow metal needles are cheap, sanitary, manufactured by the billions each year and are an established constituent of modern medical care; they have only one primary side effect of their use for patients, pain [8,9].

The Problem

Since the first development of the hypodermic needle, pain has attended the benefits of this medical tool. An acknowledgement of this complication is demonstrated by the early protocol to reduce pain, outlined in the 1862 Massachusetts Medical Society communication, “Hypodermic Injections,” by A. Ruppaner, where the importance of pressure to hold the skin tense, during needle insertion is described [10]. For reasons not clearly understood, these procedures appear to be particularly painful and distressing for children younger than eight years [11]. Hypodermic procedures are reported as those most feared by young cancer patients, who form a cohort unfortunately knowledgeable of many medical procedures, as well as by young patients undergoing inpatient venipuncture [9,12].

Pain in Child Patients

Pain is difficult to quantify and perception varies between patients [11]. Pain levels are even more difficult to determine when the patient cannot communicate well or is frightened [13-15]. When performing medical procedures on children, differences in anatomy and perception must also be taken into consideration and are often underestimated by clinicians [16]. Childhood development happens at vastly different rates for different children, further complicating care and location of vital structures [17]. Historically, there have been horrendous miscalculations of the impact of pain on neonates, resulting in analgesics being withheld during major surgery. This treatment was based on the misconception that pain was not perceived by the patient and in an attempt to protect the patients from complications due to the analgesics [18,19]. The difficulties understanding and treating pediatric pain continues today and are demonstrated by clinicians reporting an inability to accurately determine pain levels and discomfort administering pain medication [11].

Pediatric Physiology

In general, there is less physiological information available, and fewer studies on children than adults [16]. This is possibly due to the smaller pool of patients and ethical complications for studies involving subjects incapable of giving legal consent. However, there are known differences, including children having up to 3 times the skin surface area of adults while also having a small blood volume as stated by AA Figaji, 2017, in addition to the excerpt from their paper below.

"Brain metabolism in children changes with advancing age. It depends on progressive myelination and synaptogenesis and drives the substantial changes in CBF, especially in the first 8 years of life. Cerebral metabolism of glucose starts at low rates of around 60% of adults values at birth, but rapidly accelerates to over 200% adult values by age 5 before slowly decreasing to adult levels through adolescence." [16]

These drastic changes may explain differences in pain perception between children and adults and between children of different ages. It has repeatedly been found that younger children report higher levels of pain from venipuncture [20-22]. These physiological differences and studies show that adult pain experiences inadequately inform the judgement of children's actual pain levels from hypodermic access.

Effects on Patients

Pain has been viewed by the medical profession as an undesirable but minor side effect to many procedures, but is starting to be recognized as an adverse event that can and should be addressed for the best quality of patient treatment [23,24]. Beyond the immediate discomfort and trauma from the needle, if the level of distress is high enough, the pediatric patient may try to physically resist or lash out in self-defense [22,25]. If the clinician cannot rely on a calm and stationary patient, there is a higher risk of nerve puncture, as the median and radial nerves of the cubital region (bend of the inner elbow) are occasionally injured during venipuncture and the location of nerves in pediatric patients is not well identified [26,27]. In these situations, restraints are commonly used, although complete immobilization of the procedure site is not possible and there are significant psychological consequences for the patients [28-32]. In addition, repeated exposure to painful stimuli can lead to maladaptation of pain perception and pediatric patients exposed to many painful procedures report a lower tolerance for pain [33]. The pain experienced from venipuncture is the main source of children's anxiety, anticipation, and unpleasant memories associated with venipuncture and deserves greater recognition and mitigation [9,24,34,35].

Effects on Clinicians

While the most obviously effected party is the patient themselves, the toll on the healthcare workers should not be underestimated. While uncomfortable procedures cannot be eliminated from treatment, venipuncture specifically, holds such fear that in some cases the emotional stress, fear and at times violent resistance can lead to apathy or compassion fatigue in clinicians [25,36,37]. The solution to uncooperative patient behavior can include the previously mentioned use of immobilization restraints, their use impacting the clinicians by causing them to sometimes report feeling as if they had committed an assault [38]. Additionally, these encounters can be so extreme that the clinician starts to anticipate and fear the violent and defensive behavior, contributing to the charged procedure environment and in some cases resulting in significant psychological costs for the clinicians [31]. These effects are compounded by the lack of an accepted and effective standard of care that fully accounts for the impacts of pain on young patients and would provide clear guidance and expectations for clinicians [39].

Current Pain Mitigations

The methods below attempt to logically address the pain encountered and rely on generations of intuitive understanding of the pain perceptions of the human body. It is the hypothesis of this paper that these methods can be improved upon by application of current neurological research. None of the these methods alone or in combination presently constitute a widely accepted standard of care for pediatric venipuncture pain management [40].

Distraction – Is it Pediatric Behavioral Modification or Pain Relief?

Perceived pain in all human stages of development is understood to be a synthesis of the neurological system's interpretation of environment, memory, anticipation, and focus in addition to the physiological stimulation of nociceptor neurons [22,41]. While this theory applies to pediatric patients, within this theory, there is a potential for clinicians to lean heavily on the manipulation of psychological interpretations and awareness, rather than the physiological impacts of the procedures due to the limitations and absence of prevalent, standardized, and effective mitigations for the physiological pain [39,40]. While there are obvious correlations of memory and anticipation with pain perception, the relationship is inexact and varies between individuals [33,42]. This variability may possibly be due to the lack of studies that have been able to separate the event of distraction to the point of ignoring pain, encouragement of pain tolerance, consolation and comfort with actual pain reduction. Additionally, distraction appears to be especially ineffective in children 0-6 years of age, who report the greatest amount of pain from venipuncture [20,21,43].

Anesthetics – Pharmacological Nociceptor Intervention

One of the most obviously available tool to clinicians is the administration of a local anesthetic for the acute pain of venipuncture. A commonly used pharmaceutical for this purpose is Lidocaine/Prilocaine cream, which blocks the sodium ion channels present in neurons, preventing the transmission of the nociceptor signal [44]. The difficulty with this pain relief method stems from the necessary application of the analgesic to locations where they can effectively numb nociceptor nerves. Diffusion from a cream requires approximately one hour to be fully effective, and Prilocaine in rare cases can induce methemoglobinemia which can prevent proper oxygenation of body tissues [45-47]. An additional consideration is the depth of different types of pain nociceptor neurons. The diffusion of the cream must reach deeper levels from the surface and full pain mitigation efficacy is variable between individuals and application time [48]. This has been somewhat ameliorated by the use of gas pressure jet injections of anesthetic, such as with the patented J-tip device, however there is still discomfort from the jet injection and the introduction of a pharmaceutical into the patient may be of concern [49-51].

Local Application of Vibration and Low Temperature

Rubbing is an automatic response to a painful stimulus and the application of vibration has been used in a similar manner for pain relief, while cold produces a numbing effect. These two mechanisms are employed with the patented Buzzy device, which combines a small battery powered vibrating motor with attached ice packs [52]. Frequency output of the device is specified as "high" by the manufacturer and may be variable as the batteries drain [52]. Significant pain relief results during injections and venipuncture are mixed [53,54]. Sample sizes were small and control scenarios were not able to eliminate placebo or distraction effects and may account for some variability. While cold may have some effective numbing quality, its application here has been found to elicit changes in blood hematology that may compromise certain test results [55,56]. Real world application reviews appear to encounter a great deal of variability in efficacy, with particularly poor results in younger patients [57]. Interestingly, both vibration and low temperature are shown to cause vasoconstriction; the effect of this on pain perception is unclear [58,59].

Requirements for a Better Solution

The ideal pain mitigation for venipuncture in pediatrics, based on the use of the current hypodermic needle, needs to meet specific objectives to be successful in real world applications. Foremost, the withdrawn blood sample must not be compromised in any way that would affect analysis. There must be a high degree of pain mitigation efficiency, across ages or specific to age and individual differences. The pain mitigation must easily integrate into the procedure workflow, with the current number of procedural staff and not impair the clinician's phlebotomy protocol, which itself has implications in pain and injury prevention [60]. Preferably, there would not be pharmaceuticals introduced into the patient, as risks increase with the smaller weights of young children [50]. The mitigation should not require the attention or participation of the child for efficacy which limits the mitigation to older children and those with cooperative temperaments [20] . Additionally, the mitigation should not elicit fear or produce the feeling of loss of control for the patient [30,57]. Of the mitigations reviewed here, vibrational pain reduction is one area that offers effective pain relieving potential while best meeting the above specifications. Further, conceivable efficacy and functional improvements, based on an understanding of the underlying neurological mechanisms and clinician workflow, may facilitate standard of care integration superior to existing solutions.

The Mechanism of Vibration Pain Relief

Sensory Inhibition

The neurological phenomenon of sensory inhibition occurs to allow for the isolation and effective amplification of a stimulus. While the prompting stimulus results in a specific excitatory response, the body goes further to amplify the received stimulus by also inhibiting the background “noise” in the areas surrounding the initial stimulus processing area of the cerebral cortex [61]. This effectively creates a signal reductionvalley surrounding and isolating the initial excitatory response. This magnifies the difference from the surrounding baseline to the total degree of the stimulus response [61]. The exploitation of this inhibition is one factor in the efficacy of vibrational pain relief, where a certain stimulation’s inhibition flows across an area stimulated by pain sensation, resulting in an inhibition of pain processing and perception [62].

Manipulation of the Sensory Mechanism

As mentioned before, the perception of pain is complicated. Nociceptors are neurons responsive to pain and are located in most body tissues. These pain sensory neurons include two types, fast myelinated neurons, known as A delta fibers and slow, unmyelinated neurons, known as C fibers [63]. In *Dynamic Representations of the Somatosensory Cortex* by Tommerdahl, et al, it is demonstrated in animal models that the application of a 200Hz frequency effectively inhibits the perception of a 25Hz vibrational stimulus, evidenced by brain imaging cortical responses [62]. This effect is mediated by the stimulus being processed in two different, but neighboring areas of the brain, 3a and 3b for instance. It is shown the activation of one area by 200Hz (3b), creates an inhibitory surround that covers an activation area responsive to 25Hz (3a). As the 25Hz stimulus is at the frequency that activates nociceptor neurons, 200Hz will effectively interfere with the perception of pain in the study model [62]. Additionally, the same study identified time period and vibrational depth required to elicit this inhibitory response [62]. These findings demonstrate identified and specific conditions that could be implemented to improve the efficacy of vibration pain relief and warrants further investigation using age varied and human models.

Proposed Vibration Pain Mitigation

The development of vibration pain interventions can be informed by the application of the findings of neurological research. Specifically, by achieving a precise frequency shown to effectively inhibit the known pain perception activity [62]. Additionally, the most effective inhibitory frequency needs to be not only reached, but also maintained over the procedure and multiple uses. The vibration device proposed could be placed some distance from the acute pain site due to the large receptor field of the targeted mechanoreceptors [63]. This would effectively free the procedure area for normal phlebotomy protocol and familiar workflow. This slightly distant placement would lend itself to a hands-free design that could be attached to patients similarly a blood pressure cuff that is importantly already familiar to patients as a low pain procedure and clinician’s from normal patient protocol.

Remaining Questions

While hypothesis-driven research enables an informed approach to vibration pain mitigation, a number of important questions remain to be addressed. Does the animal study model behavior effectively correlate to results in young humans? Can a better understanding of pediatric physiology further reduce procedure pain? What is the onset time of the vibration pain relieving effect? What is the most effective size of vibration stimulated skin area, magnitude and distance from the acute pain site? Is consistent stimulus or pulse patterns more effective? Are corpuscles or withdrawn blood sample quality impacted from the applied vibrations? Does vibration initiated vasoconstriction have effects on the patient level of pain or the procedure? Can the device include the mitigation of pain during other procedures resulting in acute or chronic pain? After the investigation of these specifics, the real world efficacy and function of the device must additionally be confirmed by rigorous blinded studies to accurately determine the level of efficacy.

Conclusion

La estructura factorial de tres factores se mantuvo en la versión final del instrumento, con las siguientes características (ver Table 2 y .

Subdermal access to the body by hypodermic needle has been one of the most effective developments in medicine. This often lifesaving procedure has been assumed to be coupled to the discomfort that occurs during the process. When treating children, the pain from repeated transdermal access can become an underappreciated stressor. Not only does this affect the patients, but the clinicians who must contend with guilt, stress, and patients that sometimes protest violently.

Since the 1800's, efforts to reduce pain for hypodermic procedures has been in existence, but have been hindered by limited understanding and control of neurological sensory mechanisms. Improved, research based understanding of pain should motivate the evolution of pain mitigation methods to increase efficacy resulting in benefits for patients and clinicians.

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