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Medihoney

Medihoney, a brand of medical-grade honey derived from the Leptospermum species (commonly known as Manuka honey), has gained significant attention in the field of wound care and surgical applications due to its potent antibacterial, anti-inflammatory, and wound healing properties. Over the years, extensive research has been conducted to explore the efficacy of Medihoney in treating various types of wounds, including chronic ulcers, burns, and post-surgical wounds. This essay delves into the scientific basis for the surgical use of Medihoney, its mechanisms of action, clinical applications, and its potential advantages over conventional treatments.

Medihoney's antibacterial activity is one of its most well-documented properties, making it particularly valuable in surgical settings where infection control is paramount. The honey is produced by bees that forage on the Leptospermum plant, which imparts unique phytochemical properties to the honey, enhancing its antimicrobial effectiveness. The antibacterial action of Medihoney is attributed to several factors. First, its high osmolarity creates a hyperosmolar environment that draws moisture out of bacterial cells, leading to their desiccation and death. Additionally, Medihoney's low pH, typically around 3.5, is sufficiently acidic to inhibit the growth of many pathogenic bacteria. Another significant factor is the production of hydrogen peroxide through the enzyme glucose oxidase, which contributes to Medihoney's broad-spectrum antibacterial activity. Finally, Methylglyoxal (MGO), a compound found in high concentrations in Manuka honey, has been shown to possess potent antibacterial properties, particularly against antibiotic-resistant strains such as MRSA. These properties make Medihoney an effective agent for preventing and treating infections in surgical wounds, particularly in cases where antibiotic resistance is a concern.

Beyond its antibacterial properties, Medihoney has several mechanisms that promote wound healing, which are particularly relevant in a surgical context. Medihoney facilitates the autolytic debridement of necrotic tissue through its osmotic effect, which draws lymphatic fluid into the wound, softening and helping to remove dead tissue without the need for surgical intervention. Furthermore, the high viscosity of Medihoney creates a moist wound environment conducive to the healing process by promoting the migration of epithelial cells and reducing scab formation. Medihoney also reduces inflammation by drawing out excess fluid from the wound, which helps to decrease swelling and pain—an essential benefit in post-operative wound care where controlling inflammation is crucial for proper healing. By reducing bacterial colonization, Medihoney also helps control wound odor, which can be distressing for patients and caregivers.

The application of Medihoney in surgical settings has been explored in various studies, demonstrating its efficacy in both preventing and treating wound infections, as well as in promoting faster healing. Post-operative infections are a significant concern in surgical practice, often leading to complications such as delayed healing, prolonged hospital stays, and in severe cases, sepsis. Medihoney has been used effectively in the management of surgical wounds, particularly in preventing infection and promoting healing in contaminated wounds. Studies have shown that when applied to surgical sites, Medihoney reduces the bacterial load and facilitates faster healing, often with less scarring compared to conventional treatments.

Chronic wounds, such as pressure ulcers and diabetic foot ulcers, present a significant challenge in clinical practice due to their resistance to conventional treatments and their propensity for infection. Medihoney has been particularly effective in these cases, as demonstrated by its use in patients with spinal cord injuries who developed chronic pressure ulcers. In one study, 90% of patients showed complete wound healing within four weeks of treatment with Medihoney, with no negative effects reported. This underscores its potential as a non-surgical therapy for chronic wounds, reducing the need for more invasive procedures.

Burns are another area where Medihoney has shown considerable promise. Burns often become infected, complicating healing and increasing the risk of scarring. Medihoney has been used to treat both superficial and deep burns, with studies showing that it helps to control infection, reduce pain, and promote faster healing. Its ability to maintain a moist wound environment is particularly beneficial in burn care, as it helps to prevent the formation of dry, hard scabs that can impede healing.

The use of Medihoney in preventing infections related to peritoneal dialysis is another important application in surgical care. A study published in *The Lancet* reported that Medihoney was effective in preventing catheter-related infections in patients undergoing peritoneal dialysis. The study highlighted that Medihoney did not induce bacterial resistance, a significant advantage over traditional antibiotics like mupirocin, which have been shown to lead to resistance even when used topically.

Medihoney offers several advantages over conventional treatments, particularly antibiotics, in the management of surgical wounds. One of the most significant concerns in modern medicine is the growing problem of antibiotic resistance. Medihoney, with its broad-spectrum antibacterial activity, offers an alternative that does not contribute to this issue. This makes it particularly valuable in the treatment of wounds infected with multi-drug-resistant organisms. Medihoney is a natural product with a long history of use in traditional medicine. Its safety profile is well-documented, with very few adverse effects reported in clinical studies, contrasting with the potential side effects and complications associated with synthetic antibiotics and antiseptics. In many cases, Medihoney can be a more cost-effective option compared to conventional treatments. Its ability to promote faster healing and reduce the need for surgical interventions can lower overall treatment costs. Many patients prefer treatments that are perceived as natural or less invasive. Medihoney fits this preference, which can improve patient compliance and overall satisfaction with treatment.

The use of Medihoney in surgical applications represents a significant advancement in wound care, combining ancient knowledge with modern medical practice. Its potent antibacterial properties, coupled with its ability to promote wound healing and reduce inflammation, make it an invaluable tool in the management of surgical and chronic wounds. As the threat of antibiotic resistance continues to grow, the role of Medihoney and other natural therapies in surgical care is likely to expand, offering clinicians effective alternatives to traditional treatments. Continued research and clinical trials will be essential in further defining the scope of its applications and optimizing its use in surgical practice.

References:

1- Acton C. Medihoney: a complete wound bed preparation product. Br J Nurs. 17(11), S46-8, 2008
2- Biglari B, vd Linden PH, Simon A, Aytac S, Gerner HJ, Moghaddam A. Use of Medihoney as a non-surgical therapy for chronic pressure ulcers in patients with spinal cord injury. Spinal Cord. 50(2):165-9, 2012
3- Müller P, Alber DG, Turnbull L, Schlothauer RC, Carter DA, Whitchurch CB, Harry EJ. Synergism between Medihoney and rifampicin against methicillin-resistant Staphylococcus aureus (MRSA). PLoS One. 8(2), 2013
4- Biglari B, Moghaddam A, Santos K, Blaser G, Büchler A, Jansen G, Längler A, Graf N, Weiler U, Licht V, Strölin A, Keck B, Lauf V, Bode U, Swing T, Hanano R, Schwarz NT, Simon A. Multicentre prospective observational study on professional wound care using honey (Medihoney™). Int Wound J. 10(3):252-9, 2013
5- Van Biesen W, Jörres A. Medihoney: let nature do the work? Lancet Infect Dis. 14(1):2-3, 2014
6- Cooper R, Jenkins L, Hooper S. Inhibition of biofilms of Pseudomonas aeruginosa by Medihoney in vitro. J Wound Care. 23(3):93-6, 2014
7- Boekema BKHL, Chrysostomou D, Ciprandi G, Elgersma A, Vlig M, Pokorná A, Peters LJF, Cremers NAJ. Comparing the antibacterial and healing properties of medical-grade honey and silver-based wound care products in burns. Burns. 50(3):597-610, 2024

Inguinal Hernia Repair in Preterm Infants

Inguinal hernia is a frequent condition in preterm infants, and deciding when to repair it is one of the most crucial aspects of management. Timing of repair involves balancing the risk of hernia-related complications, such as incarceration, with the risks associated with anesthesia in a population prone to respiratory and neurological complications. This updated review will focus extensively on the timing of repair, integrating the latest evidence, while also covering surgical approaches and anesthesia considerations.

The optimal timing for inguinal hernia repair in preterm infants is heavily debated among neonatologists, pediatric surgeons, and anesthetists. This is because the decision directly affects the risks of incarceration, which can lead to bowel necrosis, and anesthesia-related complications, particularly respiratory failure, and neurodevelopmental outcomes. In preterm infants, the incidence of inguinal hernia varies widely, with rates as high as 30% in some populations. The thinness of the hernia sac, the fragility of the abdominal wall, and the vulnerability of associated tissues make this group particularly susceptible to complications if the condition is left untreated.

One of the primary drivers of early hernia repair is the risk of incarceration. Studies have shown that the risk of incarceration in preterm infants can be significantly higher than in term infants, with estimates of up to 30% of preterm infants experiencing incarceration. Incarceration of the hernia can lead to bowel obstruction, ischemia, or testicular atrophy, making prompt repair necessary in many cases. Data from Vaos et al. demonstrated that delaying hernia repair beyond the first week after diagnosis dramatically increases the risk

of incarceration by nearly fivefold. Infants with incarcerated hernias not only face an emergency situation but also have poorer overall surgical outcomes and increased perioperative risks.

For this reason, many surgeons advocate for repairing the hernia as early as possible, often before the infant is discharged from the neonatal intensive care unit (NICU). This approach minimizes the risk of emergency surgery for incarcerated hernia, which is associated with higher morbidity.

However, early repair also comes with significant risks, particularly related to anesthesia. Preterm infants, especially those with bronchopulmonary dysplasia or other respiratory disorders, have an increased risk of perioperative complications. Studies have shown that infants undergoing surgery under general anesthesia are at a greater risk for postoperative apnea, respiratory failure, and the need for prolonged mechanical ventilation. This has led some experts to recommend delaying surgery until the infant is older and better able to tolerate the anesthetic, typically at a post-conceptional age of around 60 weeks.

Crankson et al. reported that delaying surgery until the infant reaches at least 47 weeks of post-conceptional age can reduce the incidence of postoperative apnea and other respiratory complications, making surgery safer for the infant. This delay allows time for the infant's respiratory system to mature, potentially decreasing the risks associated with anesthesia. Additionally, some studies suggest that waiting until the infant is older can reduce the likelihood of surgical complications, such as hernia recurrence, particularly in infants who required mechanical ventilation during their NICU stay.

Given the risks of both early and delayed repair, many experts advocate for an individualized approach based on the infant's overall clinical status, gestational age, and comorbidities. Some surgeons argue for a middle ground, performing surgery shortly before the infant is discharged from the NICU to avoid the risks of delaying surgery too long but still allowing time for some respiratory maturation.

A survey of members of the American Pediatric Surgery Association showed that 63% of surgeons would prefer to repair the hernia just before the infant's NICU discharge. In these cases, the hernia repair is delayed long enough to reduce anesthesia risks but is performed while the infant is still in the hospital, minimizing the need for emergency readmissions for incarcerated hernias.

A critical factor in deciding when to repair a hernia is the infant's post-conceptional age (PCA). Research consistently shows that infants with a PCA of less than 46 weeks are at a significantly higher risk for postoperative apnea and other respiratory complications. For this reason, some clinicians recommend delaying hernia repair until the infant reaches a PCA of at least 60 weeks.

However, this delay increases the risk of hernia incarceration, particularly as the infant begins to grow and move more, placing additional pressure on the abdominal wall. Data from Lautz et al. revealed that for every month hernia repair is delayed, the risk of incarceration increases by more than twofold. Thus, while waiting for the infant's PCA to

reach a safer threshold for anesthesia is ideal, this delay must be carefully weighed against the increasing risk of incarceration.

The decision about when to repair an inguinal hernia also varies significantly based on institutional practices and available resources. Some centers have developed protocols for early repair, using spinal or caudal anesthesia to minimize the risks of general anesthesia, especially in infants with a high risk of respiratory complications. In centers where regional anesthesia expertise is available, early repair can be safely performed, minimizing the risk of incarceration while reducing the perioperative risks associated with general anesthesia.

Other institutions, particularly those without ready access to regional anesthesia techniques for infants, may opt to delay surgery and focus on close monitoring of the hernia, allowing the infant's respiratory system to mature before surgery. The lack of consensus on the optimal timing of surgery reflects the complexity of balancing these risks in a highly vulnerable population.

The choice of surgical technique can also influence the timing of repair. Open surgery is traditionally performed and remains the gold standard for many surgeons due to its well-established outcomes and lower risk of complications. Laparoscopic surgery, although less invasive, typically requires general anesthesia and is associated with an increased risk of pneumoperitoneum, which can exacerbate respiratory problems in preterm infants.

Some evidence suggests that laparoscopic surgery, while technically more demanding, may offer the advantage of inspecting both inguinal canals during the procedure, reducing the risk of missing a contralateral hernia. However, the risk of iatrogenic complications, such as injury to the spermatic cord, is higher in laparoscopic procedures. Consequently, the choice of surgical approach must consider the infant's overall condition and the surgeon's experience with both techniques.

Anesthesia is a major consideration in the timing of inguinal hernia repair. As previously mentioned, general anesthesia carries significant risks for preterm infants, particularly those with respiratory conditions. Regional anesthesia, including spinal and caudal blocks, has been shown to reduce these risks, leading some centers to prefer early repair using regional techniques.

However, regional anesthesia is not always feasible, particularly for more complex cases, such as bilateral hernias or when laparoscopic surgery is planned. In such cases, general anesthesia may still be necessary, and surgery is often delayed until the infant is older and better able to tolerate the anesthetic. For infants with a PCA of less than 46 weeks, some surgeons recommend preoperative caffeine administration and close postoperative monitoring to reduce the risk of apnea.

The timing of inguinal hernia repair in preterm infants is one of the most challenging decisions in neonatal surgery. Early repair reduces the risk of hernia incarceration but exposes the infant to the risks of anesthesia-related complications. Delaying surgery allows for respiratory maturation but increases the risk of hernia-related complications, including incarceration. An individualized approach, based on the infant's clinical status, PCA, and

the availability of anesthesia techniques, is crucial for optimizing outcomes.

References:
1- Fu YW, Pan ML, Hsu YJ, Chin TW: A nationwide survey of incidence rates and risk factors of inguinal hernia in preterm children. Pediatr Surg Int. 34(1):91-95, 2018
2- Patoulias I, Gkalonaki I, Patoulias D: Inguinal hernia management in preterm infants: addressing current issues of interest. Folia Med Cracov. 60(4):41-52, 2020
3- Pogorelić Z, Anand S, Križanac Z, Singh A: Comparison of Recurrence and Complication Rates Following Laparoscopic Inguinal Hernia Repair among Preterm versus Full-Term Newborns: A Systematic Review and Meta-Analysis. Children (Basel). 26;8(10):853, 2021
4- Lesher AP, Chess PR: Regional anesthesia may improve cardiorespiratory complications in preterm inguinal hernia surgery. J Perinatol. 41(3):370-371, 2021
5- Dohms K, Hein M, Rossaint R, Coburn M, Stoppe C, Ehret CB, Berger T, Schälte G: Inguinal hernia repair in preterm neonates: is there evidence that spinal or general anaesthesia is the better option regarding intraoperative and postoperative complications? A systematic review and meta-analysis. BMJ Open. 9(10), 2019
6- Choo CS, Chen Y, McHoney M. Delayed versus early repair of inguinal hernia in preterm infants: A systematic review and meta-analysis. J Pediatr Surg. 57(11):527-533, 2022
7- Taverner F, Krishnan P, Baird R, von Ungern-Sternberg BS. Perioperative management of infant inguinal hernia surgery; a review of the recent literature. Paediatr Anaesth. 33(10):793-799, 2023
8- HIP Trial Investigators; Blakely ML, Krzyzaniak A, Dassinger MS, et al: Effect of Early vs Late Inguinal Hernia Repair on Serious Adverse Event Rates in Preterm Infants: A Randomized Clinical Trial. JAMA. 26;331(12):1035-1044, 2024

Central Venous Catheters in Pediatric Oncology

Central venous catheters (CVCs) are indispensable tools in the management of pediatric oncology patients, providing reliable venous access for the administration of chemotherapeutic agents, blood products, and parenteral nutrition. Despite their essential role, the use of CVCs in this vulnerable population presents significant risks, including infections, thrombosis, and mechanical complications. This review examines the latest findings on the safety, efficacy, and complications of CVCs in pediatric oncology patients, focusing on issues such as catheter-related bloodstream infections (CRBSIs), venous thromboembolism (VTE), and emerging management strategies.

Several types of CVCs are utilized in pediatric oncology, each with specific advantages and risks. The most common types include peripherally inserted central catheters (PICCs), non-tunneled CVCs, and tunneled catheters such as Hickman or Broviac lines. PICCs are often favored due to their ease of insertion and lower risk of mechanical complications compared to non-tunneled CVCs. PICCs can remain in situ for extended periods, which is advantageous for children undergoing long-term chemotherapy. A study analyzing 258 PICCs in pediatric oncology patients found a median catheter life of 102 days, highlighting their suitability for prolonged treatment.

However, the choice of catheter type depends on several factors, including the duration of use, the patient's clinical condition, and the risk of infection or thrombosis. In high-risk cases, such as stem cell transplantation or intensive chemotherapy, tunneled catheters may be preferred due to their lower risk of infection and ability to be in place for longer durations. Non-tunneled catheters, typically used in emergency settings, are associated

with higher complication rates, and are usually replaced with tunneled catheters or PICCs once the patient is stabilized.

Catheter-related bloodstream infections (CRBSIs) are among the most frequent and severe complications associated with CVCs in pediatric oncology patients. Immunosuppression due to chemotherapy significantly increases the risk of infections, with bacteria such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Enterobacterales* being the most common culprits. The incidence of CRBSIs in pediatric oncology patients is reported to be 1.51 per 1,000 catheter-days, and infections can lead to serious outcomes, including sepsis, prolonged hospital stays, and even death.

Management of CRBSIs involves a combination of systemic antibiotic therapy and, in some cases, catheter removal. Recent studies have explored the possibility of catheter salvage using antibiotic lock therapy (ALT) and systemic antibiotics, especially for infections caused by organisms such as *Enterobacterales*. However, the success of catheter salvage remains variable, and in cases of persistent bacteremia or severe sepsis, immediate catheter removal is often recommended. A study conducted in pediatric oncology patients found that the cumulative incidence of ICU admission and death following CRBSIs was 16% and 5%, respectively, underscoring the severity of these infections.

Venous thromboembolism (VTE) is another significant complication associated with CVCs in pediatric oncology patients. CVCs disrupt normal blood flow and cause endothelial injury, increasing the risk of thrombosis. Studies have reported a high incidence of catheter-related thrombosis (CRT), with one study documenting a rate of 35.69 cases per 1,000 CVC-days. CRT can be asymptomatic in many cases, but symptomatic thrombosis, including pulmonary embolism, can occur and poses a life-threatening risk.

Several factors contribute to the development of CRT, including the duration of catheter placement, the method of insertion, and underlying conditions such as malignancy or infection. Prolonged catheter use has been identified as a major risk factor for CRT, with studies demonstrating that the risk of thrombosis increases with the number of catheters days. Interestingly, catheter malfunction and infection have also been associated with a higher risk of CRT, suggesting a possible link between infection, catheter occlusion, and thrombosis.

The management of CRT often involves anticoagulation therapy, although there are no specific guidelines for pediatric oncology patients. In cases of symptomatic thrombosis, catheter removal may be required, particularly if anticoagulation therapy is unsuccessful. Prophylactic anticoagulation is not routinely used in pediatric patients, and its role in preventing CRT remains controversial.

Mechanical complications such as catheter dislodgement, occlusion, and migration are also common in pediatric oncology patients. A study on PICCs in children found that catheter-related complications, including occlusion and breakage, occurred at a rate of 1.75 per 1,000 catheter-days. Catheter occlusion, often caused by fibrin sheath formation or thrombosis, can lead to treatment delays, and necessitate catheter replacement.

Catheter migration, although less common, can have serious consequences. For example, migration into the pleural space has been reported, leading to pleural effusion and respiratory distress. Proper catheter positioning, confirmed by imaging, and regular monitoring are essential to prevent these complications.

Given the high risk of complications associated with CVCs in pediatric oncology patients, several strategies have been proposed to minimize these risks. Infection prevention measures, including strict adherence to aseptic techniques during catheter insertion and maintenance, are critical. The use of antimicrobial-impregnated catheters and antibiotic lock solutions has shown promise in reducing the incidence of CRBSIs, although further studies are needed to confirm their efficacy in pediatric populations.

For thrombosis prevention, routine screening for CRT using ultrasonography has been recommended in high-risk patients, particularly those with prolonged catheter use or a history of thromboembolic events. Anticoagulation therapy, while not routinely used, may be considered in certain high-risk patients, although the benefits must be weighed against the risk of bleeding.

Mechanical complications can be minimized by ensuring proper catheter placement and securement techniques. Regular monitoring for signs of occlusion or migration is essential, and prompt intervention is required if complications arise. In some cases, replacing a malfunctioning catheter with a different type, such as switching from a non-tunneled CVC to a PICC, may be beneficial.

Central venous catheters are vital in the treatment of pediatric oncology patients, providing essential venous access for the administration of life-saving treatments. However, their use is fraught with risks, including infections, thrombosis, and mechanical complications. The management of these complications requires a multidisciplinary approach, involving infection control measures, anticoagulation therapy, and careful monitoring of catheter function. Advances in catheter technology, coupled with better prevention and management strategies, have the potential to improve outcomes for pediatric oncology patients requiring long-term venous access. Further research is needed to refine these strategies and develop evidence-based guidelines tailored to the unique needs of this vulnerable population.

References:

1- Beck O, Muensterer O, Hofmann S, Rossmann H, Poplawski A, Faber J, Gödeke J: Central Venous Access Devices (CVAD) in Pediatric Oncology Patients-A Single-Center Retrospective Study Over More Than 9 Years. *Front Pediatr*. 7:260, 2019

2- Suzuki D, Kobayashi R, Sano H, Yanagi M, Hori D, Matsushima S, Nakano T, Kobayashi K: Peripherally Inserted Central Venous Catheter for Pediatric and Young Adult Patients With Hematologic and Malignant Diseases. *J Pediatr Hematol Oncol*. 42(7):429-432, 2020

3- Cellini M, Bergadano A, Crocoli A, et al: Guidelines of the Italian Association of Pediatric Hematology and Oncology for the management of the central venous access devices in pediatric patients with onco-hematological disease. *J Vasc Access*. 23(1):3-17, 2022

4- Ardura MI, Bibart MJ, Mayer LC, et al: Impact of a Best Practice Prevention Bundle on Central Line-associated Bloodstream Infection (CLABSI) Rates and Outcomes in Pediatric Hematology, Oncology, and Hematopoietic Cell Transplantation Patients in Inpatient and Ambulatory Settings. *J Pediatr Hematol Oncol*.

43(1), 2021
5- Kelada AS, Foster TB, Gagliano GC, et al: Central-line-associated bloodstream infections and central-line-associated non-CLABSI complications among pediatric oncology patients. *Infect Control Hosp Epidemiol*. 44(3):377-383, 2023
6- van den Bosch CH, Kops AL, Loeffen YGT, et al: Central Venous Catheter-related Bloodstream Infections Caused by Enterobacterales in Pediatric Oncology Patients: Catheter Salvage or Removal. *Pediatr Infect Dis J*. 43(1):49-55, 2024
7- Narayan AS, Ramamoorthy JG, Parameswaran N, et al: Central Venous Catheter-associated Venous Thromboembolism in Children: A Prospective Observational Study. *J Pediatr Hematol Oncol*. Jul 22, 2024
8- Christison-Lagay ER, Brown EG, Bruny J, et al: Central Venous Catheter Consideration in Pediatric Oncology: A Systematic Review and Meta-analysis From the American Pediatric Surgical Association Cancer Committee. *J Pediatr Surg*. 59(8):1427-1443, 2024

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