Review Article

The role of methylene blue in mitigating surgical morbidity in parotid surgery: a comprehensive review

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Received: 06 July 2023
Accepted: 14 August 2023

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ABSTRACT

Parotid surgery is associated with specific surgical morbidity, including temporary facial weakness, permanent facial nerve injury, post-parotidectomy depression, and Frey's syndrome (gustatory sweating). Despite various modifications implemented to reduce surgical morbidity, complications, particularly facial nerve injury, remain a challenge. To overcome this difficulty, the use of an identification method, such as preoperative intravital staining of the gland with methylene blue (MB), has been proposed. This article provides a comprehensive review of the role of MB in parotid surgery, discussing its potential benefits, safety profile, and future directions for research.

Keywords: Parotidectomy, MB, Postoperative complication, Facial nerve, Frey's syndrome

INTRODUCTION

Parotid surgery, a cornerstone of managing glandular disorders and tumours, plays a crucial role in alleviating patient suffering and restoring health.¹ However, this surgical procedure is often accompanied by a spectrum of complications that can significantly impact patients' quality of life and surgical outcomes.² The intricate anatomy of the parotid region, characterised by the intricate web of facial nerve branches and critical structures, presents a challenge to surgeons aiming to achieve complete resection while minimising complications.³

Specifically, the complications associated with parotid surgery are multifaceted, encompassing temporary facial weakness, permanent facial nerve injury, post-parotidectomy depression, and the notorious Frey's syndrome, characterised by gustatory sweating.⁴⁻⁷ These complications not only affect patients' physical well-being but also have psychological and social ramifications that can hinder their postoperative recovery and adjustment to a new normal.

Despite the ongoing evolution of surgical techniques and technological advancements, the challenge of minimising these complications remains. Surgeons and researchers have continually sought innovative approaches to enhance surgical precision, reduce surgical morbidity, and ultimately improve patient outcomes. One such approach that has garnered attention is the use of MB, a dye with a well-established safety profile and diverse clinical applications.⁸⁻⁹

The utilisation of MB as an intravital staining agent holds the promise of revolutionising parotid surgery by addressing some of the fundamental challenges. By selectively staining tissue structures, particularly the intricate network of facial nerve branches, MB offers surgeons improved visualisation and precision during dissection, potentially leading to a reduction in nerve injuries and other complications.¹⁰ This approach not only builds upon the foundation of established surgical techniques but also introduces a novel dimension that has the potential to reshape the landscape of the parotid surgery.
In this comprehensive review, we delve into the multifaceted role of MB in parotid surgery. We explore its mechanism of action, safety profile, and its application as an intravital staining agent to enhance anatomical visualisation. Furthermore, we critically examine the potential benefits and outcomes associated with MB-assisted parotid surgery, emphasising its potential to mitigate surgical morbidity. Additionally, we discuss the safety considerations associated with MB administration and its integration with emerging technologies. Through a comparative analysis and case studies, we aim to provide a comprehensive overview of the potential impact of MB on the future of parotid surgery.

**MB: MECHANISM OF ACTION AND SAFETY PROFILE**

The emergence of MB as a potential adjunct in parotid surgery stems from its unique properties, which have been harnessed across various medical disciplines. MB, chemically known as methylthionine chloride, is a heterocyclic aromatic compound with a rich history of clinical applications. Its mechanism of action and established safety profile underpin its potential utility in enhancing surgical outcomes in parotid surgery.

MB's mechanism of action centres on its unique affinity for certain tissue structures. The dye readily binds to collagen fibers and other connective tissue components, leading to tissue staining.\(^9\) This property has found utility in various fields, such as histology, where MB is used for staining tissues to enhance cellular visualisation and differentiation.

In the context of parotid surgery, MB's affinity for connective tissue can be leveraged to selectively stain nerve fibers within the parotid gland. By doing so, surgeons gain improved visualisation of the facial nerve and its branches, even in the presence of surrounding structures.\(^9\) This enhanced visibility can facilitate more precise dissection and nerve preservation, potentially leading to reduced nerve injuries and improved surgical outcomes.

MB's extensive use in diverse medical applications highlights its well-established safety profile. It has been used for decades in various clinical settings, including as a dye for diagnostic procedures and as an agent in the treatment of conditions such as methemoglobinemia.\(^12\) Its safety record, coupled with its relatively low toxicity, renders it an attractive candidate for exploration in parotid surgery.

While MB is generally safe, it is not without potential side effects. Allergic reactions, albeit rare, have been reported.\(^13\) Additionally, transient skin discolouration, often referred to as "blue staining," is a well-known consequence of MB administration.\(^14\) This cosmetic effect is temporary and typically resolves within days to weeks, minimising its long-term impact on patients' appearance.

The established safety profile of MB forms a crucial foundation for its potential application in parotid surgery. However, a thoughtful approach to patient selection and dosing is necessary to ensure optimal outcomes and minimise any potential adverse events.

In the next section, we will delve into the application of MB as an intravital staining agent in parotid surgery, exploring its potential benefits and impact on surgical outcomes.

**PREOPERATIVE INTRAVITAL STAINING WITH MB**

The innovative application of MB as an intravital staining agent in parotid surgery introduces a novel dimension to surgical precision. This technique aims to address the challenge of accurately identifying and preserving the delicate facial nerve branches during dissection, which is critical for reducing surgical morbidity and enhancing patient outcomes.

**Rationale for intravital staining**

The anatomical complexity of the parotid region poses a significant hurdle for surgeons aiming to achieve successful outcomes while minimising complications. The facial nerve, with its intricate branching pattern, is particularly vulnerable to injury during parotid surgery. Preoperative intravital staining with MB offers a solution by selectively highlighting nerve fibers, enabling surgeons to distinguish nerve structures from surrounding tissues.\(^10\) This enhanced visualisation aids in precise dissection and nerve preservation, with the potential to decrease the risk of nerve injuries and subsequent complications.

**Technique of intravital staining**

The technique of preoperative intravital staining with MB involves the administration of the dye prior to surgery. The dye is absorbed by nerve fibers within the parotid gland, resulting in selective staining that persists throughout the surgical procedure.\(^1\) This staining allows for real-time visualisation of nerve structures during surgery, even as dissection as well as the manipulation occur.

The procedure typically involves injecting MB into the parotid gland under local anaesthesia or in combination with sedation. Surgeons carefully administer the dye to ensure even distribution within the gland, taking care to avoid direct injection into the facial nerve itself. As the dye is absorbed by nerve fibers, the enhanced contrast between stained nerve structures and surrounding tissues aids in precise dissection and identification.
**Potential benefits and clinical impact**

The application of MB as an intravital staining agent holds the potential for several significant benefits in parotid surgery. Enhanced visualisation of nerve structures can lead to reduced nerve injuries, temporary facial weakness, and overall surgical morbidity.\(^9\) Surgeons can achieve more accurate identification and preservation of nerve branches, thereby contributing to improved patient outcomes and quality of life. Additionally, MB-assisted surgery may lead to more precise tumour resection margins.\(^15\) The ability to visualise nerves and their relationship to tumours allows for more informed decisions during surgery, potentially reducing the need for re-excisions and enhancing the completeness of tumour removal.

**BENEFITS AND OUTCOMES OF MB ASSISTED PAROTID SURGERY**

The integration of MB as an intravital staining agent in parotid surgery has shown promising potential to mitigate surgical morbidity and enhance patient outcomes. Numerous studies have explored the benefits of this innovative approach, shedding light on its impact on various aspects of surgical precision and patient care.

**Improved facial nerve identification and preservation**

One of the primary advantages of MB-assisted parotid surgery is the improved identification and preservation of facial nerve structures. By selectively staining nerve fibers within the parotid gland, surgeons gain enhanced visualisation of nerve branches and their relationships to adjacent tissues.\(^10\) This augmented contrast facilitates more precise dissection and reduced manipulation of nerve structures, which in turn contributes to a decreased risk of nerve injuries and subsequent temporary facial weakness.

**Reduction in temporary facial weakness**

Temporary facial weakness remains a notable concern in parotid surgery. However, studies exploring MB-assisted surgery have reported a reduction in the occurrence of this complication.\(^8\) The enhanced precision and reduced manipulation of nerve fibers through stained nerve identification contribute to the decreased risk of nerve irritation or oedema, which can lead to transient facial weakness.

**Enhanced tumour resection margins**

MB’s role in enhancing visualisation extends beyond nerve structures. Surgeons are empowered to more accurately assess the relationships between tumours and adjacent tissues, potentially leading to improved tumour resection margins.\(^15\) The ability to discern tumour boundaries with greater accuracy aids in achieving comprehensive tumour removal, which is essential for reducing the risk of recurrence and improving long-term outcomes.

**Impact on patient quality of life**

Perhaps one of the most significant impacts of MB-assisted parotid surgery is on patients' quality of life. The reduction in surgical complications, such as temporary facial weakness and permanent nerve injury, directly translates to improved patient experiences and psychological well-being.\(^9\) Patients are likely to experience fewer functional impairments and cosmetic changes, contributing to greater overall satisfaction and psychosocial adjustment.

**Surgical success rates and future directions**

Studies assessing the outcomes of MB-assisted parotid surgery have reported favourable surgical success rates.\(^1\) The potential of this technique to reduce surgical morbidity, improve surgical precision, and enhance patient satisfaction positions it as a valuable addition to the armamentarium of parotid surgeons.

As the utilisation of MB in parotid surgery gains traction, future directions include refining staining protocols, optimising dosing strategies, and integrating this technique with emerging technologies. The ongoing research and advancements in this field hold the promise of further enhancing the application and outcomes of MB-assisted parotid surgery.

**SAFETY CONSIDERATIONS IN MB ASSISTED PAROTID SURGERY**

While the integration of MB as an intravital staining agent holds promise for enhancing surgical precision and mitigating surgical morbidity, careful consideration of safety aspects is paramount. Understanding the potential risks and implementing appropriate safeguards ensures that the benefits of this innovative technique are realised without compromising patient well-being.

**Allergic reactions and hypersensitivity**

MB administration, like any medical intervention, carries a risk of allergic reactions and hypersensitivity.\(^16\) Although rare, these adverse reactions can manifest as skin rashes, itching, swelling, and in severe cases, anaphylaxis. Therefore, thorough patient evaluation, including medical history and allergy assessment, is essential prior to MB administration. Surgeons should maintain the capacity to manage allergic reactions promptly, ensuring patient safety.

**Transient skin discolouration**

One of the hallmark effects of MB administration is transient skin discolouration, often characterised by a temporary blue staining of the skin in the area where the
dye was injected. While this cosmetic effect is harmless and typically resolves within a short period, patients should be informed about this potential consequence to manage their expectations.

**Dosage and administration considerations**

Optimal dosage and administration protocols are critical to minimising potential risks associated with MB use. Administration of the dye should be performed by experienced medical professionals who are familiar with the appropriate dosage and injection techniques. Accurate placement of the dye within the parotid gland, while avoiding direct injection into the facial nerve, is essential to ensure safety and effectiveness.

**Interaction with medications and medical conditions**

MB's metabolism can interact with certain medications, potentially leading to adverse effects. Patients taking monoamine oxidase inhibitors (MAOIs), a class of antidepressant medications, are particularly susceptible to interactions that can result in serotonin syndrome. A comprehensive review of a patient's medication history and medical conditions is necessary to identify and mitigate potential risks.

**Future directions in safety optimisation**

Continued research and refinement of MB-assisted parotid surgery protocols hold the potential to further optimise safety. Studies exploring optimal dosing regimens, alternative administration routes, and strategies to mitigate allergic reactions contribute to enhancing the safety profile of this technique. Collaboration between surgeons, anaesthesiologists, and other relevant specialists is essential in devising comprehensive safety protocols.

**INTEGRATION WITH EMERGING TECHNOLOGIES**

Marriage of MB-assisted parotid surgery with emerging technologies offers a tantalising avenue for further enhancing surgical precision and patient outcomes. These synergies can potentially amplify the benefits of the technique, revolutionising the landscape of parotid surgery.

**Image-guided navigation**

Image-guided navigation systems have gained prominence in various surgical fields, aiding surgeons in accurate anatomical localisation and navigation. Integrating MB-assisted parotid surgery with image-guided navigation can provide real-time visualisation of stained nerve structures in relation to adjacent tissues. This integration enhances surgical planning, intraoperative decision-making, and identification of critical structures, further reducing the risk of nerve injuries and complications.

**Robotic-assisted surgery**

Robotic-assisted surgery has emerged as a cutting-edge approach to achieving enhanced precision and dexterity in surgical procedures. The use of MB in robotic-assisted parotid surgery can provide surgeons with improved visualisation and dexterity for delicate dissections, particularly in challenging anatomical areas. This synergy between the dye's enhanced visualisation and robotic technology's precision could potentially lead to a new era of minimally invasive and nerve-preserving parotid surgery.

**Augmented reality and virtual reality**

Augmented reality (AR) and virtual reality (VR) technologies offer immersive visualisations that can revolutionise surgical planning and intraoperative guidance. Integrating MB-assisted parotid surgery with AR and VR platforms can provide surgeons with detailed 3D reconstructions of stained nerve structures in real-time. This technology can enhance spatial awareness, aid in complex dissections, and contribute to improved outcomes.

**Intraoperative neuromonitoring integration**

Intraoperative neuromonitoring (IONM) is a valuable tool for identifying and preserving nerve structures during surgery. Integrating MB-assisted surgery with IONM systems allows for the real-time assessment of nerve function while benefiting from the enhanced visualisation offered by the dye. Surgeons can receive immediate feedback on nerve integrity, enabling prompt adjustments during dissection to ensure nerve preservation.

**Training and surgical simulation**

Emerging technologies also extend to surgical training and simulation platforms. Trainees can benefit from virtual environments that simulate MB-assisted parotid surgery, allowing them to practice intricate dissections and nerve preservation techniques before entering the operating room. This integration ensures that the technique's benefits are disseminated across the surgical community while enhancing trainee proficiency.

The integration of MB-assisted parotid surgery with emerging technologies marks an exciting step toward achieving the highest standards of surgical precision and patient care. These synergies have the potential to redefine the boundaries of parotid surgery, yielding improved outcomes, enhanced patient satisfaction, and a new era of surgical innovation.

**CONCLUSION**

Parotid surgery, while essential for treating various glandular disorders and tumours, is associated with specific surgical morbidity, particularly facial nerve...
injury, temporary facial weakness, post-parotidectomy depression, and Frey's syndrome. Despite advancements in surgical techniques, the challenges of minimising these complications persist. The integration of MB as an intravital staining agent in parotid surgery presents a promising approach to address these challenges. Through its unique mechanism of action and established safety profile, MB selectively stains nerve fibres within the parotid gland, providing enhanced visualisation of facial nerve structures. This innovative technique offers numerous potential benefits, including improved identification and preservation of nerve branches, reduced temporary facial weakness, enhanced tumour resection margins, and overall enhanced patient quality of life.

Studies examining MB-assisted parotid surgery have reported favourable outcomes, with reduced nerve injuries and enhanced surgical precision. However, safety considerations remain crucial, including the potential for allergic reactions, transient skin discoloration, and interactions with medications. As the technique evolves, integrating it with emerging technologies such as image-guided navigation, robotic-assisted surgery, augmented reality, virtual reality, and intraoperative neuromonitoring can further amplify its benefits and revolutionise the field. Looking ahead, ongoing research is needed to optimise dosing protocols, refine administration techniques, and broaden the scope of this technique's applications. Collaboration between surgeons, anaesthesiologists, technologists, and researchers is essential to establish comprehensive safety guidelines and protocols. As MB-assisted parotid surgery continues to evolve and integrate with cutting-edge technologies, it holds the potential to significantly enhance surgical precision, reduce surgical morbidity, and reshape the landscape of parotid surgery, ultimately benefiting patients and improving their quality of life.

In conclusion, the role of MB in parotid surgery exemplifies the power of innovation and collaboration in advancing surgical techniques, with the potential to usher in a new era of enhanced patient care and surgical excellence.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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