

A Case Of Recreational N-acetylcysteine Use Modulating Coagulation and Analgesia in the Setting Of Subcapsular Liver Hematoma

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Introduction

- The diversity of health supplements being taken by patients make it challenging for clinicians to maintain knowledge of their side effects and interactions.
- N-acetylcysteine (NAC) is a health supplement that have become popular for its known benefits in replenishing glutathione stores.
- NAC may interact with the metabolism of medications like hydromorphone and alter its effects on pain management while reducing the effects of respiratory depression and sedation.
- NAC also interferes with blood coagulation and may require consideration for surgical and regional anesthesia procedures.

Methods

- Informed consent for this case report was obtained from the patient.

Case Report

- 20 year old male with acute onset and worsening right upper quadrant pain found to have a massive subcapsular liver hematoma, presenting for urgent arterial embolization with interventional radiology.
- Right upper quadrant ultrasound and computed tomography scans revealed a large subcapsular hematoma measuring 9.6 x 9.6 x 26.5 cm with areas suggestive of active extravasation.
- History of recent lumbar decompression surgery for work-related injury not requiring significant opioids for recovery.
- Patient had 10/10 pain treated in the medical intensive care unit with escalating IV hydromorphone doses, up to continuous infusion of 4mg/hour not requiring intubation or supplemental oxygen.
- Acute pain service consulted at this time and found patient's pain to somewhat controlled on this regimen (5-9/10 with IV pushes of hydromorphone on top of infusion at 4mg/hour).
- Patient did not report somnolence and had trouble sleeping due to pain. His respiratory rate remained normal throughout this period not dropping below 10 when observed.
- Patient reports having taken oral N-acetylcysteine (NAC) "on and off for the past 3 years" although in the month prior to presentation had increased his daily dose from 1000mg to 4000mg.
- He described NAC as self-medication for anxiety and obsessive-compulsive disorder for which he was already taking sertraline 50mg PO daily.
- Subsequent interviews later revealed a history of repeated epistaxis which required occasional emergency department visits for control.
- Patient's brother, father, and paternal grandfather all reported similar recurrent severe epistaxis.

Discussion

- Evidence suggests that N-acetylcysteine (NAC) can affect the levels of several clotting factors and functionally decrease clotting ability through modulation of platelet function.
- NAC given to healthy volunteers led to decreases in prothrombin activity through decreased factors II, VII, X independent of hepatic function (Knudsen et al 2005).
- NAC inhibited platelet functions including decreasing intracellular calcium mobilization, arachidonic metabolite synthesis, and adhesion to collagen matrix (Eligini et al 2022).
- Patients receiving NAC during abdominal aortic aneurysm repair had increased clot formation time by thromboelastography and more bleeding in a small randomized controlled trial (Niemi et al 2006).
- Some evidence exists for the use of NAC as an adjunct in chronic pain treatments (reviewed in Mohiuddin et al 2021).
- NAC generates hydrogen sulfide species (similar to cysteine) which can bind and internalize mu opioid receptors with evidence for activation (Distrutti et al., 2010).
- NAC generates reducing agents such as reduced albumin species and glutathione (Eligini et al., 2022) which may act as electron donors in the reaction that generates 14-methoxymetapone, an opioid analgesic with significantly reduced respiratory depression and other side effects (Freye et al., 2000; King et al., 2003).

Conclusions

- NAC may have contributed to this patient's underlying bleeding disorder leading to an unprovoked subcapsular hematoma. Absent more rigorous studies, care should be taken when considering safety of neuraxial analgesia in patients on NAC.
- While NAC has a half life on the order of hours, this patient's large hematoma may have acted as a NAC deposit that was reintroduced as the hematoma was reabsorbed. The circulating NAC may have affected the hydromorphone dosing and activity through the abundance electron donors which may generate 14-methoxymetopon and explain the increased dose requirements and the lack of typical narcotic side effects observed here.

References

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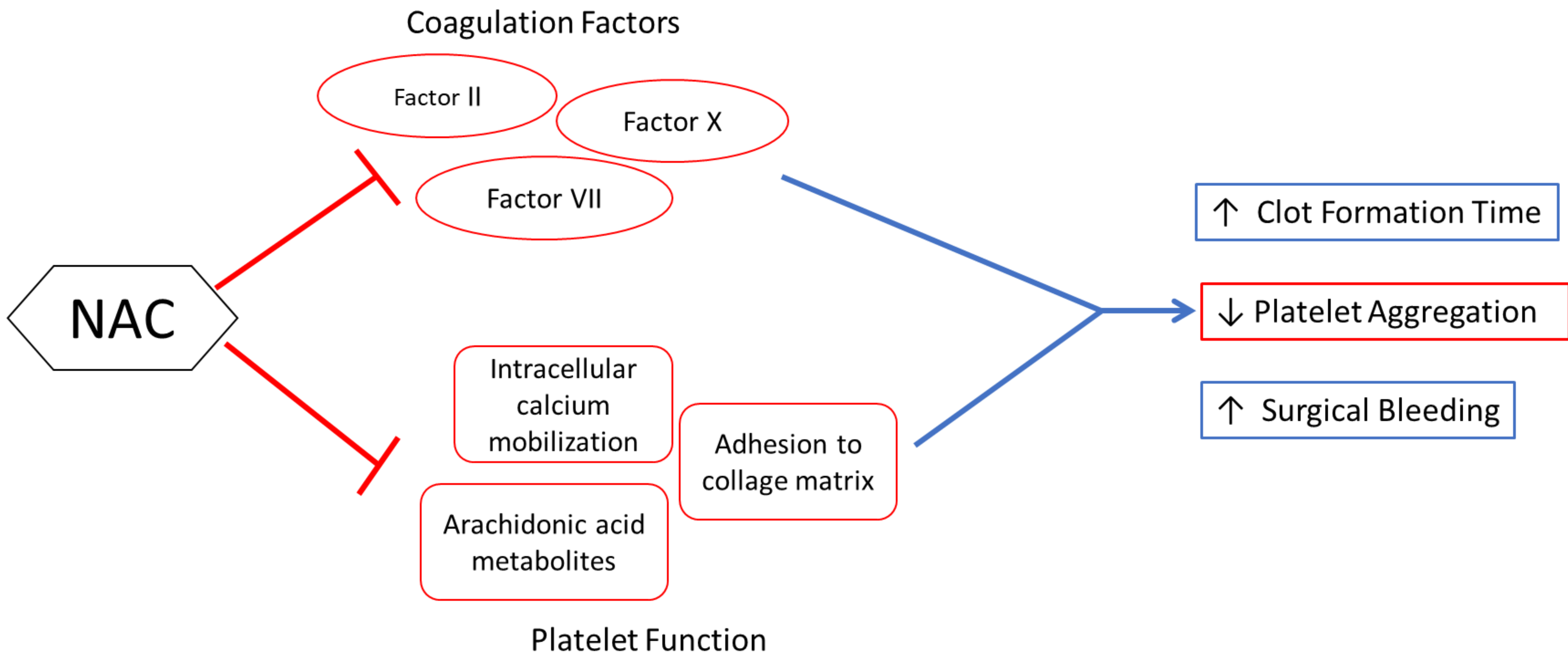


Figure 1: Proposed mechanism for NAC affecting coagulation and platelet function

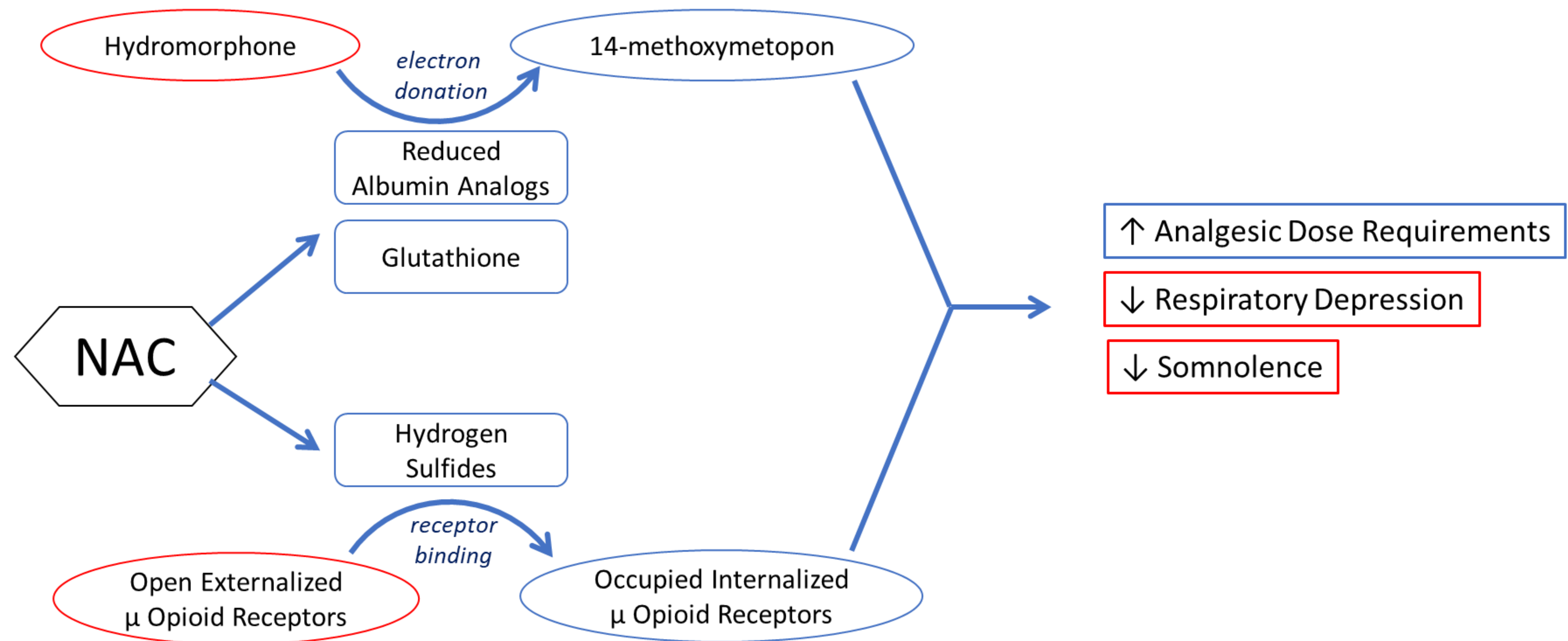


Figure 2: Proposed mechanism for NAC affecting hydromorphone analgesia and side effects