Methylene blue as the safest blue dye for sentinel node mapping: Emphasis on anaphylaxis reaction

SADEGHI RAMIN, FANI PAKDEL AZAR & HASANZADEH MALIHE

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- Anaphylaxis reaction to blue dyes being used in medical practice is a major concern for health care providers. Traditionally methylene blue is considered as the safest and its use is actually encouraged by many authors.
- A case of anaphylactic reaction to this blue dye has been published in by our group.
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- We systematically report the available literature in this regard, having in mind the evergrowing use of these dyes in oncology and sentinel node biopsy.
Accuracy

- Several blue dyes are now in use for sentinel node mapping including isosulfane blue, Patent Blue V, and methylene blue.
- The accuracy of these dyes for sentinel lymph node mapping was comparable in several studies.
Cost

- Methylene blue is the cheapest and the most available.
- This is an important concern in areas with limited resources.
Adverse reactions

- Allergic reactions
  - include urticaria, skin rash, erythema, and anaphylaxis.

- Non-allergic reactions
  - interference with pulse-oximetry, blue discoloration of the skin or body fluids, and skin necrosis
Adverse reactions

- Adverse skin reactions are more common with methylene blue and can be in the form of skin necrosis which is very problematic.
- However, interference with pulse oximetry is less common with methylene blue compared to isosulfane blue and Patent Blue V dyes.
Adverse reactions

- Allergic reactions (including life-threatening anaphylaxis) were consistently reported more frequently for Patent Blue V and isosulfan blue dyes (0.9% for ALMANAC and 0.7% for NSABP B32 trials) compared to methylene blue.
Anaphylactic reactions

- Life-threatening anaphylactic or anaphylactoid reactions to methylene blue (not related to sentinel node mapping) have been reported in the literature.
  - Trikha et al.
    - Intra-uterine injection
  - Millo et al.
    - Diagnostic laparascopy
  - Dewachter et al
    - Intra-uterine injection
  - Rzymski et al
    - Intra-uterine injection
- Only Dewatcher et al confirmed it by skin test.
Anaphylactic reactions

- Only three groups reported life-threatening anaphylaxis reaction to methylene blue during sentinel lymph node mapping
  - Oomah et al. (2011)
- The latter two confirmed it by skin test.
DNA damaging

- methylene blue and Patent Blue V can have DNA damaging effects which can be of clinical relevance
Conclusion

• In conclusion, considering the rare occurrence of anaphylactic reactions to methylene blue, it seems that this dye is the safest among the blue dyes being used in sentinel node mapping. However, the mentioned case reports show that life-threatening anaphylactic reactions do occur with methylene blue.

• Surgical teams should be aware of this fact and having the equipment to manage this grave complication is of utmost importance.