Letter to the Editor

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Comment to "Adverse Effects of Intraparenchymal and Peritumoral Application of Isosulfan Blue Dye in Sentinel Lymph Node Mapping in Breast Cancer: A Systematic Review and Meta-Analysis"

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Dear Editor,

We commend Agilinko et al. (1) for their systematic review and meta-analysis investigating the adverse effects of isosulfan blue dye in sentinel lymph node (SLN) mapping for breast cancer. Their findings provide valuable insights into the safety profile of this widely used agent, particularly in highlighting the lower adverse event rates associated with peritumoral administration compared to intraparenchymal techniques. However, we wish to highlight several methodological limitations that could have impacted the strength and interpretability of the study's conclusions.

A key limitation is the absence of a formal risk of bias assessment for the included studies. Established tools such as the Cochrane risk of bias tool or the Newcastle-Ottawa scale are integral to determining the reliability of pooled evidence (2). Without evaluating potential biases in study design, data collection, or reporting, the certainty and generalizability of the findings are less clear. The omission of such an assessment leaves room for the possibility that methodological weaknesses in the included studies may have influenced the results.

In addition, while the authors conducted subgroup analyses based on the route of administration, they did not perform a broader sensitivity analysis to assess the stability of their findings. For instance, excluding studies with small sample sizes, lower-quality reporting, or methodological inconsistencies could have provided a clearer picture of the robustness of the pooled estimates (3). This step is particularly critical given the observed heterogeneity in the meta-analysis, as indicated by the I-squared statistic. Sensitivity analysis would help determine whether the findings remain consistent under different scenarios, strengthening their applicability in clinical practice.

The study also missed an opportunity to employ the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework to evaluate the certainty of evidence. GRADE provides a structured approach to appraising factors such as risk of bias, inconsistency, imprecision, and publication bias, offering transparent guidance on the strength of recommendations (4, 5). Incorporating GRADE would have enhanced the clinical relevance of the study by providing a clearer understanding of the confidence clinicians can place in the results.

While the meta-regression exploring dose-response effects between the volume of dye administered and adverse events did not find significant associations, the analysis may have benefited from incorporating additional variables. Factors such as patient comorbidities, concurrent medications, and the use of preoperative prophylaxis could have offered a more nuanced understanding of predictors for adverse reactions. Including these variables in future studies could enhance the evidence base regarding the factors influencing patient safety.

This study raised important questions about clinical practice, particularly the finding that peritumoral administration was associated with lower adverse event rates than intraparenchymal injection. While this result is promising, additional research is needed to confirm the conclusion across diverse populations and healthcare settings. Furthermore, as novel agents, such as indocyanine green, gain traction

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in SLN mapping, future studies should compare their efficacy and safety with isosulfan blue to guide the evolution of clinical practice.

The study by Agilinko et al. (1) provides a foundation for understanding the safety profile of isosulfan blue, but further methodological enhancements could have strengthened its conclusions. Risk of bias assessment, sensitivity analyses, and the application of GRADE would have added greater clarity and confidence to the findings. We hope these points stimulate further discussion and refinement in future systematic reviews on this important topic.

Footnotes

Authorship Contributions

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References

1. Agilinko J, Borakati A, Yoong A, Pratheepan P, Samlalsingh S. Adverse effects of intraparenchymal and peritumoral application of isosulfan blue dye in sentinel lymph node mapping in breast cancer: a systematic review and meta-analysis. Eur J Breast Health. 2025; 21: 1-8. (PMID: 39744877) [Crossref]
2. Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: advantages and limitations of the Newcastle Ottawa Scale. World J Meta-Anal. 2017; 5: 80-84. [Crossref]
3. Copas J, Shi JQ. Meta-analysis, funnel plots and sensitivity analysis. Biostatistics. 2000; 1: 247-262. (PMID: 12933507) [Crossref]
4. Dewidar O, Lotfi T, Langendam MW, Parmelli E, Saz Parkinson Z, Solo K, et al. Good or best practice statements: proposal for the operationalisation and implementation of GRADE guidance. BMJ Evid Based Med. 2023; 28: 189-196. (PMID: 35428694) [Crossref]
5. Pandey P, Shabil M, Bushi G. Comment on "sodium fluorescein and 5-aminolevulinic acid fluorescence-guided biopsy in brain lesions: a systematic review and meta-analysis". J Neurooncol. 2024; 170: 677-678. (PMID: 39249668) [Crossref]