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Immediate hypersensitivity to parenteral cancer treatments

English summary

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Québec

SUMMARY

Immediate hypersensitivity to parenteral cancer treatments

Introduction

Immediate hypersensitivity reactions can occur during or shortly after the infusion of parenteral cancer treatments. Whether allergic or non-allergic, these reactions pose a significant safety issue. Rapid recognition and appropriate management are essential to prevent potentially serious complications. Given the expanding range of antineoplastic drugs and the diversity of practices in Québec, the Sous-ministériat de la santé physique et pharmaceutique of the Ministère de la Santé et des Services sociaux (MSSS) has mandated the Institut national d'excellence en santé et en services sociaux (INESSS) to develop provincial recommendations and a clinical tool. The objective is to support the harmonization of prevention, acute care and treatment resumption procedures, including desensitization criteria, for all systemic cancer treatments administered parenterally.

Methodology

For this work, the evaluation questions were designed to address the clinical dimension as well as population-based, organizational, economic and sociocultural dimensions, along with ethical and environmental issues as presented in the INESSS Statement of Principles and Ethical Foundations. A systematic review of documents presenting clinical recommendations and information was carried out based on publications listed in bibliographic databases and other sources, supplemented by an analysis of contextual factors specific to Québec, including regulatory and organizational frameworks. Stakeholder perspectives were gathered by an advisory committee made up of health professionals from various specialties and areas of expertise. The committee helped identify key clinical benchmarks and make recommendations based on the evidence obtained and the clinical experience of its members. Finally, the overall quality, acceptability and applicability of the work were assessed by external readers who are specialists in the field of interest, as well as future users who did not participate in the work.

Findings

Upon completing an analysis of the information gathered and the iterative process conducted with stakeholders, the following key messages and findings were identified as the most impactful in supporting the harmonization of clinical practice for preventing and managing immediate hypersensitivity reactions to parenteral cancer treatments in adults.

Anticipating and distinguishing the type of reaction for a more effective response

The ability to distinguish quickly between type 1 reactions, complement activation reactions and cytokine release reactions is crucial for safe management. While non-allergic reactions related to complement activation or cytokine release generally occur during the first infusion, type 1 allergic reactions occur after at least one well-tolerated cycle, usually after a few treatments, as observed with platinum salts. Primary prevention measures—including premedication and a gradual increase in flow rate—are generally ineffective in preventing type 1 reactions, unlike complement activation and cytokine release reactions, for which these measures are useful. Interrupting the infusion alone is often sufficient to resolve complement activation or cytokine release reactions, whereas type 1 reactions usually require more active management.

Harmonizing premedication, particularly for paclitaxel

This work highlights the need to harmonize premedication used during treatments involving a risk of immediate hypersensitivity reactions. More specifically, they indicate that second-generation histamine H1 receptor antagonists (anti-H1) (e.g., cetirizine, loratadine) may be considered as a replacement for diphenhydramine when an anti-H1 is required as part of a premedication protocol. In addition, the recommendations stipulate that histamine H2 receptor antagonists (anti-H2) should no longer be used as premedication during paclitaxel treatment. This is a significant change, as the use of H2 antagonists is still common in many Québec healthcare settings and is in keeping with the indications still found in the manufacturer's product monograph. Our work also indicates that the first two paclitaxel treatments could be administered at a progressive rate, which would reduce the risk or severity of hypersensitivity reactions which, in the case of paclitaxel, occur mainly during the first infusions.

Administering more epinephrine and fewer corticosteroids.

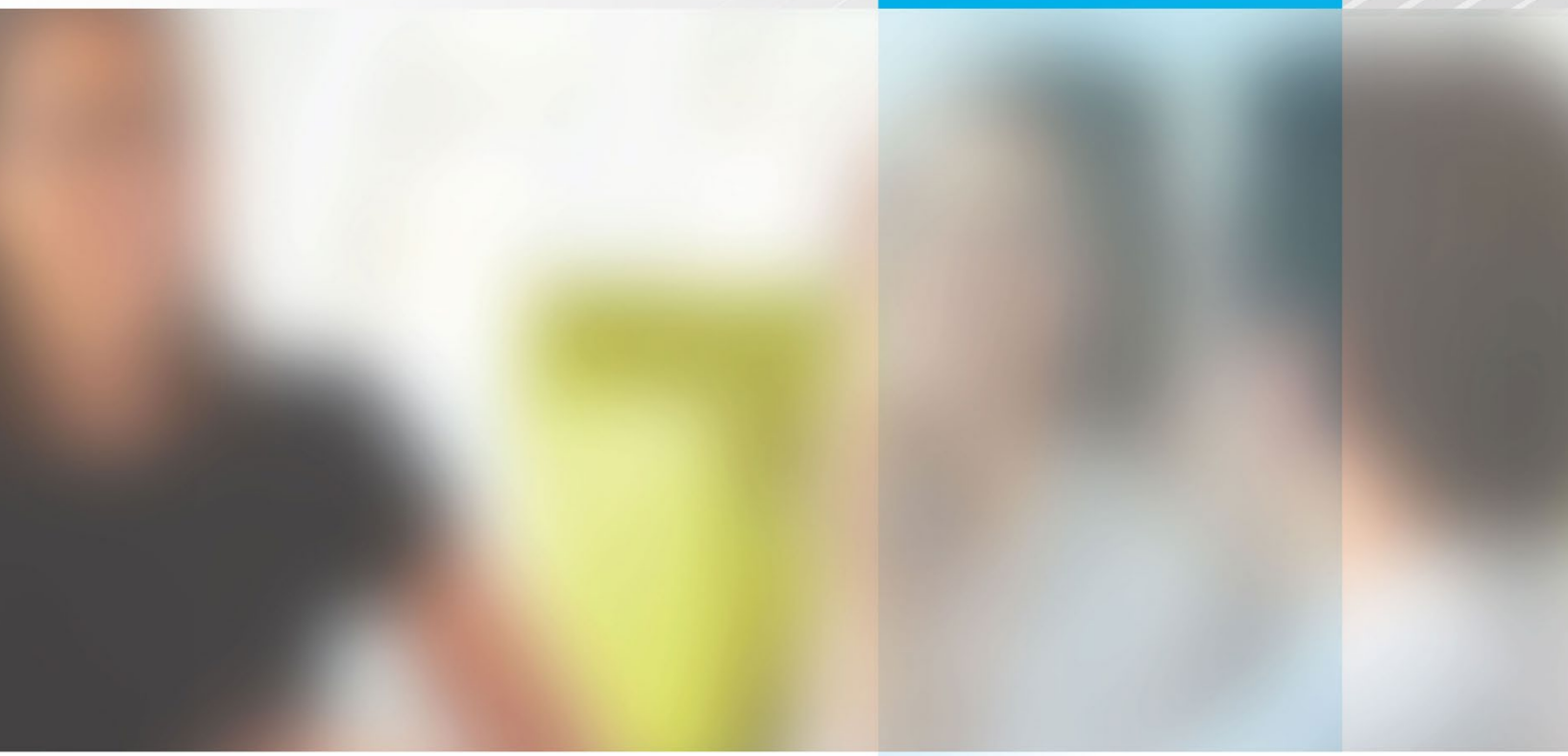
The work recommends wider and earlier use of intramuscular epinephrine. It should be administered as a first-line treatment for any severe reaction or for a moderate reaction that does not improve within five minutes of interrupting the infusion. Conversely, the use of corticosteroids should be limited to specific situations, particularly in cases of persistent hypotension, fever or chills despite all other measures taken. These adjustments represent a significant paradigm shift in many settings and will require a review of several local protocols.

Avoiding standard re-exposure to platinum salts after any type 1 reaction

Following a type 1 reaction, standard re-exposure to platinum salts is strongly discouraged, even if the initial reaction was mild or if a reduced-flow infusion was tolerated on the day of the initial reaction. Such reactions are usually recurrent and more severe despite the administration of premedication. Depending on the availability of resources, referral to an allergist and desensitization should be prioritized when no other acceptable treatment options are available.

Conclusions

The recommendations resulting from this work have been incorporated into a clinical tool designed to harmonize the prevention and management of immediate hypersensitivity reactions to parenteral cancer treatments across all Québec healthcare settings. This tool will support clinical practice without replacing professional judgment, while also helping mitigate such organizational issues as limited access to allergology and the ongoing need for training and knowledge retention. The enhancement and harmonization of practice will depend on the tool's dissemination, healthcare teams' adherence to the recommendations, and alignment with existing tools and protocols. This work can serve as a starting point for developing and updating preformatted individual prescriptions and collective prescriptions by healthcare teams.



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