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Unacknowledged adverse transfusion reactions: Are they a mine to dig?

Analyse des EIR non listés ou non précisés : une mine à creuser ?

J.-Y. Py [a,*], B. Cabezon [b], T. Sapey [c], T. Jutant [d]

[a] *EFS Centre-Atlantique Orléans, 190, rue Léon-Foucault, 45140 Saint-Jean-de-la-Ruelle, France*
[b] *EFS Centre-Atlantique Saintes, 33, chemin des Carrières-de-la-Croix, 17100 Saintes, France*
[c] *ARS Centre Val-de-Loire, 131, rue du Faubourg-Bannier, 45000 Orléans, France*
[d] *EFS Centre-Atlantique Poitiers, 350, avenue Jacques-Cœur, 86000 Poitiers, France*

Abstract

Objectives. – Haemovigilance has long tried to characterize and understand transfusion reactions in order to prevent them. Unacknowledged ones are now a minority but they question us. Are they the result of incomplete clinical setting and/or insufficient medical reasoning, or can they contain real new entities we have not yet understood?
Material and methods. – Ten volunteer experts reviewed 30 recent unacknowledged cases. Their diagnostic propositions were compared with data issued from a five-year repository we have analysed in terms of statistical links between clinical signs and diagnoses.
Results. – Experts' opinions are only quite unanimous in 60% of the cases, and the proposed diagnosis remains unacknowledged in 53%. Repository comparison shows that signs like pain or digestive symptoms are far more frequent in unknown reactions. However, it is more the absence of some other signs which drives to that conclusion, in a default diagnosis mechanism.
Conclusion. – Errors in transfusion reactions medical analysis are rare. Unacknowledged cases are more often linked to poor or unspecific clinical setting. But a particular attention must be paid with infrequent diagnoses which are far less characterised, like metabolic complications. Pain high occurrence in unknown cases also commands us to go further in the characterisation of acute pain transfusion reaction diagnosis, which is suggested by some authors.

Keywords: Transfusion reaction; Clinical reasoning; Case peer-evaluation

Résumé

But/objectif. – Depuis longtemps, l'hémovigilance cherche à caractériser et comprendre les complications de la transfusion sanguine pour mieux les prévenir. Les réactions non caractérisées sont maintenant une minorité, mais continuent de poser problème. Résultent-elles d'un tableau clinique fruste ou d'un mauvais raisonnement clinique, ou bien correspondent-elles à de nouvelles entités diagnostiques que nous n'avons pas encore comprises ?
Matériels et méthodes. – Dix experts volontaires ont accepté de revoir 30 cas conclus en diagnostic non précisé ou non listé. Leurs propositions ont été analysées en regard d'un référentiel sémiologique présentant les liens statistiques entre les signes cliniques observés et les diagnostics retenus dans les déclarations faites pendant une période de cinq ans.
Résultats. – Les propositions des experts convergent dans 60 % des cas, et le diagnostic proposé reste inconnu dans 53 %. L'analyse sémiologique du référentiel montre une présence nettement plus élevée de certains signes comme les douleurs ou les signes digestifs dans les diagnostics inconnus. Pour autant, c'est plus l'absence de certains autres signes qui aboutit à ce type de conclusion, dans un mécanisme de diagnostic par exclusion.

* Corresponding author.
E-mail address: jean-yves.py@efs.sante.fr (J.-Y. Py).

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Conclusion. – Les erreurs dans le diagnostic des réactions transfusionnelles sont rares. Les cas non caractérisés sont surtout liés à des tableaux cliniques pauvres et peu spécifiques. Mais on se doit d'y être attentif car des diagnostics plus rares, comme par exemple les accidents métaboliques, sont également bien moins décrits dans leur diversité possible. De même, la fréquence élevée des douleurs dans ces cas inconnus impose de creuser l'hypothèse d'un diagnostic spécifique de douleur aiguë post-transfusionnelle, suggéré par certains auteurs.

Mots clés : Réaction transfusionnelle ; Raisonnement clinique ; Expertise de cas

1. Background and objectives

The primary goal of French haemovigilance was and still remains to analyse adverse transfusion reactions in order to prevent them [1]. After more than 20 years, a considerable amount of data piled up but, as Williamson said, "do we know how best to use it" [2]? Hopefully, there are proofs of haemovigilance key contributions in transfusion security [3].

In French legislation [4], a healthcare professional aware of an adverse transfusion reaction must report it to the haemovigilance network regardless of its nature or gravity. This report will drive a declaration done by a local haemovigilance officer [5] using a national dedicated software called "e-FIT" [6,7].

The declaration form imposes to assign a diagnosis to the reaction. Since 2010, the diagnosis evidence has to be quoted and an alternative diagnosis can be suggested if this evidence is low. These diagnoses are found in a thesaurus, containing 27 items as of October, 2016. The most prominent ones are described in available factsheets [8,9].

Among those diagnoses, two are dedicated to unacknowledged situations:

- unspecified diagnosis when haemovigilance officers are not able to assign any diagnosis;
- unlisted diagnosis when the assigned diagnosis is not in the thesaurus.

These diagnoses represented respectively 1.4% and 1.3% of the reactions reported in 2015 in France with transfusion imputability at least possible [10].

Such diagnoses are also present in other haemovigilance organisations as "other" or "unknown" [11–14], with sometimes higher frequencies. In an international comparison [15], "other reactions" range from 1.5 to 33.7 for 100,000 transfused red blood cells concentrates. Comparison is not easy because organisations and their diagnoses definitions are different. For example, febrile non-haemolytic transfusion reactions were not in the French thesaurus before 2004 and "unknown" frequency reached nearly 50% at that time [4]. The main problem with these unknown cases is that they do not participate to haemovigilance data analysis while acknowledged diagnoses [16] are more and more studied and understood. In a recently published review [17], they were not even mentioned.

We decided to investigate those reactions to see if they can disclose some interesting aspects and we choose a cooperative approach. A previous similar study [18] had pointed out the ability to identify missing diagnoses. Another one [19] was aimed to identify diagnosis errors among cases with acknowledged diagnoses. More recently, American haemovigilance uses this method to validate its reporting software with a set of fictive cases including unknown ones [20].

2. Material and methods

We selected 30 recent cases of unacknowledged transfusion reactions in our regional database in the e-FIT software. We choose to treat without distinction "unspecified" and "unlisted" diagnoses because it seems their use was not always advisedly done.

Cases were anonymised and presented to the haemovigilance officers of our blood transfusion centre. Ten of them (63%) participated by proposing a diagnosis for each case, sometimes with a comment. Responses were transposed into thesaurus diag-

Table 1
Semeiotic analytical grid.

Sign	Items found in the declaration form
Pulm	At least one item ticked among cough, dyspnoea, bronchospasm, TACO signs
Allg	At least one item ticked among pruritus, urticarial, erythema, angioedema
DIGDig	At least one item ticked among nausea, vomiting, diarrhoea
Pain	Item pain ticked
Other	Item other clinical signs ticked
Shock	Item shock ticked
Shiv	Item shivers ticked
Hyperth	Difference between initial and reaction temperatures $\geq +1\,^{\circ}C$ Reaction temperature alone is known and $\geq 38.5\,^{\circ}C$
Hypoth	Difference between initial and reaction temperatures $\geq -1\,^{\circ}C$ Reaction temperature alone is known and $\leq 36\,^{\circ}C$
Hyperap	Difference between initial and reaction systolic arterial pressure $\geq +20\%$ Reaction systolic arterial pressure alone is known and ≥ 160 mm Hg
Hypoap	Difference between initial and reaction systolic arterial pressure $\geq -20\%$ Reaction systolic arterial pressure alone is known and ≤ 70 mm Hg
Hypercf	Difference between initial and reaction cardiac frequency $\geq +20\%$ Reaction cardiac frequency alone is known and ≥ 120/min
Hypocf	Difference between initial and reaction cardiac frequency $\geq -20\%$ Reaction cardiac frequency alone is known and ≤ 50/min
None	None of above clinical signs

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