A bedside test for methemoglobinemia, Sri Lanka

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Problem Propanil is an aniline herbicide that is widely used for rice cultivation, but is also used for self-poisoning. Toxicity from propanil is largely due to methemoglobinemia. In resource-poor settings, the capacity to determine methemoglobin concentration is insufficient and prevents effective case management, which results in increased deaths from propanil poisoning.

Approach Blood with a methemoglobin concentration greater than 15% of total haemoglobin levels appears brownish in colour. We introduced a colour reference chart that can be used to semiquantitatively determine methemoglobinemia. Each ward in three rural hospitals received a chart. Ward staff, medical officers and trainee doctors were given a presentation describing the test method and how it should be used with the relevant national treatment guidelines.

Local setting In three rural hospitals in Sri Lanka, 401 patients were admitted with a diagnosis of propanil poisoning before the introduction of this test (2003–2007) and 262 patients after it was introduced (2008–2014). 46 of 663 patients died.

Relevant changes The chart can be freely produced with any good-quality colour printer. In three rural hospitals, deaths from propanil poisoning fell from 10% of those admitted with this diagnosis in 2003–2007 (38/401) to 3% (8/262) in 2008–2014 and the use of methylene blue increased from 10% (13/136) to 55% (59/107) over this period.

Lessons learnt This simple bedside test was associated with increased use of the first-line treatment for propanil poisoning and improved survival. In 2011, the test was included in the national guidelines for the management of propanil poisoning.

Introduction

Propanil is an aniline herbicide that is widely used for rice cultivation. However, it is also used for deliberate self-poisoning. Propanil poisoning is usually manifested by methemoglobinemia and haemolytic anaemia, disorders that lead to reduction in effective oxygen transport and hypoxia. In general, the severity and symptoms of propanil poisoning correlate with the methemoglobin level in the blood. The recommended first-line treatment of methemoglobinemia is intravenous administration of methylene blue, which reduces the heme group from methemoglobin to hemoglobin. Methylene blue is inexpensive, accessible and easy to administer. The initial dose is 1–2 mg/kg of body weight with repeated doses titrated against the clinical response. Alternative treatments, such as ascorbic acid or N-acetylcysteine, are less effective, but can be used if methylene blue is unavailable. Exchange blood transfusion is only recommended when methylene blue or alternative treatments are ineffective.

The gold standard for determining methemoglobin concentration in the blood is by spectrophotometry. However, in rural areas, laboratory services are limited and it is usually not possible to measure methemoglobinemia with spectrophotometers or co-oximeters. As a methemoglobin concentration greater than 15% of total haemoglobin levels gives a brownish colour to blood, concentrations above 15% can be detected visually. Clinicians can use this visual method to diagnose patients, but to measure response to methylene blue treatment they need a more accurate method of quantification. We therefore developed a simple and low-cost bedside test for semiquantitative estimation of methemoglobin levels. The test is described in detail elsewhere. One drop of blood is placed on white absorbent paper and the colour of the blood spot compared to a reference chart (Fig. 1), corresponding to an estimated level of methemoglobinemia. We describe lessons learnt when using this bedside test in three hospitals in Sri Lanka.

Local setting

In Sri Lanka, propanil poisoning has been recognized as a significant clinical problem. Two cohort studies – from two rural tertiary referral hospitals – have shown propanil self-poisoning case-fatality of 11% (45/412). In these cohort studies, we identified treatment patterns at odds with national guidelines for the treatment of methemoglobinemia published by the Sri Lankan National Poisons Centre. The guidelines recommended the use of methylene blue as a primary treatment. We observed relatively low use of methylene blue and higher use of ascorbic acid or exchange transfusion. Although clinicians reported that it was easy to diagnose propanil poisoning, the lack of methemoglobin concentration measures made it difficult to determine whether patients were responding to methylene blue. The lack of an objective measure against which to titrate the dose lead to a recurrence of methemoglobinemia in some patients. Clinicians also raised two additional concerns in using methylene blue and in managing the subsequent reductions in methemoglobin concentration. First, methylene blue is ineffective in patients with complete glucose-6-phosphate dehydrogenase (G6PD) deficiency and may cause hemolysis. About one in every 20 people from Sri Lanka has G6PD deficiency. Second, it is known that excessive doses of methylene blue can, in theory, cause or worsen methemoglobinemia.
Relevant changes

In collaboration with clinicians at three tertiary rural hospitals, we introduced the methemoglobin colour chart into all the medical wards in 2008. For ward staff, medical officers and trainee doctors, clinical research staff gave a single 20-minute oral presentation describing the test method, and how it could be used within the current national treatment guidelines. We provided each ward with a methemoglobin colour chart. The chart was prepared using a good quality printer in a local photo studio. The accuracy of the reproduction of the colour chart was checked with colour analysis that compared its colours to the original colour values derived in the test’s development. Each ward received a poster that described the use of the colour chart and reiterated the national treatment guidelines. After introducing the colour chart in the hospitals, we validated the accuracy of the test in the field by taking an additional sample from 13 patients and analysing the blood using a spectrophotometer.

Independent of the treating team, clinical research assistants examined all poisoned patients until discharge or death. Clinical outcomes and treatment of each patient was prospectively recorded into the cohort database. We then identified, from the database, data on patients admitted with propanil poisoning. We were able to examine outcomes in 401 patients before (2003–2007) and 262 patients after (2008–2014) the introduction of the test.

Lessons learnt

After we introduced the test, case-fatality for propanil poisoning fell by two-thirds, from 10% (38/401) to 3% (8/262). Retrospective examination of available patient medical records showed an increase in the use of methylene blue after the test was introduced: from 10% (13/136) to 55% (59/107). Records showed that titrated doses of methylene blue were more common than single-dose treatment and such dosage patterns have been sustained. The use of less effective treatments and exchange transfusion were reduced, suggesting that clinicians accepted the utility of this test in the management of methemoglobinemia.

Our report has limitations. It is possible that some of the survivals may have been from unrelated improvements in care at this time. Our quasi-experimental comparison of two different time periods cannot exclude alternative explanations for the changes in number of deaths. However, the change in management and reduction in deaths was considerable and no major change in these outcomes had been observed within the study locations in the six years before the intervention.

Box 1 summarizes the main lessons learnt. The uptake of the test into practice was high, as the test quickly provided results, allowing more informed use of national treatment guidelines. Distribution of the colour chart was cheap, as it could be printed from a freely available file by any good-quality colour printer.

The simplicity and low cost of the test presented here can facilitate the treatment of methemoglobinemia in resource-poor settings. The test was included in the 2011 edition of the national guidelines: *Management of poisoning* and in the curriculum of local postgraduate training programmes for clinicians and nurses.

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Managing methemoglobinemia in Sri Lanka: Experience from a rural hospital

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Résumé
Test de la méthémoglobinémie au chevet des patients, Sri Lanka

Problème Le propanil est un herbicide à base d’aniline largement utilisé dans les cultures rurales. Mais il est aussi dans les cas d’autoempoisonnement. La toxicité du propanil se manifeste essentiellement par une méthémoglobinémie. Les établissements aux ressources limitées ne sont pas en mesure de déterminer la concentration de méthémoglobinine, ce qui empêche la prise en charge efficace des patients et la réduction du nombre de décès par empoisonnement au propanil.

Approche Le sang dont la concentration en méthémoglobinine est supérieure à 15% du taux d’hémoglobine total a une couleur brunâtre. Nous avons mis au point un nuancier de couleurs qui peut être utilisé pour déterminer semi-quantitativement la teneur en méthémoglobinine. Un nuancier de ce type a été remis à chacun des services de trois hôpitaux ruraux.

Environnement local Dans trois hôpitaux ruraux du Sri Lanka, 401 patients ont été admis avec un diagnostic d’empoisonnement au propanil avant l’introduction de ce test (2003–2007) et 262 patients après son introduction (2008–2014). 46 des 663 patients sont décédés.

Changement significatif Le nuancier peut être produit librement avec un ordinateur ou avec une imprimante couleur de bonne qualité. Dans les trois hôpitaux ruraux, le nombre de décès par empoisonnement au propanil a diminué de 10% (38/401) à 3% (8/262) en 2008–2014, et l’utilisation de bleu de méthylène a augmenté de 10% (13/136) à 55% (59/107) en 2011.

Lesions tirées Ce test simple au chevet du patient a été associé à une augmentation des traitements de première intention des empoisonnements au propanil ainsi qu’à une amélioration de la survie. En 2011, ce test a été inclus dans les directives nationales sur la prise en charge des empoisonnements au propanil.
Резюме

Тестирование на меттёмоглобинемию, выполняемое по месту оказания помощи, Шри-Ланка

Проблема
Пропанил — это анилиновый гербицид, широко применяемый для выращивания риса, который также может быть использован для самоотравления. Токсическое действие пропанила по большей части связано с меттёмоглобинемией. В условиях нехватки ресурсов отсутствует достаточный потенциал для определения концентрации меттёмоглобина, поэтому осуществлять эффективное лечение невозможно. Это является причиной большого количества смертей вследствие отравления пропанилом.

Подход
С концентрацией меттёмоглобина, превышающей 15% от суммарного уровня гемоглобина, имеет коричневый оттенок. Авторы представили справочную цветовую схему для полуколичественного определения меттёмоглобинемии. Схема была предоставлена в каждое отделение трех сельских больниц.

Результаты
Схема была представлена в каждом отделении трех сельских больниц. Для персонала, медицинских сотрудников и врач-практикantes отделений провели презентацию, в которой описывался способ тестирования и порядок его применения с соблюдением соответствующих национальных руководящих принципов лечения.

Местные условия
В трех сельских больницах Шри-Ланки 401 пациент поступил с диагнозом "отравление пропанилом". Это привело к резкому увеличению числа случаев, вовлеченных в исследование. В течение периода 2003−2007 гг. 38 (из 401) до 3% (8 из 262) в 2008−2014 гг., а количество случаев использования меттёмоглобина снизилось на 10% (13 из 136) до 55% (59 из 107) за этот период.

Выводы
Введение этого простого метода тестирования по месту оказания помощи обусловило более частое применение лечения первого ряда при отравлении пропанилом и большую выживаемость. В 2011 году метод тестирования был включен в национальные руководящие принципы ведения больных с отравлением пропанилом.

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