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Review

Safe and Appropriate Use of Insulin and Other Antihyperglycemic Agents in Hospital

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ABSTRACT

Ensuring safe and appropriate use of antihyperglycemic agents in hospital is a challenge. It requires that the contraindications and precautions to the use of non-insulin agents be observed, the incidence of hypoglycemia and severe hyperglycemia be minimized, and the risk of medication errors (including inappropriate prescribing) be reduced. Insulin is a high-alert medication with an increased risk for causing patient harm when prescribed inappropriately or administered in error. Reduction in the risk for medication error requires close attention to the many detailed steps in the various phases of the medication-use process. Hypoglycemia is often caused by failure to adjust antihyperglycemic therapy in response to a reduction in nutritional intake. Treatment needs to be more closely linked to patients' nutritional status, and nursing staff should be empowered to initiate prompt reversal of hypoglycemia. Hyperglycemia commonly results from reliance on sliding-scale insulin as the sole method of controlling blood glucose or failure to optimize treatment by increasing the dose of insulin. Suboptimal prescribing of insulin may be due to a lack of knowledge and expertise on the part of the prescriber or fear of causing hypoglycemia. Strategies for improvement of glycemic control include education of care providers on the safe and appropriate use of insulin, establishment of standardized protocols (i.e. order sets) for insulin use and provision of clinical decision aids at the point of care to guide prescribers. Considering the challenges and obstacles faced by hospitals, establishment of a multidisciplinary committee is recommended for the purpose of directing efforts at quality improvement of diabetes care within the hospital.

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R É S U M É

Il est difficile d'assurer une utilisation sûre et appropriée des agents antihyperglycémiques en milieu hospitalier. Il est nécessaire que les contre-indications et les précautions d'utilisation des agents non insuliniqes soient observées, que le nombre de cas d'hypoglycémie et d'hyperglycémie grave soit minimisé et que le risque d'erreurs de médicaments (incluant les prescriptions inappropriées) soit réduit. L'insuline est un médicament de niveau d'alerte élevé associé à un risque accru d'effets nuisibles chez le patient lorsqu'elle est prescrite de manière inappropriée ou administrée par erreur. La réduction du risque d'erreur de médicament exige de porter une attention soutenue aux nombreuses étapes minutieuses des diverses phases du processus d'utilisation des médicaments. L'hypoglycémie est souvent causée par l'échec de l'ajustement du traitement antihyperglycémique à la suite d'une réduction de l'apport nutritionnel. Le traitement doit être plus étroitement lié à l'état nutritionnel des patients, et le personnel infirmier devrait être habilité à contrer promptement l'hypoglycémie. L'hyperglycémie résulte généralement d'une dépendance à l'échelle d'adaptation aux doses d'insuline comme seul moyen de réguler la glycémie ou de prévenir l'échec de l'optimisation du traitement par l'augmentation de la dose d'insuline. La prescription sous-optimale d'insuline peut être due à un manque de connaissance et d'expertise de la part du prescripteur ou à la crainte de causer l'hypoglycémie. Les stratégies d'amélioration de la régulation de la glycémie incluent l'enseignement aux prestataires de soins de l'utilisation sécuritaire et appropriée de l'insuline, l'établissement de protocoles standardisés (c.-à-d. des ensembles de modèles d'ordonnances) d'utilisation de l'insuline, et la mise à disposition d'aides à la prise de décisions cliniques au lieu d'intervention pour conseiller les prescripteurs. Considérant les difficultés et les obstacles auxquels font face les hôpitaux, la mise en place d'un comité multidisciplinaire est

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recommandée en vue d'orienter les efforts vers l'amélioration de la qualité des soins prodigués aux diabétiques en milieu hospitalier.

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Introduction

Persons with diabetes or hyperglycemia comprise up to 40% of all inpatients and, as a result, there is a high prevalence of use of antihyperglycemic agents in hospital (1). The majority of use of non-insulin antihyperglycemic agents results from the continuation of maintenance therapy that was initiated prior to admission.

Safe and appropriate use of antihyperglycemic agents in hospital is exemplified by the following:

- Avoidance of their use in the presence of contraindications and observance of relevant precautions for their use.
- Prevention of medication errors and, in particular, safe use of insulin.
- Achievement of glycemic control, with a low incidence of hypoglycemia and severe hyperglycemia.

Safe and Appropriate Use of Non-Insulin Antihyperglycemic Agents

No large studies have investigated the effects of the use of non-insulin antihyperglycemic agents on outcomes in hospitalized patients with diabetes. The use of these agents presents challenges in the hospital setting because there are often contraindications to their use (1). In selected patients who are clinically stable, whose diabetes is well controlled and who are expected to eat normally, it is reasonable to continue selected non-insulin antihyperglycemic agents if they were successful in managing blood glucose (BG) prior to, and at the time of, admission and there are no contraindications to their use. However, if contraindications develop, or if glycemic control is inadequate, non-insulin agents should be discontinued and insulin therapy initiated (2). Hospitals should consider providing alerts to prompt care providers to reassess the appropriateness of continuing antihyperglycemic therapy when contraindications arise (3).

Metformin

The use of metformin is contraindicated in any of the situations listed in Table 1 due to an increased risk for the rare but potentially fatal complication of lactic acidosis. Because hospitalization for acute illness increases the chance that metformin use will be contraindicated, it may be prudent to discontinue metformin in most inpatients (2).

Table 1
Contraindications to the use of metformin

- Severe dehydration
- Severe hepatic dysfunction
- Severe renal impairment
- Acute or chronic metabolic acidosis or history of lactic acidosis
- Stress conditions, such as severe infection, trauma or surgery
- Conditions associated with hypoxia (myocardial infarction, cardiovascular collapse [shock], septicemia)
- Excessive alcohol intake, acute or chronic
- Intravascular administration of radiocontrast (stop metformin at time of imaging and restart after 48 hours if deterioration of renal function has been ruled out)

Metformin use is contraindicated in patients with estimated glomerular filtration rate (eGFR) <30 mL/min, and it should be used with caution if eGFR is 30 to 59 mL/min (4). Some authors have made further recommendations as follows: 1) patients with eGFR of 45 to 59 mL/min should have renal function monitored every 3 to 6 months; 2) those with eGFR of 30 to 44 mL/min should receive no more than 1000 mg per day and have renal function monitored every 3 months; and 3) metformin therapy should not be initiated in patients with eGFR 30 to 44 mL/min. Screening of inpatients receiving metformin for the presence of renal impairment and the concomitant use of nephrotoxic medications may be a useful strategy for enhancing adherence to the above recommendations. Care providers could be prompted to address issues by a system of computerized automatic alerts or in response to manual review of laboratory data and medication profiles (5). One study assessing the utility of computer alerts sent to the prescriber found that this strategy reduced the inappropriate use of metformin by 75% (6).

Heart failure requiring pharmacological therapy has in the past been listed in the metformin-prescribing information as a contraindication to its use. However, current evidence suggests that patients with heart failure fare at least as well, if not better, with metformin than with other antihyperglycemic agents in the absence of severe renal impairment. Therefore, metformin can be considered as first-line therapy in patients with heart failure, provided that eGFR is 30 mL/min or greater (7).

Insulin secretagogues

Sulfonylureas are long-acting insulin secretagogues that can cause severe and prolonged hypoglycemia, particularly in patients at risk, such as the elderly, those with renal impairment and those with inadequate or irregular nutritional intake. Use of lower doses is warranted in elderly patients who are more likely to have comorbidities and a decreased ability to tolerate the consequences of hypoglycemia (3).

The incidence of sulfonylurea-associated hypoglycemia in hospitalized patients has been reported to be 19% overall (22%, 19% and 16% for glyburide, glimepiride and glipizide, respectively) based on a 1-year retrospective review of medical records (8). Similarly, a 3-month prospective review of inpatient medical records found the prevalence of hypoglycemia among sulfonylurea recipients to be significantly higher for glyburide (19.1%) than for other sulfonylureas (glimepiride 13.6%, glipizide 10.0%). Approximately 40% of all hypoglycemic episodes in this study were related to decreased enteral caloric intake (e.g. missed meals or nil per os status due to illness or procedures) (9).

In view of the substantial risk for hypoglycemia and the unpredictability of nutritional intake in hospital, sulfonylureas should be prescribed and administered with the proviso that doses be held whenever a patient's nutritional intake is expected to be decreased. As well, the appropriateness of continuing sulfonylurea treatment should be reassessed after any episode of hypoglycemia. It has been suggested that sulfonylurea therapy be avoided in patients receiving enteral or parenteral nutrition because hypoglycemia may result if the feeding is interrupted (10).

In renal impairment, the following precautions for sulfonylurea use should be observed (4):

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