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# Improving post-hypoglycaemic patient safety in the prehospital environment: a systematic review

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## ABSTRACT

To determine the extent to which post-hypoglycaemic patients with diabetes, who are prescribed oral hypoglycaemic agents (OHA) are at risk of repeat hypoglycaemic events (RHE) after being treated in the prehospital environment and whether they should be transported to hospital regardless of their post-treatment response, a systematic literature review was carried out using an overlapping retrieval strategy that included both published and unpublished literature. Retrieved papers were reviewed by each author for inclusion. Disagreements regarding inclusion were resolved through discussion. Ninety-eight papers and other relevant material were retrieved using the developed search strategy. Twenty-three papers and other relevant material were included in the final review. A narrative synthesis of the findings is presented. Although several case reports demonstrate the risks associated with repeat or prolonged hypoglycaemia, the review was unable to locate any specific high quality research in this area. Consequently, caution is required in interpreting the findings of the studies. Post-hypoglycaemic patients treated in the prehospital environment have a 2–7% risk of experiencing a RHE within 48 h. The literature retrieved in this study recognises the potential for OHA to cause RHE. However, the extent to which this occurs in practice remains unknown. This lack of evidence has led to the recommendation that conservative management, through admission to hospital, is appropriate. The review concludes with recommendations for both practice and research.

Diabetes is a growing health concern placing increasing pressure on NHS resources.<sup>1</sup> In the UK 2.3 million people are currently diagnosed with the condition; a figure predicted to rise to 3 million by the end of the decade.<sup>2</sup> Audit data from one of the UK's largest ambulance services indicate that approximately 50% of the 6500 diabetes-related emergency calls per annum were for patients with hypoglycaemia. (R Lawrenson, Scottish Ambulance Service Audit Manager, personal communication, 2008).

In response to continuing increases in emergency department admissions,<sup>3</sup> UK ambulance services have identified new ways of working aimed at reducing unnecessary transportations and attendances at emergency departments. Initiatives such as “treat and refer” or “see and treat” (S&T) guidelines have enabled ambulance clinicians to attend, treat, discharge or refer patients with a defined list of conditions as appropriate.<sup>4–6</sup> One condition typically included in such guidelines is hypoglycaemia in diabetes.

This review focuses on patients with type II diabetes who are prescribed oral hypoglycaemic

agents (OHA). OHA are used to treat some patients with type II diabetes when there is either insulin resistance or when the pancreas produces insufficient quantities of insulin to meet the body's requirements.<sup>7–9</sup> In the latter, their action stimulates the secretion of stored insulin from pancreatic beta cells, which then acts at a cellular level enabling the uptake and utilisation of glucose by the cell.<sup>8</sup> Recurrent and prolonged hypoglycaemia resulting from renal insufficiency, drug interaction or accidental/deliberate overdose are known risks of OHA, particularly the sulphonylurea group.<sup>7–9</sup> In the prehospital setting a post-hypoglycaemic patient may be discharged by the ambulance clinician after apparent recovery, only to have a subsequent event hours or even days later. These risks have resulted in some,<sup>5 10–13</sup> but not all,<sup>4 14</sup> ambulance services advising transportation to hospital for all post-hypoglycaemic patients with type II diabetes treated with OHA, regardless of treatment response. Such service variation highlights the inconsistencies in ambulance service hypoglycaemia guidelines both in the UK and internationally.<sup>4 5 10–14</sup>

## AIM

To determine the extent to which post-hypoglycaemic patients with diabetes who are prescribed OHA are at risk of repeat hypoglycaemic events (RHE) after being treated in the prehospital environment, and whether they should be transported to hospital regardless of their post-treatment response.

## METHODS

A systematic literature review was conducted. The following search strategy was used to retrieve relevant material: (1) Medline (using Pubmed) was searched using the following search strategy: (“diabetes”[All Fields] OR “diabetes mellitus”[All Fields] OR “diabetic”[All Fields]) AND (“sulphonylurea”[All Fields] OR “sulfonylurea”[All Fields]) OR “rebound hypoglycaemia”[All Fields] OR “diabetic emergency”[All Fields] OR “oral agents”[All Fields] OR “oral hypoglycaemic agent\$”[All Fields] OR (“hypoglycaemia”[All Fields] OR “hypoglycaemia”[All Fields] OR “hypoglyc\$”[All Fields]) OR “glucose”[All Fields] OR “dextrose”[All Fields] OR “glucagon”[All Fields]) AND (“pre-hospital”[All Fields] OR “prehospital”[All Fields] OR “ambulance”[All Fields] OR “paramedic”[All Fields] OR (“therapy”[Subheading] OR “therapy”[All Fields] OR “treat”[All Fields]) AND refer[All Fields]) OR “see and treat”[All Fields]). (2)

Electronic searching of the Cochrane Library and clinicaltrials.gov using adaptations of the above search terms. (3) Hand searching of clinical text books and key journals: BNF pharmacology 2006; *Emergency Medicine Journal* (January 2000 to March 2007); Joint Royal College Ambulance Liaison Committee National Clinical Guidelines (2006). (4) Grey literature (unpublished material): "Pathfinder" course material. (5) Personal communication with other ambulance services and diabetologists.

### Inclusion/exclusion criteria

Peer reviewed papers, letters and unpublished documents were all included in the review. Retrieved material was excluded if it did not include patients with type II diabetes treated with OHA, the topic was not of direct relevance, or the paper was not published in English.

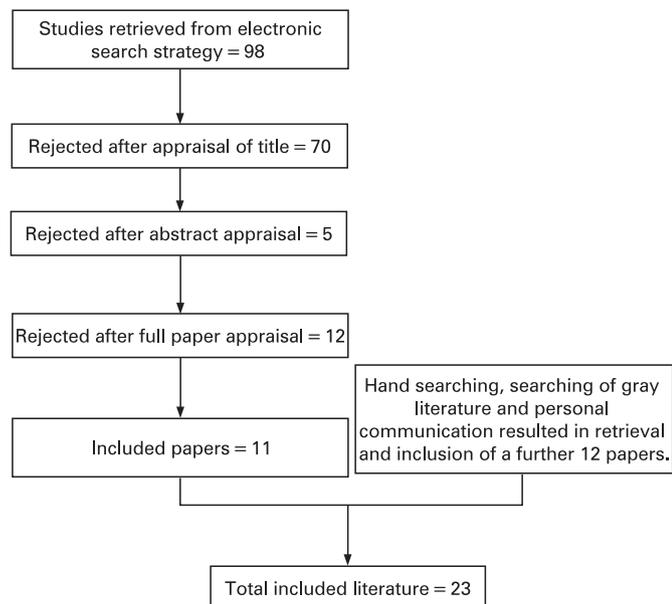
Titles and abstracts were screened for inclusion by one of the authors (DF). All potentially relevant papers and material were retrieved and the full documents were then read by both authors to check that each met the inclusion criteria. Each paper was then categorised according to publication source and research method (fig 1). References of electronically retrieved but excluded papers are available from the authors on request.

### ANALYSIS

Due to the small number, low quality and data heterogeneity of included quantitative research studies a meta-analysis of the findings was not conducted. Instead a descriptive summary of the included paper's sources and research design was developed and a narrative synthesis of key themes from these papers is provided.

### Findings

Table 1 outlines the sources of literature and types of study design of the included papers. Eighteen papers were retrieved from peer-reviewed journals, one internet site and four publications from other sources were also included. Only one controlled trial was found in this area.<sup>12</sup> Eight of the included papers were cohort studies.<sup>6 13 15-20</sup> Six papers were literature



**Figure 1** A flow chart of included literature.

reviews.<sup>8 9 21-24</sup> Two presented case reports<sup>25 26</sup> and one reported a retrospective case note analysis study.<sup>14</sup> In addition, four guidelines<sup>4 5 10 11</sup> and one well recognised reference book<sup>7</sup> were included.

Of the included studies from the retrieved literature (n = 18), 12<sup>6 12-18 22-25</sup> included patients who had had hypoglycaemic events and were treated with OHA. Twelve<sup>8 9 13 15-17 19 21-25</sup> emphasised the inherent dangers of these drugs, and 10<sup>8 9 12 13 17 20-23 25</sup> highlighted treatment in, or suggested a treatment only available within, the hospital environment. Care was taken to ensure no double counting of individual studies occurred.

### RESULTS

#### Incidence of OHA-induced hypoglycaemia

Of the included studies, which followed patients between 6 months and 3 years, the incidence of OHA-induced hypoglycaemia (in type II diabetes) was predominantly reported as being between 0.8% and 12%.<sup>6 15 16 21</sup> However, one study reported an incidence of 23% over a 3-year period.<sup>13</sup>

#### Risks and causes of OHA-induced hypoglycaemia

The potential for hypoglycaemia was highlighted as the most significant risk associated with OHA.<sup>7 8 24</sup> The primary risk to any hypoglycaemic patient is reduced levels of consciousness, leading to airway compromise, seizure, cerebral oedema (potentially resulting in permanent neurological deficit) and in rare cases, death.<sup>8 24</sup> Other risks such as prolonged hypoglycaemia or RHE result from the long-acting nature of some OHA, particularly the sulphonylurea group.<sup>8 13 24 25</sup> Cases have been described in which hypoglycaemic patients prescribed OHA have been treated appropriately with intravenous glucose only to experience RHE hours or even days after the initial event.<sup>17 25</sup>

Two reviews<sup>8 22</sup> describe the general risk factors associated with hypoglycaemia in patients treated with OHA. These include the elderly, those with a history of vascular disease, renal failure, reduced food intake, alcohol consumption and drug interactions. Specific examples of these risk factors in the included papers include medication interactions,<sup>8 26</sup> quiescent renal or hepatic disease<sup>25</sup> and accidental or deliberate ingestion.<sup>8 9</sup> Many of these arise from the clinicians' failure to consider the contribution of such risk factors to either an initial or RHE and illustrate how ignoring such risk factors unnecessarily exposes the patient to the dangers associated with hypoglycaemia.

#### Repeat calls for hypoglycaemic events

Five of the papers included in this review directly discussed repeat emergency calls for hypoglycaemic events.<sup>14 16-19</sup> These papers were examined to identify the rates of RHE and whether OHA were viewed as a contributory factor. There was no standard definition of "recurrence" in the literature. Reported recurrence times ranged between 24 and 120 h, with the incidence of RHE within a 48-h period varying between 2% and 7%.<sup>14 16-19</sup> No studies were detailed enough to determine how many of these RHE were directly related to OHA.

#### Transport to hospital

Roberts and Smith<sup>23</sup> identified post-hypoglycaemic patients treated with OHA as high risk and recommended that they be transported to hospital; no rationale was provided. Brackenridge *et al*<sup>20</sup> emphasise that patients on OHA are "special cases" (p 185) and suggest the "threshold for admission" (p 185) to be

**Table 1** Study design and core findings of included papers

Author, date and country	Patient group	Study design	Core findings and outcomes	Limitations/weaknesses
Mattila <i>et al.</i> , <sup>12</sup> 2004, Finland	Investigation of the clinical epidemiology of severe out-of-hospital hypoglycaemia 11 months (Feb–Dec 2001) 69 Participants	Control trial	90% (n = 62) of patients were left at scene  55% (n = 22) of questionnaire respondents had a RHE within 3-month follow-up period, none within 24 h  The practice of leaving selected patients at the scene after assessment and treatment was found to be effective, safe and economical  All patients with type 2 diabetes prescribed OHA were transported to hospital	Only 8.5% (n = 69) of patients left at home were included in this study  Short study duration  Only patients with type 1 diabetes were left at home  Time between emergency contact and research contact was 3 months
Steinmetz <i>et al.</i> , <sup>18</sup> 2006, Denmark	Assessed patients preferences to locality of treatment, ie, hospital or home. 139 Participants	Prospective cohort study	6% (n = 8) patients treated and discharged at the scene were admitted to hospital within 48 h  Involvement of OHA is unknown	This intervention was limited to physicians  Did not provide sufficient detail to determine the cause of admission for the eight patients who were admitted within the 48-h period  Limited information on study methods  Small sample size
Walker <i>et al.</i> , <sup>6</sup> 2006, UK	Evaluation of ambulance crew referral pathway to a DSN 3 Months (Dec 2002–March 2003) 38 Participants	Prospective cohort study	53% (n = 20) of referred patients had medication altered, 37% (n = 14) required ongoing review. Of participants who returned questionnaire, 73% (n = 19) felt more able to treat a hypoglycaemic episode in the future.  Recommends specialist pathways to DSN for patients who have had a hypoglycaemic event  Highlights the need for medication alteration and expert advice for patients	Required shorter follow-up period, ie, <7 days required to ensure safety for patients
Brackenridge <i>et al.</i> , <sup>20</sup> 2006, UK	Exploration of the use of emergency services by people with diabetes 12-Month audit (Oct 2000–Sept 2001) 89 Participants	Prospective cohort study	Management of hypoglycaemia by the emergency services was varied and not always appropriate  11% (n = 10) of sample were admitted to hospital  Many patients who attend ED were discharged with no follow-up arrangements. Education is required for healthcare professionals. Highlights challenges of identifying people who need to be admitted to hospital.  States that patients treated with OHA should be treated as “special cases”	Patients were not followed up adequately to provide detail on, and determine if, a repeat hypoglycaemic event occurred
Cain <i>et al.</i> , <sup>17</sup> 2003, Canada	Determined the outcomes of patients treated and not transported for hypoglycaemia and identified criteria for those who do not require to be transported 10 Months (Aug–June 2001) 220 Participants	Prospective cohort study	Repeat hypoglycaemic events are reported to be common, however, recurrences within 48 h are not  From the 220 hypoglycaemic emergencies, 145 patients were left at home, 27% (n = 40) of whom made a repeat call within the study period; 2% (n = 3) of these were within 48 h.  From the 75 patients transported to hospital, 22.7% (n = 17) reported a RHE, with 4% (n = 3) occurring within a 48-h period.  Given the high incidence of repeat hypoglycaemic episodes, paramedics and physicians need to emphasise the importance of follow-up	Unable to determine OHA involvement in recurrence of hypoglycaemia
Holstein, <sup>13</sup> 2003, Germany	Obtain reliable data on the care of prehospital diabetic emergencies with a view to improving quality of care 3 Years (Jan 1997–Dec 2000) 213 Patients	Prospective cohort study	Training of emergency teams with a specific intervention improved quality of treatment and prognosis outcome for patients  Treatment of severe hypoglycaemia at the scene was deemed to be safe in patients with type 1 diabetes who had previously received structured patient education  Mortality rates for sulfonylurea-induced hypoglycaemia dropped from 4.9% (n = 2) to 0%	This intervention was limited to physicians  Limited number of sulfonylurea-induced hypoglycaemia, much larger trials including comorbidity, type of OHA and dose would be required to substantiate the results of this study

Continued

Table 1 Continued

Author, date and country	Patient group	Study design	Core findings and outcomes	Limitations/weaknesses
Leese <i>et al</i> , <sup>15</sup> 2003, UK	Determine the incidence, predisposing factors and costs of emergency treatment of severe hypoglycaemia in people with type 1 and type 2 diabetes  12-Month period (June 1997–June 1998) 160 Patients	Cohort study	Hypoglycaemia requiring emergency assistance is as common in patients with type 2 diabetes as in insulin-dependent type 1 diabetes	Episodes of hypoglycaemia that were treated in environments other than ambulance, primary care and hospitals were not recorded, this may have resulted in an underestimation of all severe hypoglycaemic events.
Carter <i>et al</i> , <sup>19</sup> 2002, Canada	Determine if patients who had received prehospital iv dextrose seek additional medical care within a 72-h period post-hypoglycaemic event  12 Months (April 1999 to March 2000)  100 Patients	Retrospective cohort study	68% Refused transportation  The practice of treating patients with symptomatic hypoglycaemia and leaving them at the scene appears to be safe. Further study required to confirm this.	Hawthorne effect: as paramedics were aware that this study was taking place the potential for such an effect cannot be excluded
Socransky <i>et al</i> , <sup>16</sup> 1998, USA	Aimed to identify RHE in patients with diabetes and compare outcomes of those who refused with those who were transported to hospital  7 Months (Jan–July 1995)  374 Participants (made 571 emergency calls)	Cohort study	Out-of-hospital treatment of hypoglycaemic patients with diabetes appears to be effective and efficient independent of whether they were transported or not  Relapse rates did not differ significantly between the refusers and the transported patients  None of the 32 patients who relapsed did so within the subsequent 48 h	Did not consider clinic visits as an indicator of relapse, which may result in an underestimation of relapses
Langford <i>et al</i> , <sup>25</sup> 2003, UK	Case report describing repeat hypoglycaemic events in a 62-year-old woman with impaired renal function treated with gliclazide	Case report	Demonstrates the effects impaired renal function have on plasma insulin concentrations in a patient who is treated with OHA. The patient had repeat hypoglycaemic events.	Single case
Bussing and Gende, <sup>26</sup> 2002, USA	Two case reports highlighting the interaction between clarithromycin and sulfonylureas resulting in hypoglycaemia	Case report	Both patients received an initial bolus of iv glucose. The patient who did not receive a continuous glucose infusion had a repeat hypoglycaemic event.	Only two cases
Anderson <i>et al</i> , <sup>14</sup> 2002, Denmark	Aimed to validate the appropriateness of leaving the patient with prehospital hypoglycaemia after being safely treated at home in a physician-based EMS system  4 Years (1995–8)  1148 Hypoglycaemic patients treated by a mobile intensive care unit were used Possible predictors of transportation were identified	Retrospective case note analysis	964 Patients were released home  RHE events between 0 and 72 h post-treatment were identified. 5% (n = 46) of those treated and released home experienced a RHE within the 72-h period, 75% (n = 31) occurring within 48 h post-treatment.	This intervention was limited to physicians
Zammit and Frier, <sup>24</sup> 2005, UK	Aimed to identify the frequency and pathophysiology of hypoglycaemia in type 2 diabetes  Search via PubMed 1984–2005	Systematic literature review	Results suggest that insufficient and misleading information may have contributed to the perception that hypoglycaemia is considered to be a mild and infrequent side effect of treatment in type 2 diabetes. Identifies sulfonylurea-induced hypoglycaemia as a significant problem.	Narrative synthesis of findings, not meta-analysed  Variations in design, heterogeneity of study populations and varying classifications of hypoglycaemia. Looking at the elderly patients with type 2 diabetes with hypoglycaemic events confounded attempts in this review to determine the frequency of hypoglycaemia in type 2 diabetes.
Roberts and Smith, <sup>23</sup> 2003, UK	Identified outcomes for patients who were treated for hypoglycaemia out of hospital and included set of recommendations for the safe follow-up of patients  Search strategy was defined using MeSH terms and conducted via Medline	Systematic literature review	Advised transportation to hospital of all post-hypoglycaemic patients treated with OHA, no rationale was provided	Narrative synthesis of findings, not meta-analysed.  Search terms do not include hypoglycaemia or other condition-specific terms Limited retrieval of papers

Continued

Table 1 Continued

Author, date and country	Patient group	Study design	Core findings and outcomes	Limitations/weaknesses
Spiller, <sup>9</sup> 1998, USA	Focuses on antidiabetic medications in overdose (deliberate and accidental)	Systematic literature review	Overdose with antidiabetic drugs produces major morbidity, requires intensive care medicine and prolonged hospital stays Monitored for at least 24 h  When overdose does occur prompt recognition results in an improvement in successful outcomes	No search strategy defined, difficulty in reproducing review  Narrative synthesis of findings, not meta-analysed
Harrigan <i>et al</i> , <sup>3</sup> 2001, USA	Review of oral antidiabetic agents describing the treatment of type 2 diabetes regarding the pharmacology, toxicity and treatment	Review	Pharmacology of OHA described, adverse effects, ie, hypoglycaemia, drug interactions and toxicities  Patients with hypoglycaemia in the setting of therapeutic error, impaired renal function etc should be admitted for observation	Search strategy is not defined, difficulty in reproducing review
Murphy and Colwell, <sup>22</sup> 2000, USA	An educational review that details the pathophysiology of the condition as well as treatments and emergencies relating to the condition	Review	Describes prehospital treatment for diabetes-related emergencies. Prolonged hypoglycaemia in patients treated with OHA is highlighted.  Patients on OHA are at risk of prolonged hypoglycaemia	Search strategy is not defined, difficulty in reproducing review. Some of the treatments are either specific to region or dated.
Lheureux <i>et al</i> , <sup>21</sup> 2005, Belgium	Focuses on the antidotal treatment of sulphonylurea-induced hypoglycaemia with octreotide	Review	Hypoglycaemia is a major potential adverse effect of sulphonylurea agents. Causes and treatments are described, specifically the use of octreotide. Clearly describes pharmacological actions of sulphonylureas.	Limited number of studies on the use of octreotide in sulphonylurea-induced hypoglycaemia. Search strategy not defined.
Basics, <sup>10</sup> Pathfinder guidelines, 2004, UK	n/a	Guideline	Advises transportation of all post-hypoglycaemic patients with diabetes treated with OHA to hospital	n/a
Welsh Ambulance Service, <sup>3</sup> T&R guidelines, 2006, Wales	n/a	Guideline	Advises transportation to hospital for patients treated with OHA who have experienced a hypoglycaemic event	n/a
Joint Royal College Ambulance Liaison Committee, <sup>11</sup> 2006, UK	n/a	Guideline	Advises that all patients treated with OHA who have experienced a hypoglycaemic event should be transported to hospital	n/a
Scottish Ambulance Service, <sup>4</sup> T&R guideline, 2004, Scotland	n/a	Guideline	Does not specifically advise transportation to hospital for patients treated with OHA who have experienced a hypoglycaemic event	n/a
British National Formulary, <sup>7</sup> 2006, UK	n/a	n/a	The BNF provides specific detail on sulphonylurea-induced hypoglycaemia and highlights the prolonged effects and the need for treatment in hospital	n/a

BNF, British National Formulary; DSN, diabetic specialist nurse; ED, emergency department; EMS, emergency medical services; iv, intravenous; OHA, oral hypoglycaemic agent; RHE, repeat hypoglycaemic event; T&R, treat and refer.

low, while Socransky *et al*<sup>16</sup> state that patients taking OHA who have had a hypoglycaemic event should be convinced to travel to hospital. The British National Formulary (BNF)<sup>7</sup> recommends that such patients should always be treated in hospital. A recent review<sup>9</sup> supports this stance and recommends patients are observed for at least 24 h; whereas less conservatively, Harrigan *et al*<sup>8</sup> suggest a minimal observation time of 8 h. The length of time patients should be observed, therefore, remains unclear.

The reviews by Murphy and Colwell<sup>22</sup> and Harrigan *et al*<sup>8</sup> reveal the dangers of hypoglycaemia caused by OHA and highlight treatments such as continuous glucose infusions and constant blood glucose monitoring. A strong case for such treatments and transportation of patients with OHA-induced hypoglycaemia is demonstrated in the study by Holstein *et al*,<sup>15</sup> in which the authors specifically targeted sulphonylurea-induced hypoglycaemic patients with a treatment protocol. This consisted of mandatory additional glucose infusions and hospital admission for further treatment and observation. The study's pre-intervention statistics on mortality rates associated with all sulphonylurea-induced hypoglycaemia were 4.9% and 1.7% for all other causes. After intervention, mortality rates from severe hypoglycaemia caused by sulphonylureas were reduced to 0%.

## DISCUSSION

This systematic review has retrieved and analysed 23 documents in an attempt to establish if post-hypoglycaemic patients with diabetes who are prescribed OHA are at risk of RHE after being treated in the prehospital environment and whether such patients should be transported to hospital regardless of treatment response.

### Risks associated with OHA

Although a relatively rare occurrence, patients with diabetes treated with OHA can and do experience hypoglycaemic episodes. This review clearly exposes the risks associated with OHA and the possible dangers of RHE when leaving post-hypoglycaemic patients treated with OHA at home.<sup>7 8 20 25 26</sup> A decision not to transport these patients may result in unnecessary and unacceptable risks, including repeat or prolonged hypoglycaemia leading to seizure, cerebral oedema, permanent neurological deficit and, rarely, death.<sup>8 9</sup>

### Repeat calls and OHA

It cannot be determined from the five papers<sup>14 16-19</sup> documenting repeat call-outs if OHA were directly involved, but it is evident

that unrecognised risks, such as those outlined in the study by Harrigan *et al*<sup>8</sup> and failure to treat accordingly may lead to a RHE posing a direct risk to patients. Repeat calls also directly impact on ambulance resources reducing ambulance availability and consequently affecting response times. On the basis of the limited available evidence, the safest action to be taken by ambulance clinicians attending a post-hypoglycaemic patient with diabetes treated with OHA is to transport them to hospital to be admitted for a period of observation, appropriate treatment and follow-up care. The potential benefits of admission may include extended monitoring, continuous glucose infusions, pharmacological interventions, exploration of underlying causes and medication alteration if required. In the UK the standard prehospital treatment for hypoglycaemia includes either intramuscular glucagon or the intravenous administration of 10% glucose, in 100 ml boluses to a maximum of 300 ml (30 g).<sup>11</sup> Similar guidelines to those used in the study by Holstein *et al*,<sup>13</sup> ie, continuous infusion of 10% glucose after the initial bolus, could be considered for UK ambulance clinicians. This may be particularly beneficial in remote and rural areas, should such a situation arise, where transportation times can be prolonged and repeat intervention may be required.

#### Future directions: education and referral processes

Some ambulance service guidelines currently enable clinicians to refer or discharge patients with certain conditions, including hypoglycaemia. However, although basic ambulance service education includes the recognition of and emergency treatments for patients with hypoglycaemia, there is little specific education on the risks associated with OHA or the provision of appropriate care plans (ie, what to do with patients). Lack of awareness of the possibility of a RHE may result in patients being left at home inappropriately by ambulance clinicians. The literature currently suggests a minimum observation period of 24 h for post-hypoglycaemic patients treated with OHA. Extended observation would be difficult in an outpatient setting, the literature did not suggest this as an alternative and it is unlikely that the current health service infrastructure would enable this to be achieved safely. Therefore, patients treated with OHA who have had hypoglycaemic events requiring treatment from an ambulance clinician should be transported directly to hospital so they can be observed, treated and receive appropriate follow-up care. Ambulance clinicians should be educated to this effect.

Although it is not always necessary to transport the post-hypoglycaemic type 1 insulin-dependent patient with diabetes, this review has highlighted other issues that require to be addressed with this population. Some S&T guidelines place the responsibility of contacting the general practitioner following a hypoglycaemic event on the patient;<sup>4</sup> ambulance clinicians typically leave a carbon copy of the S&T form containing details of the event and the patient is asked to pass this on to their general practitioner. This system is ineffective. Patients' attendance for follow-up in primary care (which enables medication alteration and specialist education to be provided) is low,<sup>17</sup> and when patients do make an appointment the time delay between the original referral and attendance can often be several days, during which time a relapse may occur.<sup>6</sup> Walker *et al*<sup>6</sup> developed and evaluated a referral process for post-hypoglycaemic patients. Patients who had had a hypoglycaemic episode were referred by the ambulance service to a diabetic specialist nurse (DSN) who then contacted the patient within 7 days of the event. Fifty-three per cent (n = 20) of the

referred patients required medication alteration and 37% (n = 14) required additional appointments for ongoing care issues. One patient had a further hypoglycaemic event in the period between being referred and being seen by the DSN.

Irrespective of the type of diabetes, efforts should be made to increase the attendance of these patients to primary or specialist care within as short a timeframe as possible. This would enable more patients to receive expert advice, medication review and subsequent follow-up care. Evidence-based interventions to increase post-hypoglycaemic patient attendance in primary care should be developed.

#### LIMITATIONS

Only English language publications were included in this review. Although we have comprehensively searched and appraised the available literature, little high quality research was retrieved. Consequently, caution is required in interpreting the findings of the studies.

#### CONCLUSION

The findings of this study indicate that post-hypoglycaemic patients treated in the prehospital environment are at a 2–7% risk of experiencing a RHE within 48 h. The potential for OHA to cause RHE is highlighted in the reviewed literature. However, the extent to which this occurs in practice remains unknown. This lack of evidence has led to the recommendation that conservative management, through admission to hospital, is appropriate. The review has also highlighted that appropriate follow-up care of all other post-hypoglycaemic patients is required.

Several practice and research recommendations arise from this review.

Practice recommendations:

- ▶ All hypoglycaemia S&T guidelines should recommend that patients treated with OHA are transported to hospital for appropriate observation and treatment. Ambulance clinicians should receive education on the appropriate management of hypoglycaemic patients treated with OHA.
- ▶ Referral pathways should be developed to ensure appropriate follow-up care for all patients with diabetes.

Research recommendations:

- ▶ Evidence-based interventions to increase post-hypoglycaemic patient attendance in primary care should be developed and evaluated.
- ▶ An investigation into the causes of RHE, the timeframes in which these occur and the length of observation time required to ensure patient safety.

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#### REFERENCES

1. **Scottish Government.** *Scottish diabetes framework action plan.* Edinburgh: Scottish Government, 2006.
2. **Diabetes UK.** *Reports and statistics: diabetes prevalence.* [http://www.diabetes.org.uk/Professionals/Information\\_resources/Reports/Diabetes-prevalence-2007/](http://www.diabetes.org.uk/Professionals/Information_resources/Reports/Diabetes-prevalence-2007/) (accessed: 19 Sept 2008).
3. **Scottish Executive.** *A national framework for service change: building a service fit for the future.* Edinburgh: Scottish Executive, 2005.

4. **Scottish Ambulance Service.** *Scottish Ambulance Service: treat and refer guidelines.* Edinburgh: SAS, 2004.
5. **Welsh Ambulance Service.** *Welsh Ambulance Service: treat and refer guidelines.* Denbighshire: WAS, 2006.
6. **Walker A,** James C, Bannister M, *et al.* Evaluation of a diabetes referral pathway for the management of hypoglycaemia following emergency contact with the ambulance service to a diabetes specialist nurse team. *Emerg Med J* 2006;**23**:449–51.
7. **British National Formulary.** *BNF.6.1.2.1 sulphonylureas.* [http://bnf.org/bnf/bnf/57/4164.htm?q=%22sulphonylureas%22#\\_hit/](http://bnf.org/bnf/bnf/57/4164.htm?q=%22sulphonylureas%22#_hit/) (accessed: 19 Sept 2008).
8. **Harrigan RA,** Nathan MS, Beattie P. Oral agents for the treatment of type 2 diabetes mellitus: pharmacology, toxicity, and treatment. *Ann Emerg Med* 2001;**38**:68–78.
9. **Spiller HA.** Management of antidiabetic medications in overdose. *Drug Safety* 1998;**19**:411–24.
10. **BASiCs Education Scotland/Scottish Ambulance Service.** *Basics Education Scotland: paramedic extended skills course.* Aberthven: BASiCs Education Scotland/SAS, 2004.
11. **Joint Royal College Ambulance Liason Committee.** *UK Ambulance Service Clinical Practice Guidelines (2006): glycaemic emergencies in adults.* London: JRCALC, 2006.
12. **Mattila EM,** Kuisma MJ, Sund KP, *et al.* Out-of-hospital hypoglycaemia is safely and cost-effectively treated by paramedics. *Eur J Emerg Med* 2004;**11**:70–4.
13. **Holstein A,** Plaschke A, Vogel MY, *et al.* Prehospital management of diabetic emergencies—a population-based intervention study. *Acta Anaesthesiol Scand* 2003;**47**:610–15.
14. **Anderson S,** Hogskilde PD, Wetterslev J, *et al.* Appropriateness of leaving emergency medical service treated hypoglycemic patients at home: a retrospective study. *Acta Anaesthesiol Scand* 2002;**46**:464–8.
15. **Leese GP,** Wang J, Broomhall J. Frequency of severe hypoglycemia requiring emergency treatment in type 1 and type 2 diabetes: a population-based study of health service resource use. *Diabetes Care* 2003;**26**:1176–80.
16. **Socransky SJ,** Pirralo RG, Rubin JM, *et al.* Out-of-hospital treatment of hypoglycemia: refusal of transport and patient outcome. *Acad Emerg Med* 1998;**5**:1080–5.
17. **Cain ED,** Ackroyd-Stolarz S, Alexiadis P, *et al.* Prehospital hypoglycemia: the safety of not transporting treated patients. *Prehosp Emerg Care* 2003;**4**:458–65.
18. **Steinmetz J,** Nielsen SL, Rasmussen LS. Hypoglycaemia in patients with diabetes: do they prefer prehospital treatment or admission to hospital? *Eur J Emerg Med* 2006;**13**:319–20.
19. **Carter AJ,** Keane PS, Dreyer JF. Transport refusal by hypoglycemic patients after on-scene intravenous dextrose. *Acad Emerg Med* 2002;**9**:855–7.
20. **Brackenridge A,** Wallbank H, Lawrenson RA, *et al.* Emergency management of diabetes and hypoglycaemia. *Emerg Med J* 2006;**23**:183–5.
21. **Lheureux PE,** Zahir S, Penalzoza A, *et al.* Bench-to-bedside review: antidotal treatment of sulphonylurea-induced hypoglycaemia with octreotide. *Crit Care* 2005;**6**:543–9.
22. **Murphy P,** Colwell C. Prehospital management of diabetes. *Emerg Med Serv* 2000;**29**:78–85.
23. **Roberts K,** Smith A. Outcome of diabetic patients treated in the prehospital arena after a hypoglycaemic episode, and an exploration of treat and release protocols: a review of the literature. *Emerg Med J* 2003;**20**:274–6.
24. **Zammit NN,** Frier BM. Hypoglycemia in type 2 diabetes: pathophysiology, frequency, and effects of different treatment modalities. *Diabetes Care* 2005;**28**:2948–61.
25. **Langford NJ,** Krentz AJ, Martin U, *et al.* Severe relapsing sulphonylurea-induced hypoglycaemia: a diagnostic and therapeutic challenge. *Postgrad Med J* 2003;**79**:120–3.
26. **Bussing R,** Gende A. Severe hypoglycemia from clarithromycin-sulphonylurea drug interaction. *Diabetes Care* 2002;**25**:1659.