Management of diabetes in end of life care

Nuala Creagh
Consultant diabetes NGH
November 20th 2014
Outline of talk

• Epidemiology

• A case

• Is there an evidence base?

• National guidance

• Local guidelines for glycaemic management
National diabetes audit data 2012-2013

Figure 2: Age and gender of patients with Type 2 diabetes in NHS Sheffield CCG
Prevalence of diabetes in palliative care setting

• 27% diabetes in 3yr retrospective survey of 563 patients

• 80% patients cancer, 20% other severe chronic disease

• No difference in survival

• Increased BMI and days in hospital

• Significant impact on health care burden

Dionisio et al Am J Palliative Care 2014
84 yrs male – first admission

- PMH
  - Type 2 DM
  - Hypertension on ramipril

- Drugs
  - gliclazide 160mg bd, metformin 1 g tds, pioglitazone 30mg od
  - Ramipril 10mg od, nifedipine
  - Simvastatin and aspirin

- Presentation with anorexia, weight loss, anaemia

- Diagnosis: Gastric cancer with liver metastases
Management and Progress

• Transfused

• Omeprazole instituted

• No other changes to medications

• BP 110 – 140 systolic

• BGs 8 -10

• Discharged day 7 for discussion at UGI MDT
2\textsuperscript{nd} admission 5 days later

- Found unconscious by daughter – BG 1.3 in A+E

- HbA1c 95mmol/mol

- Gliclazide stopped on admission

- Gliclazide 80mg daily reinstituted before discharge because BGs rising to 28mmol/L

- Discharge plans to GP: ‘To monitor his BMs when able please’
3rd and final admission – 1/12 later

- Hypoglycaemic coma, prolonged
- Acute renal failure
- GCS 3
- No improvement with iv glucose at 24 hrs
- Treatment withdrawn
Is there an evidence base?

• No large observational studies or RCTs

• Current knowledge based on expert opinion, surveys and retrospective studies

• Clinical recommendations derived from these

• Need for prospective studies
Common diabetes problems in end of life care

- Hypoglycaemia
- Hyperglycaemia, including steroid induced
- Adverse effects of medications eg metformin
- Withdrawal of medications in last few days of life
Expert opinion and clinical recommendations

• Hypoglycaemia is the main metabolic threat

• Glycaemic control should be relaxed – in order to avoid symptomatic hypoglycaemia

• Insulin should be continued in type 1 diabetes, together with regular glucose monitoring, as long as the patient is conscious.

• Communication between different HCPs caring for dying patients with diabetes needs to be improved
Blood glucose monitoring in end of life care

Against

• Futile
• Invasive
• Painful

For

• Useful screening test for treatable symptoms
• No more invasive than other procedures
• Glucose monitoring not overly burdensome

Pikey et al, J Palliative med 2012
Palliative care and type 2 diabetes: a need for new guidelines?

- Diabetes patients in Palliative care units managed according to standard guidelines
- International recommendations for tight glucose control
  - Have no scientific basis in end-of-life population
    - Time for therapeutic effect > life expectancy of patient
- Go against quality-of-life goals
  - Discomfort caused by insulin injections, frequent glucose monitoring, hypoglycaemic episodes

*Vandenhaute, American Journal of Medicine 2010*
ABCD position statement on diabetes and end of life care 2011

• Care of dying patient with diabetes had been neglected

• Need for diabetes MDT to liaise with EOLC services

• Frequent glucose monitoring and complex insulin regimens should be avoided

• Avoidance of long term complications an irrelevant goal

• Patients and carers may need sensitive counselling re shift in glycaemic targets
ABCD 2011 – Glycaemic goals

• To avoid symptomatic hyperglycaemia
  • Thirst
  • Dehydration
  • Confusion
  • Drowsiness

• To avoid symptomatic hypoglycaemia
Factors predisposing to altered glucose control at the end of life

<table>
<thead>
<tr>
<th>Hyperglycaemia</th>
<th>Hypoglycaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stress response to severe illness</td>
<td>• Anorexia</td>
</tr>
<tr>
<td>• Steroid therapy</td>
<td>• Weight loss</td>
</tr>
<tr>
<td>• Co-existent infection</td>
<td>• Renal and or hepatic failure</td>
</tr>
</tbody>
</table>
ABCD recommendations 2011

- Avoid symptomatic hyper- and hypoglycaemia
- Minimum blood glucose monitoring
- Target blood glucose range 5 - 15 mmol/L
- Detailed treatment algorithms best avoided
- Early involvement of the specialist diabetes team for individualised advice
Type 1 diabetes

• A disease of absolute insulin deficiency: insulin withdrawal will lead to death

• Continue treatment with a simplified regimen where possible, unless patient specifies otherwise
  • Twice-daily fixed insulin mixtures (Humulin M3, Humalog Mix 25)
  • Twice-daily isophane (Humulin I or Insulatard)
  • Once daily long-acting insulin analogue (Lantus or Levemir)
Type 2 diabetes

- Insulin treated may be able to discontinue insulin
  - If reintroduction needed simple regimen such as once daily analogue (Lantus etc) or twice daily isophane (Humulin I etc)

- Tablet treated patients may be able to discontinue treatment

- Blood glucose monitoring should not be performed unless
  - Plans to adjust treatment based on results
  - Patient’s preference
End of Life Diabetes Care: Clinical Care Recommendations Oct 2013

• Commissioned by Diabetes UK

• Steering group
  • Co-Chairs i) Director, Institute of Diabetes for Older People (IDOP)
    ii) Consultant diabetologist
  • 2 x Nurse consultants in diabetes
  • Professor of Diabetes nursing
  • GPwSI Older people

• Aim to build on July 2008 DoH End of Life Strategy
Key Principles of Care 2013

• Tailor glucose lowering therapy and minimise diabetes related treatment effects
• Avoid metabolic decompensation and diabetes-related emergencies
  • Frequent and unnecessary hypoglycaemia
  • Diabetic ketoacidosis
  • Hyperosmolar hyperglycaemic state
  • Persistent symptomatic hyperglycaemia
• Avoid foot complications in frail, bed-bound patients
• Support and maintain the empowerment of the individual patient and their carers to the last possible stage
Management goals – glucose control targets

• No published evidence for any particular glucose or HbA1c range

• Target ranges based on consensus:
  Aim 1 – no glucose level less than 6mmol/L
  Aim 2 – no glucose level higher than 15mmol/L

• Patients may need explanation and reassurance re relaxed targets
Tailoring medications in end of life diabetes care
Four stages A- D

• A – Blue ‘All’ from diagnosis stable with year plus prognosis

• B - Green ‘Benefits’ DS1500 Unstable/Advanced disease months prognosis

• C – Yellow ‘Continuing Care’ Deteriorating weeks prognosis

• D – Red ‘Days’ Final days/Terminal Care days prognosis
Recommendations for A – Blue ‘All’ from diagnosis stable with year plus prognosis

• Use of ACE inhibitors, ARBs, aspirin, statins should be reviewed
  • In light of diagnosis and comorbidities
  • Consider dose reduction or even withdrawal of some

• Review oral agents and glucose control targets
  • Weight loss may mean reduced need for OHA or potential to simplify regimens including insulin
Sheffield guidelines for management of diabetes during last few months of life

1. Aim of treatment to avoid symptoms of hyper- and hypoglycaemia; BG targets 6 – 15mmol/L
2. Treatment usually needs to be reduced
3. Not necessary to aim for tight glucose control
4. Dietary restriction should be avoided – but avoid large quantities of sugary drinks
5. Important to understand views of patients and carers; if treatment stopped should not be misconstrued as medical team having given up
6. Each patient needs individualised treatment
Adjustment of oral agents, insulin and GLP1 analogues in type 2 diabetes

<table>
<thead>
<tr>
<th>Metformin (standard or modified release)</th>
<th>Sulphonylureas (gliclazide / glimepiride / tolbutamide)</th>
<th>Pioglitazone and SGLT2 agents (Dapa-gliflozin)</th>
<th>Gliptins</th>
<th>GLP-1 analogues (exenatide/liraglutide/lixisenatide/Bydureon)</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop if anorexia and weight loss or distressing nausea, heartburn, diarrhoea, flatulence</td>
<td>Reduce dose, eg halve if anorexia and/or weight loss</td>
<td>Stop</td>
<td>Review dose if renal impairment</td>
<td>Stop if significant anorexia, weight loss, nausea or abdominal pain</td>
<td>Reduce dose by 25 - 50% if BGs &lt; 7mmol/L HbA1c &lt; 60 or if new renal impairment</td>
</tr>
<tr>
<td>Reduce dose or stop if hypoglycaemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stop if eGFR &lt; 30ml/min/1.73m²</td>
<td>Reduce dose if new renal impairment or liver dysfunction or HbA1c &lt; 60mmol/mol</td>
<td>Linagliptin can be used in all stages of renal disease</td>
<td></td>
<td></td>
<td>Reduce dose by ~ 50% if recurrent hypoglycaemia</td>
</tr>
</tbody>
</table>

Patients on oral agents: check blood glucose only if symptoms of hypoglycaemia or hyperglycaemia and see overleaf for guidance if blood glucose levels high.
Adjustment of oral agents, insulin and GLP1 analogues in type 2 diabetes (2)

- Increase hypoglycaemic treatments only if symptoms of hyperglycaemia AND blood glucose > 15mmol/L

- Increase gliclazide in steps of 40 – 80mg daily

- Increase insulin by ~ 10% if BGs > 15mmol/L, ~ 20% if BGs > 20mmol/L

- If advice needed, ring diabetes nurse specialist on centre cover
Diabetes and steroid therapy for malignancy

• Steroids prescribed in 30 - 60% patients

• Steroid induced hyperglycaemia in ~ 30%

• Diabetes incidence correlated with dose not duration of steroids

*Pikey et al, J Palliative med 2012*
Management of diabetes during steroid therapy for malignancy

NICE guidance
• Test for DM before starting, at one month and then 3 monthly
• Monitor people with existing diabetes more closely

ABCD guideline - Oct 2014
• Monitor BG daily if considered to be at risk of DM – obese, family history, ethnic origin
Sheffield guidelines for management of diabetes during steroid therapy for malignancy

High dose steroids
- Increase BG levels in people with diabetes
- Increase risk of developing DM esp if at high risk
- Typically raise BG levels later in the day after a morning dose, BGs falling overnight

*Test* for diabetes
- Before starting steroids, at one month, then 3 monthly
- If suspicious symptoms arise
Sheffield guidelines for management of diabetes during steroid therapy for malignancy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Fasting blood glucose</th>
<th>Blood glucose 2hrs post 75g glucose or random blood glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 6.1mmol/L</td>
<td>&lt; 8mmol/L</td>
</tr>
<tr>
<td>Impaired fasting glucose</td>
<td>6.1 – 6.9 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td></td>
<td>≥ 8mmol/L – 11mmol/L</td>
</tr>
<tr>
<td>Diabetes</td>
<td>≥ 7 mmol/L</td>
<td>&gt; 11mmol/L</td>
</tr>
</tbody>
</table>

If blood glucose abnormal **before** starting steroids refer to diabetes nurse specialist for education and self glucose monitoring.
Sheffield guidelines for management of diabetes during steroid therapy for malignancy

Emergency management of steroid induced diabetes

• Consider admission if patient dehydrated or drowsy or vomiting
• Refer urgently for insulin if BG > 25mmol/L

Elective management

• Diet – exclude sugary drinks
• Daily BGs if symptoms – pre evening meal if am dose
• Start gliclazide 80mg if BG > 15 on am steroid, increasing to 160mg if BG remains > 15mmol/L
• Start insulin eg Humulin M3 8 – 12 unit am if BGs don’t fall
Management of known diabetes during steroid therapy if osmotic symptoms and BG > 15mmol/L

<table>
<thead>
<tr>
<th>Previous treatment</th>
<th>Recommended intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet alone</td>
<td>Start oral agent eg gliclazide 80mg mane</td>
</tr>
<tr>
<td></td>
<td>Increase to 160mg mane if symptoms persist or BG &gt; 15 mmol/L</td>
</tr>
<tr>
<td>Oral agents at maximum dose</td>
<td>Stop oral agents except metformin (unless contraindicated)</td>
</tr>
<tr>
<td></td>
<td>Start insulin eg Humulin M3 8-12 units mane, or bd if twice daily steroids (higher doses if overweight); Refer diabetes nurse specialists</td>
</tr>
<tr>
<td>Insulin</td>
<td>Increase morning/lunchtime insulin doses by 20–50% if morning steroid, all insulin doses if bd steroids - consult diabetes nurse specialists</td>
</tr>
</tbody>
</table>

*If diabetes well controlled on high dose steroids anticipate need for reduction in doses of insulin/oral agents when steroid dose reduced*
Type 1 diabetes (likely if patient on insulin since diagnosis or within 2 years)

• If anorexia, weight loss or hypos reduce insulin by ~ 25%, monitor BGs and may need to reduce further but DO NOT DISCONTINUE

• Many patients, esp those DAFNE trained, can self manage

• If intercurrent illness eg infection may need increased insulin doses

• Check urine for ketones if symptoms suspicious of ketoacidosis – if > ++ admit
Terminal phase – last few days of life

Practice points

1. In Type 2 DM insulin and oral agents can usually be stopped
2. BG monitoring should be kept to the minimum necessary and targets relaxed to 7 – 17 mmol/L
3. It is important to ensure clinical deterioration not due to hyperglycaemia or hypoglycaemia
4. Regular review of the patient and management plan is necessary
5. If death imminent may be appropriate to discontinue all monitoring and insulin
6. If advice needed contact DSN (diabetologist or on call palliative care team if out of hours)
Type 2 Diabetes (likely if treated with diet/tablets for >2 years before insulin)

STOP hypoglycaemic treatment (Insulin, GLP1 analogues and oral agents)

If symptomatic: thirst/polyuria/dry mouth - check meter blood glucose (BG)

**Is BG > 17**

Yes

Previous oral agent
Give human insulin (or equivalent) 8 - 12 units once daily at teatime

Check BG once daily before breakfast

**Is BG 7 - 17**

Yes

BG < 7
Reduce insulin dose by 25-50%

BG > 17
Increase insulin dose by approximately 25%

No

Repeat random BG daily if symptoms persist
Diabetes Management in the Last Few Days of Life

Type 2 Diabetes (likely if treated with diet/tablets for >2 years before insulin)

STOP hypoglycaemic treatment (insulin, GLP1 analogues* and oral agents)

If symptomatic - thirst/polyuria/dry mouth - check meter blood glucose (BG)

Is BG > 1.7

No  Repeat random BG daily if symptoms persist

Yes
Is BG > 17

- Yes
  - Previous oral agent: Give Human Insulatard or Humulin I 8 – 12 units once daily at teatime.

- No
  - Repeat random BG daily if symptoms persist

Check BG once daily before breakfast

- Is BG 7 – 17
  - Yes
  - No
    - BG < 7: Reduce insulin dose by 25-50%
    - BG > 17: Increase insulin dose by approximately 25%
Type 1 Diabetes (likely if on insulin since diagnosis or within 2 years)

Give 40% usual insulin dose split twice daily as Insulatard Humulin L (or as Detemir [Levemir] twice daily or Glargine [Lantus] once daily at bedtime if already on one of these preparations)

Check meter blood glucose (BG) once daily before breakfast

Is BG 7-17

Yes

No

BG < 7
Reduce insulin dose by 25-50%

BG > 17
Increase insulin dose by approximately 25%
Type 1 Diabetes (likely if on insulin since diagnosis or within 2 years)

Give 40% usual insulin dose split twice daily as Insulatard/Humulin L (or as Detemir/Levemir) twice daily or Glargine/Lantus once daily at teatime if already on one of these preparations

Check meter blood glucose (BG) once daily before breakfast

Is BG 7-17

Yes
Check meter blood glucose (BG) once daily before breakfast

Is BG 7-17

Yes

No

BG < 7
Reduce insulin dose by 25-50%

BG > 17
Increase insulin dose by approximately 25%
Management of Hypoglycaemia in the last few months of life

- Treat according to Sheffield Hypoglycaemia guideline
- Adjust oral agents/insulin as advised in Table
  - Reduce or stop gliclazide if hypo
  - Reduce if new renal impairment or liver dysfunction or if HbA1c < 60mmol/mol
Would our guideline have prevented the fatal hypoglycaemic episode in the case?

- HbA1c 95mmol/mol on first hypo admission, gliclazide reduced from 160mg bd to 80mg od

- ? BG monitoring in the community – guideline advises check only if symptoms of hypo or hyper

- No advice re stopping ramipril – likely major contributor to AKI
Management of Hypoglycaemia in the last few months of life

- Need to identify patients at high risk
  - Poor appetite/erratic eating
  - Weight loss
  - Impaired/deteriorating renal function
  - Liver impairment/cancer
  - Previous major hypo
- Educate patient/carers re hypoglycaemia
- Stop gliclazide if possible
- Consider switch to a gliptin if alternative treatment necessary
Conclusion

• Diabetes is one of the commonest comorbidities in end of life care

• The evidence base for diabetes management is very weak

• Consensus supports relaxation of glucose control to avoid hypoglycaemia

• Prospective studies are needed to guide improvements in diabetes care
Message from Mr Dorries

- Law now requires an inquest to be held if DOLS in place at time of death

- Inquest with a jury needed if unnatural cause
  - Fall
  - Mesothelioma

- Need to report death to coroner if DOLS in place