PostScript

NHS Greater Glasgow and Clyde

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This edition contains articles on:

HbA1c Reporting Units

On 16th January 2012, the way in which HbA1c results are reported across the UK will change.

What is HbA1c?

Glucose in the blood binds irreversibly to a specific part of haemoglobin in red blood cells, forming HbA1c. The higher the glucose is, the higher the formation of HbA1c. HbA1c circulates for the lifespan of the red blood cell, so reflects the prevailing blood glucose levels over the preceding 2–3 months.

What does it tell us?

The Diabetes Control and Complications Trial (DCCT) in Type 1 diabetes and the UK Prospective Diabetes Study (UKPDS) in Type 2 diabetes both showed that the risk of microvascular and macrovascular complications of diabetes increases as HbA1c increases. HbA1c gives a measure of an individual's risk of the long-term complications of diabetes.

What is changing?

After the DCCT, a new standard specific for HbA1c was prepared by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). Assay manufacturers will supply IFCC standardised values for their calibrators as well as DCCT aligned values. The units for reporting HbA1c have also changed to mmol per mol haemoglobin for results traceable to the IFCC reference method.

When is the changeover to new units?

Since June 2009, results have been provided in the UK as both IFCC-standardised units (mmol/mol) and DCCT-aligned units (%). This was to give everyone time to become familiar with the new units and how they relate to DCCT numbers, and thus to the risk of complications. From **16th January 2012**, results will be reported in the new IFCC units only.

What are the targets in new units?

DCCT HbA1c (%)	IFCC HbA1c (mmol/mol)
4.0	20
6.0	42
6.5	**48**
7.0	53
7.5	**59**
8.0	64
9.0	75
10.0	86
12.0	108
14.0	130
16.0	151

The equivalent of the former DCCT HbA1c targets of 6.5 and 7.5% are 48 mmol/mol and 59 mmol/mol in the new units, with the non-diabetic reference range of 4.0 – 6.0% being 20 mmol/mol to 42 mmol/mol.

What are the limitations of HbA1c measurement?

HbA1c results (DCCT or IFCC) will be misleading in certain situations, eg a variety of haematological conditions where there is abnormal red cell turnover, where there is abnormal haemoglobin, and in some patients with renal or liver disease. In pregnancy, HbA1c falls by around 0.5% due to a variety of factors. In the presence of abnormal haemoglobin, HbA1c results can vary depending on the method used to measure HbA1c and the particular haemoglobinopathy involved.

Further Information

For further information please see www.diabetes.org.uk/HbA1c or contact your local Biochemistry Department.

Webwatch

Therapeutics Handbook

We know that staff find this a very useful resource, but as paper copies go missing it can be difficult to access. There is an electronic version available on the new website or on Staffnet which has navigation tools to help you find information easily. Refer to the "quick guide to using the handbook" on page 12. It can also be downloaded onto PCs or handheld devices. However, remember it is updated every August. Make sure you use the most recent version.

Dabigatran: ADTC Decision

Dabigatran (Pradaxa®) was added to the *Total Formulary* for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) with one or more risk factors. It has been restricted to patients currently receiving warfarin who have poor INR control despite evidence that they are complying with treatment, or patients with allergy or intolerable side effects from coumarin anticoagulants. Use in other patient groups remains non-*Formulary* at present. Clinical information on dabigatran was published in *PostScript* 66.

For the majority of non-valvular atrial fibrillation patients who are well controlled on warfarin, then warfarin should remain the treatment of clinical choice.

The national consensus statement on its use contains the following advice:

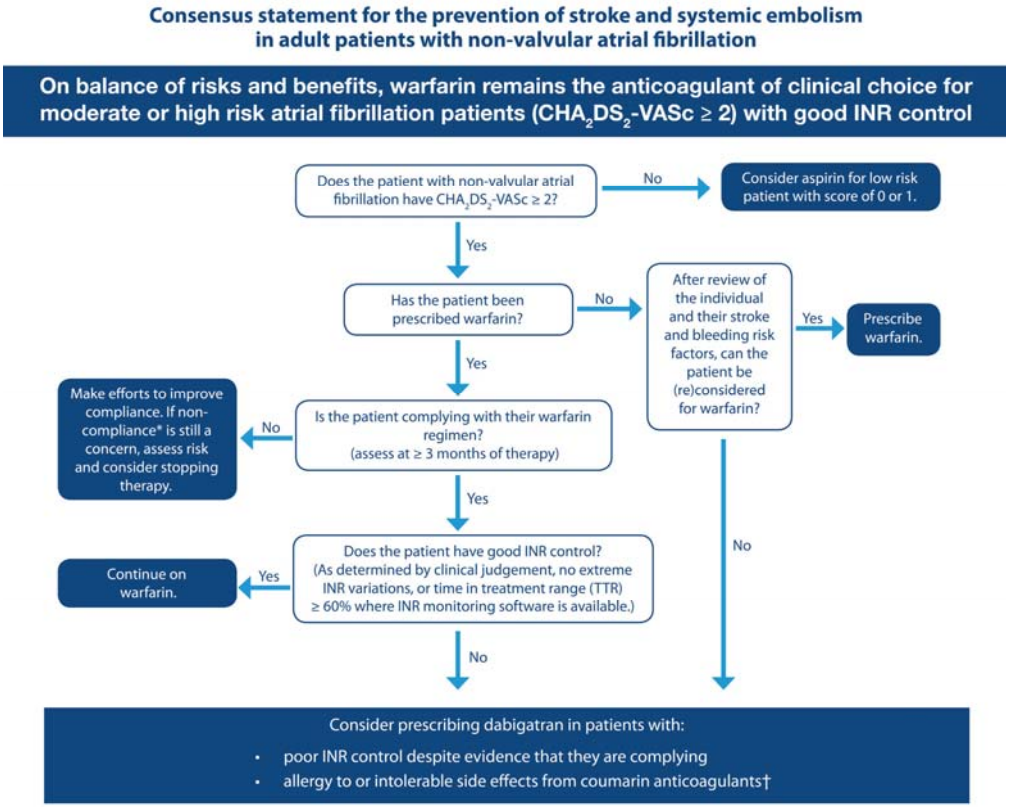
It was agreed that, for the majority of non-valvular atrial fibrillation patients who are well controlled on warfarin, then warfarin should remain the treatment of clinical choice. Particular patient groups were identified where dabigatran should be considered as a treatment option.

On balance of risks and benefits, warfarin remains the anticoagulant of clinical choice for moderate or high risk atrial fibrillation patients (CHA_2DS_2-VASc ≥ 2) with good INR control.

Clinicians should consider prescribing dabigatran in patients with:

- *poor INR control despite evidence that they are complying,*
- *or allergy to or intolerable side effects from coumarin anticoagulants.*

This consensus was reached with recognition that dabigatran is a new type of anticoagulant and there is little experience of its use outwith clinical trial settings.



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Voluntary Ban on Oral Methotrexate 10mg in NHSGGC in Adult Patients

Methotrexate is a safe and effective medicine if taken at the right dose and with the appropriate monitoring. Without close monitoring, it can cause serious long term complications or death. In July 2004, the National Patient Safety Agency (NPSA) produced "*Towards the safer use of oral methotrexate*" as a result of 137 patient safety incidents, including 25 deaths, in the previous 10 years in England and Wales.

In 2009, NHSGGC ADTC endorsed a 2.5mg methotrexate only policy, supported by the *Formulary*. However, significant use of 10mg tablets remains and there are still patient safety incidents caused by confusion between the two strengths by patients and healthcare professionals.

- 10mg methotrexate tablets were dispensed in error instead of 2.5mg tablets.
- A patient took 80mg (8 x 10mg tablets) instead of the intended 20mg dose (8 x 2.5 tablets).
- A patient took 40mg (4 x 10mg) instead of the intended 10mg dose (4 x 2.5mg) and subsequently required hospital admission.

To improve patient safety, further attempts must be made to reduce risks. All other Health Boards support a 2.5mg only policy. Although there has been some increased use of 2.5mg tablets, NHSGGC is the third lowest health board area in Scotland for the proportion of methotrexate 2.5mg tablets prescribed.

From 1st February 2012, GP practices will start all new patients on 2.5mg tablets and begin to switch all patients currently using the 10mg tablet to an equivalent dose of 2.5mg tablets. Hospital dispensaries will only supply 2.5mg tablets and will provide patients with a standard letter highlighting the different strengths and the reason for the 2.5mg being the only product supplied.

To assist this, specialists involved in prescribing methotrexate are asked to implement the following:

- All new patients should be prescribed / supplied only 2.5mg tablets.
- All patients receiving 10mg tablets from hospital should be identified, educated and switched onto the 2.5mg tablets as soon as possible.
- All clinic letters should be updated to communicate that only 2.5mg tablets should be prescribed and supplied.

Medical, pharmacy and nursing staff in non-specialist areas dealing with patients on methotrexate should:

- Establish the strength of methotrexate used prior to admission.
- Provide patient education on discharge regarding the switch.

Actinic Keratosis

Actinic keratosis (solar keratosis) is a form of chronic sunlight damage occurring on the most exposed skin surfaces, ie head, neck and dorsa of hands. Those at increased risk are fair skinned, immunocompromised or those who work or recreation takes place outside. Changing social habits (holidaying in sunny locations, fashion for a suntan) means the onset age has fallen. A recent UK study shows prevalence in men under 40 years of 15% (women 6%) and 34% in men 70 years or less (women 18%). NHSGGC may be higher due to the number of fair and redheaded individuals.

Lesions range from superficial scale to hyperkeratotic nodules. In the former spontaneous resolution has been shown to occur with avoidance of excessive sun exposure. In the latter, treatment will be required. The overall risk of progression of a single lesion to squamous cell carcinoma is about 1%. Patients rarely present with a single lesion; very sun damaged persons will have confluent change over large areas, eg a balding scalp.

Treatments that can be used in primary care by someone experienced in their use include:

- Cryotherapy is best aimed at discrete or individual lesions; less effective for large / confluent lesions.
- Actikerall® (fluorouracil 0.5% and salicylic acid 10% (5-FU-SA)) is a new product probably best for early lesions. This has recently been added to the *Total Formulary*.
- Diclofenac 3% gel for early lesions. The treatment period is three months. Currently non-*Formulary*. The skin section is currently under review.
- Fluorouracil 5% cream (non-*Formulary*) or imiquimod cream are used for more advanced lesions. Large areas can be treated in small sections over a period of time.

Most patients with early disease can be treated appropriately in primary care. Those with extensive disease or persistent lesions or those where there is diagnostic uncertainty should be referred to secondary care. Specialist options include:

- Photodynamic therapy is a hospital outpatient service. Good for resistant lesions which are not too large.
- Surgery is used where other treatments have failed or where there is concern about progression to squamous cell carcinoma.

What is the Evidence for 5-FU-SA?

5-FU-SA has been compared with diclofenac 3% gel and the cutaneous solution vehicle over a 12 week treatment period and 8 weeks after treatment cessation. The active drugs showed reduction in number of AK lesions per patient with more patients in the 5-FU-SA group (55%) having complete clinical clearance of lesions than either diclofenac gel (32%) or vehicle (15%). Treatment-emergent adverse events were mainly of mild or moderate intensity and were no treatment-related serious adverse events.

Case Study: Dopamine Agonist Withdrawal Syndrome in Parkinson's Disease

Treatment with dopamine agonists (DAs) in Parkinson's disease can cause some unusual side effects. Unfortunately, reducing the dose of causative drugs can cause other problems which can be difficult to recognise and treat appropriately. Dr. Anne-Louise Cunnington discusses a case where specialist involvement allowed resolution of symptoms and a return to normal daily activity for one of her patients.

Key learning points

- DAs play a key role in management of Parkinson's disease.
- Impulse Control Disorders (ICDs) occur in 14-17% of patients receiving DAs and must be asked about and documented at every clinic attendance.
- If ICDs occur, DA dose reduction or cessation of therapy (depending on the extent of the ICD) under close specialist supervision must be considered. The severity of the ICD must be assessed and monitored and additional support offered where appropriate.
- A significant withdrawal syndrome can occur when tapering DAs. This can mimic undertreated Parkinson's disease, but it does not improve with levodopa dose escalation, antidepressants or anxiolytics.
- Ongoing research is required to elucidate dose tapering regimens and management of DAWS.
- Clinicians should report any suspected adverse drug reactions not defined in the BNF or drug information sheet via the Yellow Card system.

A man in his late 70s with a five year history of Parkinson's disease, developed an ICD in the form of gambling, while taking ropinirole (a DA). His dose had been slowly increased since diagnosis and he was taking the maximum dose (24mg daily) when he developed an ICD. Despite his years he was otherwise fairly fit and played golf regularly. Up to 17% patients on DAs may develop ICDs and this can occur at any dose. Signs include pathological gambling, binge eating, increased libido and hypersexuality, generally reversible upon reduction of the dose or treatment discontinuation.

He was advised to gradually reduce his DA over four weeks and start co-beneldopa increasing up to 25/100 three times a day over the same period. Within 24 hours of stopping his DA he felt much slower and stiffer with worsening of his tremor. Telephone advice to increase his co-beneldopa to 25/100 four times a day was given and an urgent clinic review arranged.

At review he stated that he had stopped playing golf altogether as he felt so undertreated and non-specifically unwell. The possibility of either infection or DA withdrawal was postulated. He was advised to recommence his ropinirole modified release at 4mg, increasing up to 8mg the following day if no improvement. Routine bloods and urine culture were negative.

At review two weeks later he still had profound apathy and complained of low mood, feeling undertreated, and described symptoms of the levodopa wearing off before his next dose. He had not gone up to the higher dose of DA as suggested. Entacapone 200mg four times a day was added to prolong the effect of levodopa (given as co-careldopa 100 /25), and the DA continued at 4mg.

Clinic review a week later found him to have become house bound with suicidal ideation and no change in his motor symptoms. He also complained of severe nausea, an inner restlessness and excessive sweating. He was admitted to hospital and his dose of ropinirole was increased to 8 mg with levodopa reduced to co-careldopa 25/100 three times a day. Dopamine agonist withdrawal syndrome (DAWS) was postulated. Within 48 hours of the ropinirole dose being increased, his withdrawal symptoms dramatically improved.

He was back at the driving range within two weeks of hospital discharge. He has not had recurrence of ICD, but he and his wife are aware of the ongoing risk whilst continuing on ropinirole. Given the emergent thinking on this condition, it is difficult to quantify that risk. Extra support is provided through the movement disorder team. This case was yellow carded as a suspected adverse drug reaction.

DAWS occurs exclusively in Parkinson's patients with ICD. It is a severe stereotyped cluster of physical and psychological symptoms that correlate with DA withdrawal and causes clinically significant distress and is refractory to levodopa.

ADTC Decisions Summary

The following were among those added to the *Formulary*:

- Paliperidone injection for schizophrenia (specialist use)

The following were among those not added to the *Formulary*

- Naproxen and Esomeprazole (Vimovo®)
- Decisions deferred for telaprivir and boceprivir for hepatitis C