

Ovarian Hyperstimulation Syndrome

Strategic delivery

Safe, ethical, effective treatment

Consistent outcomes and support

Improving standards through intelligence

Details

Meeting Authority

Agenda item 10

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Author Hannah Verdin, Head of Regulatory Policy

Output

For information or decision? Information

Recommendation That the Authority considers whether OHSS is being reported accurately (section 2) and the proposed actions for improving reporting (section 3).

Resource implications Within budget

Implementation date Over time, dependent on issue

Communication(s) Over time, dependent on issue. Some strands tied to Code of Practice review for October 2018 implementation. Some strands can be communicated through Clinic Focus and stakeholder publications during Spring/Summer 2018.

Organisational risk

Low

Medium

High

1. Introduction

- 1.1.** Ovarian Hyperstimulation Syndrome (OHSS) is a potentially serious side effect which some patients develop in reaction to the drug treatment necessary for IVF. As a consequence, we require licensed clinics to report all 'severe' and 'critical' cases of OHSS to us. In May 2017 a national newspaper alleged that there was under-reporting by clinics of OHSS evidenced by the wide disparity between the number of cases reported to the HFEA and the number of hospital admissions apparently due to OHSS reported to NHS Digital. 60 cases of serious or critical OHSS were reported to us in 2015 and a further 38 cases in 2016; compared with the 865 admissions to hospital for OHSS in England, 836 of which were emergency admissions.
- 1.2.** Our initial assessment of the issue was presented to the Authority in September 2017, as part of a wider paper. The Authority agreed the following actions in respect of OHSS:
- **Work with NHS Digital to:**
 - analyse the data to establish, as far as possible, how many of the 865 hospital admissions were severe and critical OHSS because of IVF treatment
 - set up an arrangement to receive regular updates on hospital admissions relating to OHSS, to check whether the number of cases reported to us is in line with those figures (while acknowledging that the different statistical definitions employed means that the figures are unlikely to be identical) and in relation to their proportion of the overall number of cases.
 - **Meet with the RCOG (Royal College of Obstetricians and Gynaecologists) and the BFS (British Fertility Society) to discuss:**
 - what proportion of mild, moderate, severe and critical cases we should expect to see, bearing in mind there are no reporting requirements for mild and moderate OHSS
 - whether there is any room for improvement/update of our definitions (in guidance note 27 – Adverse incidents, taken from the RCOG Green-top guideline), and how RCOG promotes its guideline to ensure it reaches the appropriate clinicians
 - whether implementation of a specific OHSS incident form would be useful, or if the information we glean from our reviews of severe and critical cases is sufficient
 - the possibility of requiring clinics to have procedures for the prevention and management of OHSS.
 - As part of the **review of Code of Practice guidance** regarding information which clinics are required to provide patients, we will consider **what information clinics should provide patients on OHSS**, including reporting requirements and information which patients should give an Accident and Emergency clinician or any other clinician involved with their

care. This should encourage patients to alert their treating centre if they suffer from OHSS (and are admitted to hospital).

- Depending on the outcomes of the actions above we may wish to **review what inspectors ask clinics about their application of the OHSS/adverse incident definitions** (guidance note 27) and/or the **information clinics provide patients about OHSS**.

- 1.3.** This paper updates the Authority on our work undertaken regarding OHSS since then, including outcomes of a meeting with stakeholders (including representatives of the BFS and the RCOG) held on 13 December 2017.

2. Are clinics underreporting cases of OHSS?

Our analysis of NHS Digital data

- 2.1.** As noted above, clinics are required to report all cases of 'severe' or 'critical' OHSS to us. Our analysis of the NHS Digital hospital episode statistics, and discussion with stakeholders, reveals that this data includes all women admitted to hospital where it is judged that they have OHSS. The vast majority of these women have mild or moderate OHSS, admissions which currently do not need to be reported to the HFEA. We are also certain that the diagnosis a patient received cannot be properly deduced from this data as it is also likely that cases were labelled as OHSS when it was possible the patient did not receive a diagnosis of OHSS.
- 2.2.** In considering this issue it is also important to bear in mind the limitations of the coding used in hospital episode statistics. In 2004, the payment by results system was introduced to the NHS in England. In this system, a tariff is paid for each activity, for example clinic attendance, emergency admission, a procedure or operation. It is known that coding information varies greatly in accuracy and veracity, and is not designed to capture information that may be more relevant for our purposes here. This is consistent with the view the Authority expressed at its September 2017 meeting and findings of a study referred to below.
- 2.3.** Whilst it is agreed, on examining and discussing this data with stakeholders, that few conclusions can be drawn from these NHS Digital data, it was agreed it would be useful to review it on an annual basis to keep an eye on any trends. This is not to ignore the issue and in any event, it raises significant concerns and questions about the safety of patients undergoing IVF – and which the next section explores further.

So how many cases should we expect to see reported?

- 2.4.** In discussion with stakeholders it was agreed that the data on incidence of OHSS (Delvigne and Rozenburg, 2002) referred to in the RCOG Green-top guideline no.5, 'The Management of Ovarian Hyperstimulation Syndrome' (February 2016) is out of date and does not take account of the impact of recent changes in practice. For example, the use of egg freezing will have led to a reduction in the cases of OHSS.

- 2.5.** We were advised, and accept, that overall clinics are aware of what ‘severe’ and ‘critical’ cases of OHSS look like, and there is good awareness of the reporting requirements. However, we cannot assume that the number of cases reported to us is always accurate.
- 2.6.** Here, it is relevant to reflect on findings of an audit carried out at St. Mary’s Hospital Manchester, specifically undertaken in response to our concerns following the media allegations¹. The study was carried out to investigate whether the discrepancy in the hospital admission data and the number of cases of OHSS reported to the HFEA was due to errors in the admission code, or actual under-reporting of cases. The study proposed that incorrect coding may arise because emergency admissions are often handled by a relatively junior clinician who may not have sufficient experience of OHSS. The audit was carried out in a tertiary hospital with an affiliated (and large) IVF clinic performing 1100 fresh non-donor IVF cycles annually. It was identified that there were 55 emergency attendances resulting in 33 admissions of patients coded for OHSS (on the hospital coding database) in 2016. Following review of these cases two were considered to be severe OHSS, although only one was reported to the HFEA. Of the remainder of cases 12 were mild, 11 moderate and the remaining admissions were incorrectly coded, based on the RCOG classification system (Green-top guideline no.5, February 2016). This study concludes (as our initial assessments did – as set out in 2.1) that the NHS coding system does not appear to be a reliable method of identifying cases that meet the criteria for reporting, so attempting to draw conclusions about the adequacy of incident reporting from data concerning admissions is only likely to mislead.
- 2.7.** In summary, this single-centre study covering admissions for one year did not find evidence of systematic under-reporting of OHSS. It recommended that further work across a number of acute trusts and covering a longer time period is required to see whether this finding can be generalised. We agree.
- 2.8.** On discussing this further with stakeholders it was agreed that in order to get a better idea of whether or not there is underreporting of severe and critical cases similar audits should be carried out at a number of clinics. These audits would involve a fertility clinic contacting its primary local hospital(s) to see how many patients they have seen with OHSS in a given year and to consider the reasons for these cases, what definitions (in the RCOG green top guideline) the cases fall under and whether or not they were admitted. We will be seeking volunteer clinics to carry out these audits.

¹ Sood and Mathur, 2018: ‘Are fertility clinics “covering up” the incidence of OHSS?’, Poster presented at Fertility 2018

3. What can we do to improve reporting?

Change to reporting requirement and form

- 3.1. Currently HFEA Directions 0011 requires that OHSS “which requires a hospital admission and has a severity grading of severe or critical” is reported to the HFEA.
- 3.2. On discussion with stakeholders it was agreed that a change should be made to this reporting requirement: clinics will be required to report all severe and critical cases of OHSS to the HFEA *irrespective of whether or not they involved a hospital admission*. This will bring the reporting requirements more in line with the criteria for assessing and classifying the severity of OHSS set out in the RCOG green top guideline. Hospital admissions and the length of time spent in hospital is not part of this classification system and is therefore not in itself an indicator of severity.
- 3.3. It was also agreed that a new proforma specifically for severe/critical OHSS case reviews should be developed in the coming months. This proforma could ask for more detail than is currently collected - eg, how many follicles were present, what stimulation protocol was used, how was the risk of OHSS assessed etc. and will be sent to centres to complete when they report a case of severe or critical OHSS. Information gleaned from these completed forms will be analysed by the HFEA, in conjunction with the BFS and RCOG, to ensure appropriate clinical interpretation and recommendations, then themes/learning points will be reported on in a thematic review (possibly every two years) to make it easier for clinics to learn from their incidents.

Agreement between IVF clinics and local hospitals

- 3.4. One reason for potential underreporting is that hospitals do not inform fertility clinics when patients are admitted. One way round this is for fertility clinics to build up relationships with their local hospitals and for clinics to follow up at risk patients so they know when they are admitted, these ideas could be further explored with the sector.

Inspections

Discussion with stakeholders suggest that the best way to check for unreported cases of severe or critical OHSS will be at inspection. The trigger for this is likely to be clinics who have not reported any cases of OHSS. This might be a particular issue where clinics have a number of cases of patients with a high number of follicles (eg, more than 20-25). However, it's important to bear in mind that a high number of follicles is not always an accurate predictor of OHSS. There was discussion about targeting clinics with high success rates and no or low OHSS incident reporting (in particular high pregnancy rates in fresh treatment). This will be considered as part of the next review of inspection themes/notebook.

Information for patients

- 3.5.** Stakeholders were in agreement that more could be done to encourage patients to report cases of OHSS to fertility clinics. For example, including more guidance in the Code of Practice outlining what clinics should include about this in patient information. This will be considered as part of the current review of the Code of Practice, which will come into force in October 2018.
- 3.6.** Even though hospital admission is not an indicator of severity of OHSS the fact that there were 865 hospital admissions, apparently as a result of fertility treatment, in England in one year, is of obvious concern, even if most of them were classified as mild or moderate (and many of these admissions would have been precautionary or for assessment, and not emergency). Given this, we will consider whether or not the risk of hospital admission (even though this affects a very small percentage of total treatment cycles) is accurately reflected in patient information on the HFEA website.

Raising awareness of RCOG green top guidelines

- 3.7.** The definitions in the RCOG green top guideline were discussed with stakeholders. It was agreed that in practice it is hard to distinguish between mild and moderate cases and it should be accepted that there may be some slight variation in the interpretation of definitions in the guideline. Given this, we should recommend that clinics should take a precautionary approach to reporting and report cases which are borderline moderate/severe.

Patient follow-up

- 3.8.** In addition, clinics should also be encouraged to follow up patients after they become pregnant. It is possible that patients who do not have good follow-up contact with their clinics are more likely to seek help from emergency services and potentially a lack of specialist knowledge will mean a low threshold for admission. Improving post treatment follow-up may help to reduce the number of hospital admissions.
- 3.9.** The points outlined at 3.7 and 3.8 will be conveyed to clinics in a Clinic Focus article alongside the new form for reporting OHSS incidents and in any relevant stakeholder publications.

4. What can we do to reduce the number of cases of OHSS?

- 4.1.** Reducing the incidence of OHSS is not simply the responsibility of the regulator. The professional bodies recognise that they too have a role to play, that work has already started. In addition the BFS will survey its members on the measures they currently take to prevent OHSS, follow-up mechanisms and risk reduction strategies/management. This would cover measures in cases recognised as 'high-risk' prior to start of stimulation and in cases which are only recognised during stimulation or after egg collection as 'high-risk'. This will give

an idea of current UK practice and how far it reflects BFS guidelines, and possibly focus minds on the issue.

- 4.2.** The BFS and RCOG will use their various publications to promote the green top guidelines and strategies for preventing and managing OHSS: bulletins, a scientific impact paper and an article in The Obstetrician & Gynaecologist (TOG) journal will be suggested to the editor.
- 4.3.** The wording in the Code of Practice guidance regarding OHSS management protocols will be checked to make sure its sufficiently clear that clinics should have protocols in place for the prevention of OHSS. Currently guidance note 15 states that “centres should, where appropriate, have documented procedures that coversuperovulation regimes and management of ovarian hyper-stimulation syndrome”.