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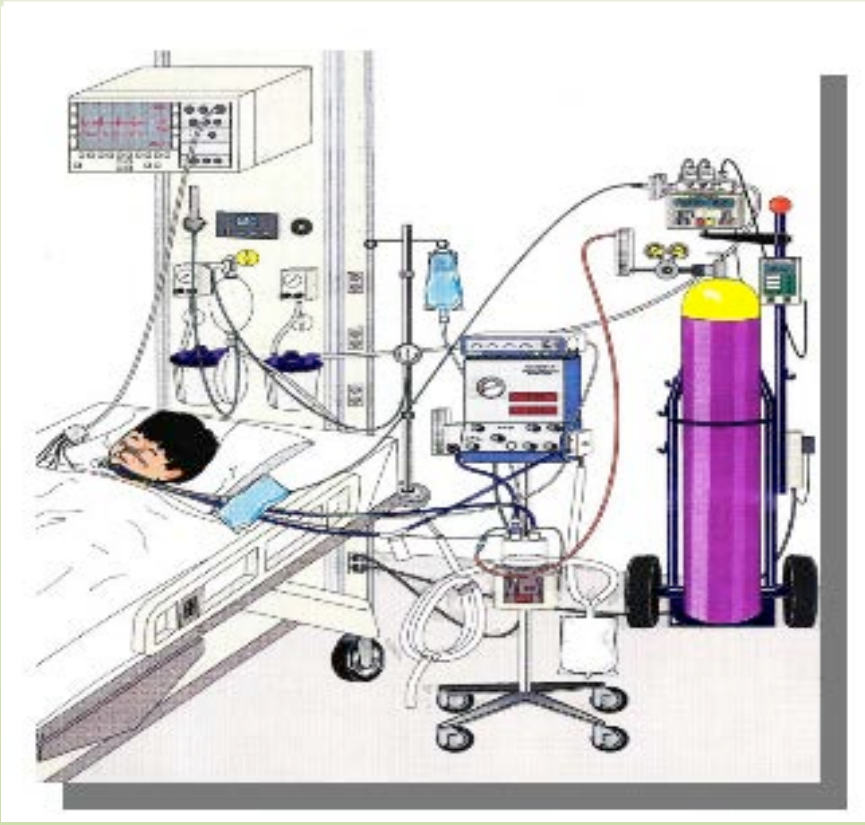

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Introduction

Inhaled Nitric Oxide (INO) is finding its place in adult cardiac surgery more and more. It provides selective vasodilation of the pulmonary arterioles without systemic effect. Vasodilation of the pulmonary arterioles will provide a decrease in pulmonary vascular resistance (PVR), which should improve blood flow to the lungs, thus improving the oxgenation and right heart function. It is licensed for use in adult cardiac surgery in UK. Nitric Oxide (NO) has become a common drug in the immediate postoperative period and this means it needs guidelines at national level. There is no national guideline that governs the use of INO in cardiac surgery in UK. With this in mind a survey was undertaken with approval of Association of Cardiothoracic Anaesthetists (ACTA) through Survey Monkey web programme.

Methods

Survey monkey electronic survey was designed to gather information about the use of INO in adult cardiac surgery. The survey was used to determine the extent and safety of use, monitoring levels of INO in the immediate post operative period after cardiac surgery in

different cardiac centres across UK. Forty-five centres are registered with the ACTA website, although after exclusions 35 centres with an identified linkman, were found to be performing adult cardiac surgery. By surveying the Linkmen we hoped to get the information on the utilization of INO in the respective centres rather than individual anaesthetists' preference. The survey was opened for response and analysed for 35 centres only (See Table 1). The initial response was poor and hence a postal survey was sent to improve the response rate.

Table 1

Cardiac surgical activity across UK and response to survey of INO therapy		
Total Number of Centres		45
Number of paediatric centres	5	
Number of centres with no identified Linkman	2	
Number centres that do not have INO therapy	3	
Full response (46%)	**16**	
Partial Response	**6**	
No response	**13**	
Total	45	45

Results

Sixteen ACTA Linkmen from different cardiac centres across UK completed the questionnaire in full and the response rate was 46% in all. There was partial response from 6 Linkmen and 13 did not respond at all and these 19 centres were excluded from this survey. The report is based on the responses from 16 centres only.

We split the survey in to four categories

1. Cardiac activity in each centre and case load
2. Inhaled Nitric Oxide use in each centre
3. Monitoring INO levels and complications
4. Comments

Activity of adult cardiac surgical centres across UK

All sixteen cardiac centres have dedicated cardiac surgical intensive care units (CSICU) with bed availability and caseload as shown in Table 2 & 3. Adult congenital heart disease (ACHD) patients represent a small proportion of the annual caseload in many centres. ACHD patients present with various levels of heart dysfunction and pulmonary hypertension and invariably they require INO therapy after cardiac surgery. Table 4 shows the level of adult congenital heart surgery activity in 16 centres.

Table 2

CSICU beds	Number of Centres	Percentage of 16 centres
5-10	3	19
10-15	4	25
15-20	5	31
>20 beds	4	25

Table 3

Case load /year	Number of Units	Percentage of 16 centres
500-1000	7	44
1001-1500	5	31
1500-2000	2	12.5
>2000	2	12.5

Table 4

ACHD cases/year	Number of Centres	Percentage of 16 centres
None	3	19
<50	9	56
50-200	3	19
No response	1	6

Inhaled Nitric Oxide therapy in adult cardiac surgery

INO therapy is in practice for more than10 years in 75% of 16 centres that completed the survey and 69% of centres have a local guideline or protocol for initiation and management of INO therapy. Table 5 shows the number of patients treated with INO per year in most of centres and ACHD patients form a very few in them in almost all centres. The decision to initiate INO therapy is a combined responsibility of the consultant anaesthetist and the surgeon in 69% of centres while in other centres it is the consultant anaesthetist or the intensivist who initiates INO therapy. All CSICUs except one (93%) use continuous INO introducing the gas into the breathing circuit near the patient end. Forty-four percent of

centres use INO for intra hospital transfers and it is not used in cardiac catheterisation laboratory in 93% of the centres probably due to different Trust policies.

Table 5

Patients treated with INO therapy/year	Number of Centres	Percentage of 16 centres
1-10	9	56
11-40	6	38
>40	1	6

Indications for initiation of INO therapy

INO therapy is commenced mostly by the anaesthetist either in the operating room or on the CSICU in the immediate postoperative period. Common indications include resistant hypoxia, pulmonary artery hypertension and right heart failure. INO therapy to resistant hypoxia was triggered in most of units (50%) secondary to arterial blood gas analysis or Oxygenation Index (PaO_2/FiO_2). There was no response to this question from 38% of the centres. Pulmonary artery hypertension may be pre-existing or secondary to inadequate myocardial function, long cardiopulmonary bypass and cross clamp times or right heart dysfunction or failure during cardiac surgery. Pulmonary artery pressures and the pulmonary vascular tone were the key vital signs used to trigger INO therapy in all centres. In isolated right heart failure INO was commenced in 94% of all centres after clinical judgment, echocardiographic assessment, high levels of inotropic support or combination of multiple factors. The concentration at which the INO is commenced varies between centres, 69% of centres starting at 10-20ppm, 19% at less than 10ppm and 6% of centres did not respond to this question. We analyzed how centres titrate and manage the INO therapy before a decision is made to start weaning INO. Less than 20% of the Linkmen

think that a change of 10 % or more of the initial arterial oxygen tension (PaO2) or reduction pulmonary arterial hypertension is a positive response to INO therapy while 35% think it is between10-20 %. Thirty one percent of centres look for a change of more than 20% before any reduction in the INO therapy. About 56% of the centres reduce INO levels by 1-2 or less than 5ppm once it is effective and safe, while in 31% of centres it is variable. Sixty two percent of centres start weaning INO once a positive response is seen in the patient's clinical status within two hours while one unit (6%) adjusts every six to twelve hours (See Table 6 & 7). With regard to the difficulties faced by different centres while treating patients on INO therapy, 56% of centres did not face any difficulties, and 31% of centres faced problems such as rebound pulmonary hypertension and decrease in the Oxygenation Index, probably related to the speed at which INO was reduced.

Table 6

INO weaning after effective response	**Number of centres**	**Percentage of 16 centres**
1-2, <5ppm	9	56
Variable	5	31
No response	2	13

Table 7

Time intervals between changes in INO therapy (hours**)**	**Number of Centres**	**Percentage of 16 centres**
<2	10	62
6-12	1	6
Variable	2	13
No response	3	19

Monitoring Nitric Oxide levels and complications

Inhaled Nitric Oxide, though beneficial in cardiac patients, has its own disadvantages. In high concentration, INO is profoundly toxic and causes a condition identical to Acute Respiratory Distress Syndrome (ARDS). In the presence of oxygen, NO is broken down to form nitrogen dioxide (NO_2). In the blood NO interacts with hemoglobin. The byproduct of this reaction produces increased levels of methemoglobin. Methemoglobin will not carry oxygen, and therefore, its level must be closely monitored during INO therapy and it can cause decrease in the platelet count. The INOvent delivery system is an integrated, single unit, designed to administer and monitor inhaled NO. The INOvent delivery system connects to the inspiratory limb of the patient breathing circuit. It functions by measuring gas flow in the breathing circuit and injecting the required flow of NO to deliver the concentration set by the user in parts per million. It is designed to deliver a constant concentration of NO, independent of ventilator flow patterns. There is no other monitoring in 57% of centres relating to INO or NO_2 levels. In thirty eight percent of centres baseline values are recorded for platelet count and methaemoglobin before initiation of INO therapy, and then once every 24 hours, when the circuits are changed or when levels of INO are changed. While this practice is variable in 19% of the centres, there was no response from 44% of centres. We also analyzed the adjunct drugs, such as milrinone and sildenafil, used during INO therapy. Around 50% of centres use either milrinone or sildenafil either to wean or in addition to INO therapy.

Comments

Guidelines do not replace clinical judgement but it provides a clear safety network within which one can exercise clinical judgement. With regard to INO therapy 69% of the centres

have a local guideline or protocol for INO therapy and 56% of the linkmen expressed interest in a national guideline to assist in decision-making. However, 44% of centres did not think they need a national protocol probably as they have their own. Most of the Linkmen did not make any further comments while one appreciated the survey and wanted to participate in drawing up the national guidelines for INO therapy.

Conclusion

Sixteen ACTA Linkmen from different cardiac centres across UK completed the questionnaire in full and the response rate was 46%. It is unfortunate that some big centres, that have an established adult cardiac surgical programme, have not responded and hence this survey may not fully reflect the practice of inhaled nitric oxide therapy across UK. Inhaled Nitric Oxide therapy is toxic at high doses and expensive and should be titrated to effect, weaned and discontinued once it is no longer beneficial to the patient.