ASSESSMENT OF THE CASE FOR UNIVERSAL ANTENATAL HEPATITIS C SCREENING

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1. BACKGROUND

Screening can be defined as

"A public health service in which members of a defined population, who do not necessarily perceive they are at risk of, or are already affected by, a disease or its complications, are asked a question or offered a test to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of disease or its complications"

Screening for a disease can be targeted or universal

Hepatitis C (HCV) is a communicable viral disease, spread from person to person by contact with infected blood or bodily fluids. Those at highest risk in Ireland are injecting drug users (IDU)

Like HIV, HCV can be transmitted from mother to child during pregnancy or at delivery. Universal antenatal HIV screening is well established and recognised as an effective method in reducing mother-to-child transmission (MCT)

The rationale for universal antenatal HCV screening is primarily to prevent MCT and secondarily to detect asymptomatic infection in women of childbearing age and to diagnose and treat infected infants at an early stage

There is no uniform approach to antenatal screening for HCV at present in Ireland. Some maternity hospitals implement universal screening, whereas others carry out targeted screening for those at high risk of infection.

2. AIMS AND OBJECTIVES

Aim: provide evidence-based recommendations on universal antenatal screening for HCV in Ireland.

Objectives:

Review the literature to evaluate current evidence

Establish screening policies or positions internationally

Outline the arguments for and against the implementation of universal screening

3. METHODOLOGY

Modified Jungner and Wilson criteria were applied

Relevant literature was sought and appraised for each criteria (a summary of the most relevant findings are presented in this poster)

Formal and grey literature were reviewed for International policies

4. CRITERIA FOR DISEASE

1 Relatively common?

~ 3% of the world's population are infected

~ 1% prevalence in the general antenatal population

MCT occurs in ~5% of cases (up to 15% if co-infected with HIV)

2 Important health problem with significant morbidity ± mortality?

Chronic infection occurs in 70-85% of cases

Cirrhosis occurs in 20-30% of those infected in 30 years

Complications + death may occur in those with cirrhosis e.g. risk of hepatocellular carcinoma 1-4%/ yr

No evidence that HCV results in a higher risk pregnancy or higher incidence of poor obstetric outcome

3 Natural history of the disease should be known, including development from latent to declared disease?

Hepatitis C virus was only identified in 1989 and only became notifiable in Ireland in 2004

Difficult to determine date of onset as most infections are asymptomatic or paucisymptomatic. Symptoms, if present, are usually non-specific

Natural history is even less clear in children, particularly those infected through MCT

4 Detectable preclinical phase which is not recognisable to the general population?

The disease is often diagnosed in the preclinical phase as many are asymptomatic and do not progress beyond mild disease

5 Treatment should be acceptable to general population?

Haematological and psychiatric/psychological side-effects are of the greatest concern in adults but milder side-effects occur with common frequency making treatment difficult to tolerate.

NICE Guidelines 2006 - might be better not to subject all people with mild disease to the side effects of treatment as few may progress to moderate disease or beyond

Side effects in children include diabetes, thyroid disease, suicidal ideation and decreases in mean linear growth + weight. Long term effects of treatment are unknown

6 Treatment should be more effective if condition recognised & treated at an earlier stage?

NICE in 2004 recommended that mild disease should not be treated. On review in 2006, treatment of mild disease was found to be cost-effective. However, if a higher proportion of people with mild disease were diagnosed, e.g. through a screening programme, progression rates could be so low that it might not be optimal to offer early treatment. Therefore, guidance to date does not apply to a screened population.

Treatment is contraindicated during pregnancy and breastfeeding

No evidence at present that any form of obstetrical intervention reduces the risk of MCT

Most studies to date have not found an association between breast feeding and MCT

Early diagnosis in infants is complex. Anti-viral agents only licensed for treatment of children > 3 years

Deficit of literature on the early treatment of children, particularly those infected through MCT

NICE 2006 -insufficient evidence to recommend treatment for mild chronic HCV in patients < 18 years

7 Facilities for diagnosis and treatment should be available and shown to be working effectively for classic cases of the condition in question?

Response to treatment varies from 40-85% and by genotype - higher response rates genotype 2 + 3

Response also affected by compliance and adherence which can be difficult due to side-effects

Impact of additional cases, both adult and paediatric, detected through universal screening, on existing services must be considered

8 There should be an agreed definition of what is meant by a case of the target disorder

In Ireland a confirmed case is any case that is laboratory confirmed. Possible and probable case definitions do not apply

5. CRITERIA FOR THE TEST

The **screening test** detects antibodies to HCV. If positive it is confirmed by a 2nd test (usually a alternate antibody test). A confirmatory positive result indicates exposure to HCV. Further testing is required to distinguish between resolved infection or ongoing presence of the virus (viral RNA). If the virus is still present further testing is necessary to determine activity and viral damage.

1 The screening test which is a blood test is **simple and quick**

2 As a blood test **it is capable of being performed by paramedics**

3 As part of a screening programmes it is not **inexpensive –** 2005 cost-effectiveness analysis which compared no screening with screening and treatment or screening, treatment and elective C-section found a cost-effectiveness ratio of ~$1million per QALY. In the UK it was estimated that it would cost up to £6million to carry out the initial screening test on all antenatal patients

4 It is an **acceptable test to the population being screened.** London study found that 92% believed all women should be offered testing

5 Test is reported to have a high level of **accuracy**

6 Test is **reproducible**

7 Sensitivity is good (94-100%)

8 Specificity is high, up to 99%

HOWEVER

The predictive value of the test is dependent on the prevalence of the disease in the population being screened. False positive and false negative results are not without significant impacts on patients

•CDC (Centre for Disease Control USA) found that in populations with prevalence rates < 10%, the proportion of false-positives averaged 35% (range 15 -60%)

•US Preventive Services Taskforce (USPSTF) found that in a population with a prevalence of 2%, 59% of positive tests were false-positive

Testing newborns is complex due to the persistence of maternal antibodies up to 18 months of age. Therefore testing for viral RNA is required which has a low sensitivity at birth (~22%). Transient and fluctuating viraemia further complicates early diagnosis

6. POLICIES ELSEWHERE

•**USA** – USPSTF, CDC, National Institutes of Health (NIH) and American Gastroenterological Association do not recommend universal screening

•**Canada** – Public Health Agency of Canada does not recommend universal screening

•**Australia/New Zealand** – Royal Australian and New Zealand College of Obstetricians and Gynaecologists state that all women should be offered screening

•**European Paediatric Hepatitis C Network** - selective screening more appropriate

•**France** - "general screening is scarcely any more efficient than targeted screening, while its overall cost is out of all proportion to the cost of targeted screening".

•**Italy** – NIH conclude that screening for HCV during pregnancy unjustified

•**UK** – National Screening Committee, NICE, Dept of Health, Scottish Intercollegiate Guidelines Network do not recommend universal screening

Advisory Group on Hepatitis recently (July 2007) reviewed the evidence and found that "hepatitis C antenatal testing was a tool for case-finding rather than interrupting vertical transmission for which there were no proven or safe interventions; targeted hepatitis C testing in at-risk groups such as current or former injecting drug users was likely to be a more efficient and cost-effective method of case-finding, although it could be difficult to identify such groups"

7. ARGUMENTS FOR UNIVERSAL SCREENING

Targeted antenatal screening does not identify all maternal infections

MCT is now the commonest source of infection in children

Women can be referred for treatment after delivery

Recent NICE guidelines recommend treatment of mild disease (however these recommendations are not based on screened populations)

Detection of infection allows for advice on e.g. safe injecting practices or cessation of injecting drug use, alcohol intake, hepatitis A+B vaccination

Diagnosis of maternal infection may be the only means of detecting asymptomatic children

If children with chronic HCV are untreated they may suffer chronic morbidity incurring significant health care costs

Undiagnosed women and children will remain as a potential source of infection

8. ARGUMENTS AGAINST UNIVERSAL SCREENING

Prevalence in the general antenatal population is low – 1% or less

Low prevalence populations have high false-positive rates

Studies argue that the prevalence of HCV in antenatal populations is consistent with the prevalence of IDU in that population

No randomised controlled trials (RCTs) have been performed to demonstrate reduced mortality or morbidity in screened Vs unscreened patients or to show that benefits outweigh risks

Cost effectiveness of screening has not been established

There is insufficient evidence as yet to recommend specific interventions during pregnancy or labour to prevent vertical transmission

Breast feeding is not contra-indicated in HCV positive mothers

Treatment is contra-indicated during pregnancy or lactation

Treatment is not without significant side-effects and those who will progress beyond mild disease cannot be identified.

Diagnosis of HCV in infancy is difficult

Natural history of infection in children, particularly those infected through MCT, is unclear

Benefits of treating children early in life not clearly established. Concerns exist with regard to long-term effects of treatment

9. RECOMMENDATIONS

At present evidence indicates that targeted antenatal screening is the most efficient and cost-effective method

It is recommended that women presenting for antenatal care are assessed adequately for risk factors for HCV and if present are offered testing

Further research is required

- Evidence that screening reduces mortality or morbidity and that the benefits of screening outweigh the risks
- Prospective studies on risk factors for MCT
- Adequately designed studies on obstetrical interventions to prevent MCT
- Long term prospective studies on children to determine natural history of HCV
- Larger studies on children infected through MCT (will be difficult due to very low prevalence)
- RCTs of long-term duration to determine outcomes of treatment in children
- RCTs of children detected through screening programmes Vs other methods
- Quality of life issues for those with mild disease who undergo treatment (adults and children)

Research evidence should be regularly appraised and recommendations updated accordingly

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