Clinical implications

- Good management of urinary tract infections in children is important because of the risk of renal scarring
- In this study a more than 10-fold difference existed between general practices in the rate of referral of urine samples for testing and in the rate of confirmation of urinary tract infection
- Only a minority of children aged under 2 with a confirmed infection were referred for renal tract imaging
- General practitioners' answers to a questionnaire showed that their views on the need for renal tract imaging differed from recent recommendations
- Greater awareness is needed of the importance of the investigation and management of children's urinary tract infections

urinary tract infection. The general practitioners' views on the need for renal tract imaging differed from those of the royal college's working group but may reflect previous teaching. The replies to the questionnaire showed that general practitioners would be more likely to refer boys than girls. Over 75% of respondents would plan to refer boys aged under 1 after a first episode of urinary tract infection, but only just over half would refer girls of the same age. Most would plan to refer both boys and girls of all ages after a second urinary tract infection.

This study shows that urinary tract infections in children in Gloucester health district are underinvestigated and may be underdiagnosed, that only a small proportion of children have a follow up urine specimen taken, and that only a minority of young children with confirmed infection are referred for renal tract imaging. We believe that these findings do not apply to the Gloucester district alone, where family practitioner standards are high, but probably reflect practice throughout the country.

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Prospective study of prenatal screening for Down's syndrome with free β human chorionic gonadotrophin

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Abstract

***Objective*—To assess the value and impact of a screening programme for Down's syndrome that uses the two maternal serum markers: α fetoprotein and free β human chorionic gonadotrophin.**

***Design*—All women booked into clinics were screened. Further tests were offered to women with a risk of one in 300 or greater of having an affected baby. Follow up of outcome of all pregnancies.**

***Setting*—Biochemical screening laboratory serving two health districts.**

***Subjects*—8179 women of all ages with singleton pregnancies screened between 15 and 22 weeks' gestation from 1 April 1991 to 31 March 1992.**

***Main outcome measures*—Detection rate of Down's syndrome, false positive rate, uptake of screening, uptake of amniocentesis in women identified as at increased risk, prevalence of Down's syndrome at birth.**

***Results*—Overall 89% (8317/9345) of women underwent screening. The rate of detection of Down's syndrome was 69% (11/16; 95% confidence interval 41 to 89%) with a 5·2% false positive rate (426/8179; 4·7 to 5·7%). In women under 30 the detection rate was 50% (four out of eight; 32 to 86%) Uptake of amniocentesis was 89% (389/437), resulting in a reduction of prevalence of Down's syndrome at birth from 1·1 per 1000 in previous years (66/59 696) to 0·4 per 1000 during the screening year (4/9345). Additionally, several other abnormalities were identified.**

***Conclusion*—The benefit of a high detection rate with this approach and the additional anomalies identified should encourage others to introduce screening programmes for Down's syndrome that use free β human chorionic gonadotrophin and α fetoprotein.**

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Introduction

In 1984 Merkatz *et al* observed a link between low maternal serum concentration of α fetoprotein in the second trimester and babies affected by fetal trisomy.[1] Cuckle *et al* subsequently confirmed this observation and proposed a screening programme for Down's syndrome (trisomy 21) based on the use of specified cut off values of α fetoprotein at various maternal ages.[2] Detection rates for Down's syndrome with this procedure at best would achieve a rate of detection of 30%, with false positive rates often as high as 10%.[3]

During subsequent years other biochemical markers in maternal serum have been shown to be linked to the birth of babies affected by fetal trisomy. Unconjugated oestriol was shown by Canick *et al* to be lowered in Down's syndrome[4] and total human chorionic gonadotrophin was shown by Bogart *et al* to be raised.[5] These observations led Wald *et al* to propose a screening programme for Down's syndrome based on a combination of maternal age and the measurement of maternal serum α fetoprotein, unconjugated oestriol, and total human chorionic gonadotrophin concentration.[6] They predicted that 61% of affected pregnancies could be detected with a 5% false positive rate. This estimated rate of detection has since been revised to 58%.[7] More recently the role of unconjugated oestriol in such screening has been questioned, largely as a result of its positive correlation with other markers, doubts about the different assays, and the observation that in practice detection rates with unconjugated oestriol were not greater than those without the analyte.[8-10]

In 1990-1 two groups of workers independently showed that free β human chorionic gonadotrophin concentration was also raised in cases of Down's syndrome.[11,12] Several retrospective studies have shown that maternal serum concentration of free β human chorionic gonadotrophin in combination with α fetoprotein concentration and maternal age can achieve detection rates of Down's syndrome higher than those achieved by using total human chorionic gonadotrophin, α fetoprotein, and maternal age in combination.[8,12,13] Furthermore, in early gestation (14-16 weeks) detection rates as high as 75-80% can be achieved with a 5% false positive rate.[8,11,13,14] More recently the potential value of the free β human chorionic gonadotrophin analyte in biochemical screening in the first trimester has been identified.[15-17]

To test the true efficiency of our proposed screening strategy of α fetoprotein, free β human chorionic gonadotrophin, and maternal age we undertook a prospective study over one year in over 8000 pregnancies presenting to four antenatal clinics in two adjacent health districts.

Methods

LOCATION

In 1980 this unit began providing screening services for neural tube defects for two district health authorities (Redbridge and Barking, Havering and Brentwood) in the North East Thames Regional Health Authority. The two districts are located at the eastern boundary of outer London and serve a total population of 685 900. The area to the west is largely high density housing with some ethnic minorities whereas the areas to the north and east are more rural communities of a largely white population. The antenatal care for the area is concentrated in four centres (King George's Hospital, Ilford; Barking Hospital; Rush Green Hospital; and Harold Wood Hospital).

Screening for Down's syndrome with free β human chorionic gonadotrophin was introduced in all centres from 1 April 1991. We report on the outcome of all pregnancies screened between 1 April 1991 and 31 March 1992—the first year of prospective intervention screening.

ANALYTICAL PROCEDURES

Measurement of α fetoprotein concentration in maternal serum was carried out by using a radioimmunoassay as described before.[3] Measurement of free β human chorionic gonadotrophin concentration was carried out by using a specific solid phase two site immunoradiometric assay (ELSA-FbHCG; CIS (UK) Ltd) incorporating the monoclonal antibody FBT11 as capture antibody. The performance of this assay has been described previously.[8,12,18]

To allow for gestational variation of analyte concentration with age the concentration of each marker was expressed in terms of multiples of the median for unaffected pregnancies with the same gestational age.

Calculation of the risk of Down's syndrome from combinations of analyte concentration and maternal age was based on the likelihood ratio approach,[19] in which the bivariate gaussian frequency distribution of the two markers is used to generate a likelihood ratio, which then in turn is used to modify the age specific risk of Down's syndrome derived from the data of Cuckle *et al*.[20] The population statistics and model used in generating the likelihood ratio were those identified in our previous large retrospective study.[8] Correction of maternal serum concentration of α fetoprotein for maternal weight was carried out, but at this stage maternal serum concentration of free β human chorionic gonadotrophin was not corrected.

SCREENING PROCEDURE

The screening policy in both districts is essentially an opt out policy so that all women booked with the clinics have blood taken for screening for neural tube defects and Down's syndrome at 15-22 weeks unless they specifically ask to be excluded. Ultrasound dating of pregnancy before screening was undertaken in only one centre. In all other centres gestational dating was largely by known date of last menstrual period. In cases of uncertain dates ultrasonography was performed before screening. All relevant clinical information was provided on a comprehensive request form.

The results of biochemical screening in which the risk of Down's syndrome (at term) was one in 300 or greater were telephoned directly to the sister in charge of the relevant antenatal clinic. The risk cut off point was chosen to provide a 5-6% false positive rate based on our previous retrospective study.[8] The clinics were instructed that in all cases which were at increased risk an ultrasound scan should be performed to check the gestational age. If the gestational age required revision then an updated calculation of risk was initiated and a revised report issued. In cases when the report still indicated at increased risk the patients were counselled and amniocentesis and karyotyping offered, with an offer of termination in all cases in which a Down's syndrome karyotype was found.

OUTCOME GATHERING

Follow up of the outcome of all patients with increased risk of Down's syndrome was carried out regularly by use of an increased risk outcome request form, which was sent to the sister in each clinic with a copy of the original report about two months after the screening.

Identification of pregnancies associated with Down's syndrome and identification of those infants born with Down's syndrome was carried out in three ways to cross check complete ascertainment during the study period. Firstly, the records of the two cytogenetics laboratories used by the four antenatal clinics were examined to identify both prenatally and postnatally diagnosed cases of Down's syndrome from each centre. Secondly, an informal information gathering network, which has been in place since the introduction of screening for neural tube defects, was also used in which the antenatal clinic sisters informed the laboratory of any abnormality detected, missed, or found in the population. Finally, birth outcome notification records were checked for final confirmation. In this way only 68 cases (0·8%) of the screened population were lost to follow up.

Information on the total number of pregnancies in the two districts was taken from the number of

bookings in the four antenatal clinics during the calendar year 1991.

Results

During the study a total of 8317 pregnancies were screened; this represents a screening uptake of 89%. Of the 8317 pregnancies, 8179 were singleton pregnancies and 135 twin pregnancies; there were three cases of triplets. Risks of Down's syndrome were calculated only in cases of a singleton pregnancy, although it is now possible to extend screening to twin pregnancies (K Spencer, *et al*, personal communication). Of the women with singleton pregnancies, 6584 were white, 793 were Asian, 221 were Afro-Caribbean, and 270 were of other ethnic origin; the ethnic origin was not stated in 311. The mean (SD) maternal age (at delivery) was 28·22 (4·90) years with a median of 28 years. There were 867 (10·6%) women aged 35 and over and 401 (4·9%) 37 and over. This age distribution compares with a distribution for England and Wales of 8·7% for women 35 or over and 4·6% for women 37 of over[21] and is similar to that in the study by Wald *et al.*[22]

Most women in our screening programme book at the antenatal clinics quite early in pregnancy and it is therefore not difficult to obtain maternal serum samples for screening at the appropriate time. By the 17th week of gestation 87% (7236/8317) of the total number of pregnant women who were eventually screened had had blood samples taken for screening for neural tube defects and Down's syndrome. In our population gestational dating solely by dates of last menstrual period occurred in 57·5% (4782/8317) of the population. In 21·6% (1796/8317) of the cases dates were confirmed by ultrasound scan (primarily biparietal diameter measurement) and in 20·9% (1738/8317) of the population dating by ultrasound scan differed from that calculated from date of last menstrual period or this date was not known. Information on maternal weight was available in 91% (7568/8317) of our screened population; the mean (SD) maternal weight was 64·01 (12·34) kg with a median weight of 64 kg.

The incidence in the general population of babies born with Down's syndrome is 1·3 per 1000; on this basis in our screened population of 8179 singleton pregnancies we would have expected to see 10·6 cases of Down's syndrome at birth. When corrected for the 25% rate of fetal loss in Down's syndrome between second trimester and birth[23] we expected to see 13·3 cases at the time of second trimester screening. We identified from our outcome gathering procedures 16 cases of Down's syndrome in the screened population and one case in the unscreened population. This unscreened case was in a 41 year old woman who refused both biochemical screening and the direct offer of amniocentesis. The observed incidence of Down's syndrome in the screened population at second trimester was therefore one in 511. This annual figure may be higher than the average figure, but over the past 10 years in our screening area the annual total incidence fluctuates widely, averaging out at 1·3 per 1000.

Of the 16 cases of Down's syndrome, biochemical screening identified 11 cases, giving a detection rate of 69% (95% confidence interval 41 to 89%). Among women 37 years or older the detection rate was 100% (three out of three; 29 to 100%), in women under 37 62% (11/13; 32 to 86%), and in women under 30 50% (four out of eight; 16 to 84%).

In the screened population 566 unaffected pregnancies initially presented with a risk of Down's syndrome of one in 300 or greater, this represented an initial false positive rate of 6·9%. After revision of gestational age by ultrasound scanning 426 unaffected pregnancies still remained at increased risk, representing a false positive rate of 5·2% (confidence interval 4·7 to 5·7%). Among the cases of Down's syndrome 12 of the 16 were initially classified at increased risk, and one of these cases was reclassified as not at increased risk after revision of gestational age after ultrasound scanning. The odds of being affected given a report of increased risk were therefore 1:39.

The false positive rate in women 37 years or older was 19% (76) and in women under 30 was 2·9% (154). This age dependent difference in detection rate and false positive rate is due primarily to using maternal age as the a priori risk, although biochemical markers such as free β human chorionic gonadotrophin are better predictors of Down's syndrome than maternal age.[8]

The uptake of amniocentesis among the 437 women (426 unaffected plus 11 affected cases identified at increased risk) offered amniocentesis or cordiocentesis was 89%. Only one case of fetal death within 28 days of the amniocentesis procedure could be identified.

Of the 11 women in whom a Down's syndrome fetus was identified by the screening procedure, 10 underwent a termination of pregnancy. In the one case in which the patient declined an offer of termination the pregnancy ended with a stillborn delivery of a baby with Down's syndrome.

When the detection rate for Down's syndrome was examined by gestational age band, at 15-16 weeks' gestation the observed detection rate was 80% (four out of five; confidence interval 28·4 to 99·5%) whereas at 17-19 weeks' gestation the observed detection rate was 64% (seven out of 11; 30·8 to 89·1%). Although the difference between these detection rates was not significant, they do follow the same trend observed in previous retrospective studies.[8 11 13 14] The median maternal age of the group screened at 15-16 weeks was 31 compared with 29 in the group screened at 17-19 weeks. This difference could also have contributed to the difference in detection rate. The median concentration of free β human chorionic gonadotrophin in the Down's syndrome group was 2·62 multiples of the median and for α fetoprotein was 0·615 multiples of the median. The median concentration of free β human chorionic gonadotrophin was consistent with the combined data from 480 cases of Down's syndrome, which showed a median of 2·64 multiple of the median.[24]

In addition to the cases of Down's syndrome follow up of outcome also identified a number of other abnormalities which had been highlighted by the screening programme and which had produced reports indicating at increased risk of Down's syndrome (with the exception of case 19). Table I identified these additional benefits in detection for the screening programme, although some of these cases would

TABLE I—*Additional abnormalities identified by screening programme for Down's syndrome*

Case No	Maternal age (years)	Multiple of median: α Fetoprotein	Multiple of median: Free β human chorionic gonadotrophin	Risk of Down's syndrome	Abnormality
1	30	1·31	3·63	220	46XX t(2:12) (p13;q13)
2	36	0·69	1·74	211	45XY-13,-14,+t(13;14)(q11;q11)
3	31	1·28	3·15	295	45XX-13,-14,t(13q;14q)+
4	28	0·65	2·68	247	45X0
5	31	0·91	2·95	224	45X0
6	36	0·82	2·88	79	45X0
7	25	0·71	2·82	298	Renal agenesis
8	30	0·68	4·68	41	Hydronephrosis
9	34	1·05	8·01	4	Hydronephrosis
10	21	0·91	5·33	63	Kartagener's syndrome
11	27	0·68	3·23	171	Fetal death
12	31	0·49	2·24	171	Fetal death
13	36	3·79	4·46	74	Fetal death
14	29	0·77	4·06	86	Fetal death
15	27	0·74	4·62	64	Fetal death
16	30	8·27	4·69	181	Fetal death
17	31	3·58	5·42	89	Fetal death
18	37	0·33	1·62	55	Molar pregnancy
19	41	0·85	0·64	461	Trisomy 13

possibly have been picked up by scanning for anomalies at 18-19 weeks. Cases 1 to 3 were cases of common non-lethal chromosomal translocations. Cases 4 to 6 were cases of Turner's syndrome (45 X,0) and were typical of cases that we have identified both with and without cystic hygroma by using free β human chorionic gonadotrophin in screening.[25] Cases 7 to 9 were cases of renal impairment. Case 10 was a case of the autosomal recessive congenital heart-lung disorder, Kartagener's syndrome, in a family with two previous babies affected by this condition. The cases of fetal death (11 to 17) were either fetal death at the time of blood sampling or fetal death later in pregnancy. No chromosomal abnormality was suspected at necropsy in these cases. Case 18 was a case of a partial molar pregnancy. Finally, case 19 was a case of trisomy 13 in which the concentrations of free β human chorionic gonadotrophin and α fetoprotein were below the median. This case serves to emphasise that current algorithms are designed only to make predictions about the risk of trisomy 21. In our view until algorithms are used which can also routinely predict the risks of trisomy 13 and trisomy 18,[23] then all women over the age of 37 should automatically be offered amniocentesis irrespective of the risk of Down's syndrome as they also have an increased risk for other genetic anomalies.

Discussion

The results of our prospective study in which we have achieved a detection rate for Down's syndrome of 69% with a 5·2% false positive rate confirm the data published in retrospective studies[8 11-13] and establish further the benefits of screening by using free β human chorionic gonadotrophin and α fetoprotein. We have indicated that once again detection rates may be better earlier in gestation and that in women under 30 the detection rate with this approach is as good as that achieved in one study of the triple test when applied prospectively to women of all ages.[7]

Table II summarises the results and those from four major prospective studies of the triple test. The study of Cheng *et al* is clearly atypical of all prospective studies of Down's syndrome screening.[28] The highly significant increased incidence of Down's syndrome in this study suggests either a truly unusual population or more likely hidden population bias in the study design. If one averages the performance of the remaining studies of the triple test the detection rate by using free β human chorionic gonadotrophin is about 10% higher. We have consistently shown this difference in retrospective studies,[12 13] and by using a modelling approach, Cuckle and Lilford have also shown an 8-10% higher detection rate when using free β human chorionic gonadotrophin.[30] Wald and Hackshaw have recently suggested that the benefits of free β human chorionic gonadotrophin screening may not be achievable in practice and have disputed the projected detection rates based on their own claims[31] which have been further refuted by Cuckle and Lilford[32] and by Spencer *et al.*[33] The detection rates in our study and those unpublished studies summarised by Spencer *et al*[33] are totally consistent with the earlier direct observation of an 8-10% improvement in detection rate when using the free β approach rather than the triple test.[8]

Haddow *et al* estimated the number of cases of Down's syndrome in the study population by taking the number of subjects at each year age band and multiplying this by the age specific risk of Down's syndrome in the second trimester.[23] They then proceeded to back calculate from published retrospective estimates of detection rates of Down's syndrome to find the number of cases likely to reach term among the group of women who were classified as not at increased risk. They then found their estimated number of cases by examining birth records. The problem with this type of approach to ascertainment is that it assumes from study population to study population that the incidence of Down's syndrome is constant; that the population sample size does not introduce any bias; that the estimates of incidence rates of Down's syndrome per age band are valid; and, finally, it could lead to complacency once the expected number of cases in the study group are found. If we had used this approach the number of cases expected in our population would have been 12 at second trimester, and we would have then been claiming a 92% detection rate. In our view there is no substitute for good outcome gathering and we caution any group on using the method of Haddow *et al* to estimate the number of cases of Down's syndrome in their population. Indeed Wald *et al* in a similar sized study to our own also found that the number of observed cases of Down's syndrome was greater than that predicted from the prevalence of Down's syndrome.[22]

The policy of revision of gestational age after ultrasonography in pregnancies considered to be at increased risk, as shown by both Wald *et al*[22] and Haddow *et al*[27] results in a loss of detection; it is, however, not possible to estimate accurately the proportion of cases of Down's syndrome in the group not considered at increased risk that would have been detected if ultrasound dating had been carried out on all cases. Wald *et al* advise that all women should have an ultrasound scan before screening.[6 22] In an ideal world this would happen, but many health authorities do not routinely offer this until the scan for anomalies at 18 to 19 weeks. Any introduction of screening for Down's syndrome which required all patients to be scanned before screening and then to have a further second scan at 18 to 19 weeks must look seriously at the cost implications for any extra benefit that might occur in introducing such a policy. In practice we have shown good detection without having ultrasound dating in place in most centres.

The impact of screening in our two health districts is

TABLE II—*Comparison of data from prospective studies of triple test and free β human chorionic gonadotrophin*

Variable	Haddow *et al*[27]	Wald *et al*[22]	Cheng *et al*[28]	Phillips *et al*[29]	Current study
No of women	25207	12603	7718	9530	8179
Test studied	Triple	Triple	Triple	Triple	α Fetoprotein and β human chorionic gonadotrophin
Proportion (%) of mothers >35 years (37 years)	4·9	(4·8)	10·7	0	10·6 (4·9)
Proportion of pregnancies dated by ultrasound (%)	41·6	65	–	–	42·5
Risk cut off	One in 190	One in 250	One in 195	One in 274	One in 300
Time of assessment	Mid-trimester	Term	Mid-trimester	Mid-trimester	Term
Initial rate of positive risk (%)	6·6	5·7	8·0	7·2	6·9
Positive rate of risk after scan (%)	3·8	4·1	6·0	3·2	5·2
No of cases of Down's syndrome found	21/36	12/25	20/22	4/7	11/16
Detection rate (%)	58	48	91	57	69
Incidence of Down's syndrome per 1000 screened	1·43	1·98	2·85	0·73	1·96
Screening uptake (%)	–	74	–	–	89
Acceptance of amniocentesis (%)	79	75	69	–	89

perhaps most visibly shown when we look at the performance of screening over the past 10 years. Table III shows the proportion of cases of Down's syndrome avoided over the 10 year period when firstly maternal age (equal to or over 37 years) was the criterion for screening during 1982-8 and when this was supplemented with maternal age and α fetoprotein concentration during 1989-90. The introduction of free β human chorionic gonadotrophin into screening in 1991 has had a dramatic effect. Looked at from a perspective of birth prevalence of Down's syndrome table III also shows the annual birth prevalence during the same 10 year period. The introduction of α fetoprotein in screening for Down's syndrome in 1989, while enabling a third of cases to be avoided, made little impact on birth prevalence because in these years the incidence of Down's syndrome was increased. Screening with free β human chorionic gonadotrophin, however, has reduced the prevalence to 0·4 per 1000. Although statistically this may be deemed a chance occurrence, we think that subsequent monitoring will show a significance when screening has been carried out for a longer period.

TABLE III—*Avoidance of births of babies with Down's syndrome and birth prevalence during past decade in two screening districts. In 1982-8 screening was by maternal age (≥37) only; in 1989-90 screening was by maternal age plus α fetoprotein; and in 1991 screening was by free β human chorionic gonadotrophin, fetoprotein, and maternal age*

Year	Live births with Down's syndrome	Total cases of Down's syndrome	% Avoidance (95% confidence interval)	Birth prevalence per 1000 births
1982	9	10	10·0	1·0
1983	8	9	11·1	0·9
1984	12	14	14·3	1·3
1985	6	6	0	0·7
1986	10	10	0	1·1
1987	11	13	15·4	1·2
1988	10	11	9·1	1·1
1982-8	66	73	9·6 (0·4 to 18·8%)	
1989	9	14	35·7	1·0
1990	12	18	33·3	1·3
1989-90	21	32	34·4 (18·8 to 53·2%)	
1991	4	13	69·2 (38·6 to 90·9%)	0·4

Unlike colleagues in Tower Hamlets,[34] which was part of the project by Wald *et al*,[22] we are confident that screening for Down's syndrome has successfully reduced the birth prevalence. There may be many reasons for the difference between the outcome of the two programmes, one of which obviously relates to the cultural and socioeconomic differences between our districts which enabled us to achieve an 89% uptake of screening and an 89% uptake of amniocentesis and for us to have screened 90% of our population by the 18th week of pregnancy.

Our results show that screening with free β human chorionic gonadotrophin can match the promise displayed in retrospective studies. We have shown that screening for Down's syndrome with this approach also identifies additional abnormalities for which a great number require considerable clinical intervention. We conclude that the protocol of free β human chorionic gonadotrophin-α fetoprotein-maternal age is now an accepted protocol for screening for Down's syndrome because of its applicability across a wide gestational window (eight to 20 weeks) and its performance in prospective screening.

Clinical implications

- The birth prevalence of Down's syndrome in our screening district before the introduction of screening was 1·1 per 1000
- Our prospective study has shown that a detection rate of 69% can be achieved, confirming previous retrospective studies
- High uptake of screening, high detection rates, and high uptake of amniocentesis have resulted in the birth prevalence of the disorder falling to 0·4 per 1000
- The two test protocol using free β human chorionic gonadotrophin also identifies other anomalies requiring early clinical intervention
- The two test protocol using free β human chorionic gonadotrophin achieves a detection rate some 10% higher than that using the triple test protocol

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Chronic constipation in long stay elderly patients: a comparison of lactulose and a senna-fibre combination

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Abstract

***Objectives*—To compare the efficacy and cost effectiveness of a senna-fibre combination and lactulose in treating constipation in long stay elderly patients.**

***Design*—Randomised, double blind, cross over study.**

***Setting*—Four hospitals in Northern Ireland, one hospital in England, and two nursing homes in England.**

***Subjects*—77 elderly patients with a history of chronic constipation in long term hospital or nursing home care.**

***Intervention*—A senna-fibre combination (10 ml daily) or lactulose (15 ml twice daily) with matching placebo for two 14 day periods, with 3-5 days before and between treatments.**

***Main outcome measures*—Stool frequency, stool consistency, and ease of evacuation; deviation from recommended dose; daily dose and cost per stool; adverse effects.**

***Results*—Mean daily bowel frequency was greater with the senna-fibre combination (0·8, 95% confidence interval 0·7 to 0·9) than lactulose (0·6, 0·5 to 0·7; $t=3·51$ $p \leq 0·001$). Scores for stool consistency and ease of evacuation were significantly higher for the senna-fibre combination than for lactulose. The recommended dose was exceeded more frequently with lactulose than the senna-fibre combination ($\chi^2=8·38$, $p \leq 0·01$). As an index of the standard daily dose, the dose per stool was 1·52 for lactulose and 0·97 for the senna-fibre combination, at a cost per stool of 39.7p for lactulose and 10.3p for senna-fibre. Adverse effects were no different for the two treatments.**

***Conclusions*—Both treatments were effective and well tolerated for chronic constipation in long stay elderly patients. The senna-fibre combination was significantly more effective than lactulose at a lower cost.**

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Introduction

Constipation may affect up to 20% of people aged over 65 years.[1] In the elderly person constipation develops in association with poor mobility and is common in long term hospital or nursing home care. Prolonged laxative treatment is often necessary to avoid serious morbidity. Laxative use has been reported in 75% of long stay hospital patients and 32% of nursing home patients.[2]

Treatment of constipation involves bulking agents initially, followed if necessary by stimulant or osmotic laxatives.[3] The chosen laxative should be efficacious, safe, without excess unwanted effects, and relatively inexpensive but cost effective. There are no good comparative clinical studies of the commonly used laxatives.[3] Our study compared lactulose, a relatively expensive synthetic disaccharide,[4] with a granular senna-fibre combination (ispaghula 54·2%, senna 12·4%; Manevac, Galen UK), both of which are more effective than placebo in treating constipation.[5,6] The object was to compare the relative efficacy and cost effectiveness of the senna-fibre combination and lactulose at recommended doses in long stay elderly patients with chronic constipation.

Methods

PATIENTS

This multicentre study was conducted in long stay elderly patients in hospital or nursing home care (five hospitals and two nursing homes). Subjects had a history of chronic constipation (fewer than three bowel movements a week) or a need for regular laxatives. Exclusion criteria were important bowel pathology, diabetes mellitus, severe renal impairment, antidiarrhoeal therapy, and faecal incontinence. The protocol was approved by local ethics committees, and written informed consent was obtained from patients or relatives.

STUDY DESIGN

According to a randomised, double-blind, cross over design, patients received active senna-fibre combination 10 ml daily with lactulose placebo 15 ml twice daily, or active lactulose 15 ml twice daily with senna-fibre placebo 10 ml daily for two 14 day periods, according to a computer generated randomisation code. Doses could be increased or decreased according to response. The maximum daily dose for active or placebo senna-fibre was 20 ml (10 ml twice daily) and for lactulose or lactulose placebo 60 ml. Dosage alterations and weight of medication before and after each period were recorded. Before entry into the first phase, and between treatments, subjects had a three to five day period free of laxatives. For ethical reasons the maximum period without a bowel movement was three days.

The number of stools and their consistency and ease of evacuation, together with any other symptoms or adverse effects (scoring system, see box), were noted daily. From the weight of medication administered the number of doses per patient and the daily dose for each treatment were estimated. Total cost and cost per stool for each treatment were calculated.