Oncology and haematology

G132 FRESH FROZEN PLASMA USE IN A LEVEL 2 NEONATAL UNIT: COMPLIANCE WITH NATIONAL GUIDELINES

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Background: Prophylactic fresh frozen plasma (FFP) to prevent adverse neurological outcome in neonates is not effective according to a large multicentre trial (1996). The British Society of Haematology Guidelines (2004) suggests that FFP should only be used in neonates who have a significant coagulopathy with associated bleeding or those who are about to undergo an invasive procedure.
Aims: To audit our unit's practice against the above guidelines. To compare end-outcomes in all babies receiving FFP with pre-transfusion clotting values.
Methods: Retrospective survey over 18 months on FFP transfusions.
Results: Data were available for 24 transfusions in babies <36 weeks gestation and four transfusions in babies >36 weeks gestation. In babies born <36 weeks, three of 24 (12%) transfusions were given without prior coagulation screening. In six of 21 (28%) FFP was given despite normal clotting values. In nine of 15 (60%) with abnormal clotting values, FFP was given despite no active bleeding or imminent invasive procedure. In the four transfusions given to babies >36 weeks, clotting was checked in three cases prior to transfusion. In all three cases clotting was abnormal but in none was there active bleeding or imminent invasive procedure. Pre-transfusion clotting values were higher in the babies who subsequently suffered no serious end-outcomes (death, intraventricular haemorrhage, severe bleeding): mean activated partial thromboplastin time 70.1 vs 63.3 in the group with serious end-outcomes ($p = 0.21$). Mean prothrombin time 21.6 vs 15.92 in the group with serious end-outcomes ($p = 0.009$).
Conclusions: These data suggest that clotting values alone are not predictive of serious adverse bleeding-related events. Transfusions of FFP were given outside current guidelines in the majority of cases. Unpublished audit suggest that this reflects practice in other larger units. Clotting factors are reduced in all newborns.[1,2] There should be written guidelines in all units for FFP transfusion using appropriate normal values.

1. **Andrew M,** *et al*. *Blood* 1987;**70**:165–72.
2. **Andrew M,** *et al*. *Blood* 1988;**72**:1651–7.

G133 UK VALIDATION AND INITIAL TESTING OF AN IMMUNE THROMBOCYTOPENIC PURPURA QUALITY OF LIFE INSTRUMENT

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Aim: We describe the UK "translation" of an immune thrombocytopenic purpura (ITP)-specific quality of life (QoL) tool developed in Canada. Cross-cultural testing resulted in important changes to the measure. Ultimately, the Kids ITP Tool (KIT) will be an essential outcome measure in clinical trials and in making clinical treatment decisions.
Methods: The KIT is a disease-specific QoL measure developed by Dorothy Barnard in Canada and validated in North America. The KIT consists of 26 questions. A child version is completed by children of 7 years or older. Parents complete a proxy version and a parent impact KIT. The KIT produces scores with a range of 0 (worst) to 100 (best). Following cognitive debriefing and cross-cultural translation with 11 families a UK version of the KIT was produced. We report initial testing of the UK KIT on 40 UK families affected by childhood ITP.
Results: Feeling tired, cranky and upset, headaches, activity restrictions, bruises, having bloods taken, more hungry than usual, worry over the platelet count and more than usual frustration with parents were highlighted as particular burdens. Children with acute ITP had a significant worse HRQoL compared with children with chronic ITP ($p<0.05$). Parents completing the proxy version reported male patients have a better HRQoL than female patients ($p<0.05$) and children with a platelet count $>20\times109$/litre had a significantly better HRQoL than children with a platelet count $<20\times109$/litre ($p<0.05$). In our analysis we did not find any significant effect of age on HRQoL in ITP.
Conclusions: HRQoL analysis is a vital measure for children with ITP. We have demonstrated the cross-cultural translation of the North American KIT for use in children in the UK. HRQoL measures should be incorporated into registry data such as the UK Paediatric Registry http://www.uk-itp.org and provide an important outcome measure for upcoming interventional and non-interventional studies.

G134 VACCINATION PRACTICES OF PAEDIATRIC ONCOLOGY AND SHARED CARE ONCOLOGY CONSULTANTS: A UK SURVEY

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Background: In March 2002, the Royal College of Paediatrics and Child Health (RCPCH) introduced guidelines for the re-vaccination of children with cancer after completion of standard dose chemotherapy, and after haematopoietic stem cell transplant (HSCT). There is now published evidence from the UK to support the efficacy of these guidelines.
Aims: To ascertain whether these guidelines have been incorporated into standard unit policies by undertaking a cross-sectional survey of UK paediatric principal treatment centre (PTC) consultants and shared care (SC) consultants.
Methods: In October 2008, an online anonymised survey was sent by e-mail to all UK PTC consultants in the Children's Cancer and Leukaemia Group (CCLG) centres and to SC consultants linked to eight of these centres.
Results: Responses were received from 55 PTC consultants (representing all 21 CCLG centres) and 54 SC consultants linked to eight CCLG centres. As per the RCPCH guidelines, most PTC and SC consultants recommend initiating vaccinations at 6 months after completion of standard dose chemotherapy (99 of 105, 94.3%) and re-vaccination after HSCT at the times recommended for each transplant type (mean n = 35, 96.6%). There was no significant difference between PTC and SC consultants for any responses except in their practice of prophylaxis following significant varicella zoster virus (VZV) contact in patients non-immune to VZV prior to HSCT. PTC consultants favoured VZ immune globulin alone (15 of 37, 40.5%) or aciclovir alone (17 of 37, 45.9%) while SC consultants favoured VZIG alone (16 of 35, 45.7%) or VZIG and aciclovir (15 of 35, 42.9%, $p<0.05$). Vaccine-specific antibodies were not routinely checked after chemotherapy but six of 40 (15%) checked antibodies prior to re-vaccination following HSCT. Surrogate markers to indicate immune reconstitution in HSCT recipients were used by seven of 36 (19.4%) of PTC consultants. Annual influenza vaccine was recommended by 84 of 108 (80%) of all consultants during chemotherapy and 65 of 74 (87.8%) in HSCT recipients. Pneumococcal conjugate vaccine (PCV) was not recommended after chemotherapy by 20 of 60 (33%) of respondents.

Conclusions: There is a high level of stated compliance within the RCPCH guidelines. However, PCV has a lower than expected uptake that may reflect the absence of PCV recommendations. Policy variation in prophylaxis after significant VZV exposure suggests more evidence is required in this area.

G135 BEHAVIOURAL PROBLEMS, ADAPTIVE BEHAVIOUR, COGNITIVE STATUS, EMOTIONAL STATUS, HEALTH STATUS AND HEALTH-RELATED QUALITY OF LIFE IN THE FIRST 12 MONTHS AFTER DIAGNOSIS IN CHILDREN WITH BRAIN TUMOURS: A PROSPECTIVE LONGITUDINAL STUDY

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Introduction: Mortality from paediatric brain tumours has fallen significantly over recent years, but few detailed prospective data exist concerning quality of survival.
Aims: (1) To investigate parent and self-rated quality of survival (QOS) in patients with childhood brain tumours in the first year after diagnosis, and (2) to compare QOS in patients with brain tumour with normal matched controls.
Methods: Longitudinal prospective study. Assessments took place at 1 (t1), 6 (t6) and 12 (t12) months after diagnosis. Behavioural problems were measured by the Child Behaviour Checklist; adaptive behaviour by Vineland Adaptive Behaviour Scales; verbal IQ (VIQ) and performance IQ (PIQ) scores by WISC-III; psychological status by Revised Children's Manifest Anxiety Scale (RCMAS) and Birleson Depression Scale (BDS); health status (HS) by Health Utilities Index (HUI); and health-related quality of life (HRQL) by Paediatric Quality of Life Inventory (PedsQL). Parent reports were used, except for RCMAS and BDS, which are self-reported, and for HUI and PedsQL, where parent and child reports were used. Repeated measures analyses of variance, compound symmetry model and Mann–Whitney U-test were employed as appropriate.
Results: 38 patients and 45 controls were alive at t12. Mean age at t12 was 10.1 years (range 1.3–17.3). Brain tumour children had significantly more internalising and total behaviour problems and lower adaptive behaviour scores than controls at all time points, though behaviour tended to improve over time. Patients scored significantly lower than controls for VIQ and PIQ at all time points. PIQ improved significantly over time, but VIQ did not. HS and HRQL were lower in patients than controls at all time points, apart from self-rated HRQL and HS at t12. However, the suggested minimally clinically important difference of 4.4 for overall HRQL was met at t12. There were no significant differences in self-reported symptoms of depression or anxiety between patients and controls. There was a significant improvement in parent and self-report HRQL, parent-report HS and self-report anxiety over time.
Conclusions: Brain tumour children have significant deficits in QOS in the first 12 months after diagnosis.

G136 INITIAL RESULTS FROM THE THIRD INTERNATIONAL STUDY (2001–07) OF THERAPY FOR LANGERHANS CELL HISTIOCYTOSIS

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Introduction: Langerhans cell histiocytosis (LCH) is a heterogeneous granulomatous disorder that affects approximately 50 children/year in the UK and ROI. It ranges from mild single system disease to a severe multisystem (MS) form with risk organ (RO) involvement (liver, spleen, bone marrow and lungs). Treatment ranges from no intervention, through topical/local steroids or curettage to combination chemotherapy. International treatment trials have been organised by the Histiocyte Society. LCH I (1991–95), revealed no difference in the efficacy of vinblastine (VBL) and etoposide (VP16) in the treatment of LCH. LCH II (1996–2000) did not demonstrate any benefit of combining VP16 and VBL compared with VBL alone. The prognostic significance of a poor early response in multisystem RO-positive (RO+ve) patients was confirmed (75% mortality) and it was established that age <2 years was not an independent predictor of poor outcome. LCH III (2001–07) was designed to test whether (1) adding methotrexate (MTX) to VBL and prednisolone (PDN) would increase the early response in the RO+ve group, and (2) extending maintenance from 6 to 12 months in RO–ve children would result in a lower reactivation rate and a decrease in permanent consequences.
Results: A total of 529 MS (RO+ve 269, RO–ve 260) and 602 special site (SS) patients were entered into the study. In the RO+ve group, 234 were randomised to arm A MTX+VBL+PDN (115 patients) or arm B, VBL+PDN (119 patients). Early response data are currently available on 204 with 31 of 102 (30%) being non-responders in arm A and 29 of 102 (28%) in arm B. In the RO–ve group there were 186 patients with MS treated in standard induction with VBL+PDN and then randomised to either 6 (97 patients) or 12 months (89 patients) of maintenance therapy. The longer maintenance therapy reduced reactivation from 24% to 16% in year 1, 44% to 30% in year 2 and 55% to 42% in year 3. More follow-up is needed for the patients with SS.
Conclusions : Addition of MTX does not improve initial response. Increasing maintenance from 6 to 12 months significantly reduces reactivation rates. LCH IV is currently being designed to evaluate whether (1) poor responders can be identified before 6 weeks and thereby benefit from an early move to salvage therapy, and (2) reactivation rates can be further reduced using longer maintenance or alternative drug combinations.

G137 CHRONIC MORBIDITY IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER

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Objectives: Long-term follow-up (LTFU) is recommended for all survivors of childhood cancer to monitor, treat and ultimately prevent morbidity. National guidelines recommend risk-stratified levels of follow-up by a multidisciplinary team, in an age-appropriate environment. Many survivors do not attend late effects clinics. This study aimed to evaluate LTFU of childhood cancer survivors and to assess treatment-related morbidity in survivors lost to follow-up.
Methods: All survivors of childhood cancer diagnosed between 1971 and 1 July 2003 more than 5 years from diagnosis, were identified. Patients were retrospectively assigned a 5-year and current level of follow-up: level 1, postal or telephone LTFU; level 2, nurse-led or primary care LTFU; level 3, medically supervised LTFU clinic. All lost to follow-up survivors (not seen in clinic >2 years) were sent a postal questionnaire.
Results: 831 patients were diagnosed with childhood cancer (overall survival rate 69%). Information was available on 550 survivors (290 (53%) male): median age (range) 18.8 (5.4–44.2) years, at diagnosis 5.0 (0.0–18.8) years, and disease-free survival (range) 10.8 (1.0–37.4) years. Retrospective assignment of follow-up level 5 years from diagnosis identified: 71 (13%) survivors level 1; 230 (42%) level 2; and 249 (45%) level 3. Reassignment of current level identified 231 (42%), 125 (23%) and 194 (35%) as level 1, 2 and 3 respectively. 90 (46%) of level 3 patients were >18 years old. 256 (46%) survivors were lost to follow-up, 49 (19%) of whom were currently assigned level 3. 96 (38%) of lost to follow-up survivors returned completed postal questionnaires (57.6% female, response rate 38%). 45% of responders reported at least one late effect, 36%

mild–moderate and 8% severe–life-threatening. 19% reported two or more late effects.

Conclusions: Almost half of all long-term survivors of childhood cancer were not followed-up in late effects clinics, one-fifth of whom were classified currently as level 3. Of survivors lost to follow-up, half had at least one late effect. Risk-stratified levels of follow-up change with time. Those survivors at significant risk of chronic morbidity should be encouraged to attend late effects clinics.

G138 VISUAL OUTCOMES OF CHILDHOOD OPTIC PATHWAY GLIOMA TREATED ACCORDING TO A STANDARDISED MULTIDISCIPLINARY STRATEGY: A CHILDREN'S CANCER AND LEUKAEMIA GROUP STUDY

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Aims: Optic pathway gliomas (OPG) present most commonly in early childhood and threatens vision. They have been treated recently with chemotherapy to save vision but there are no studies correlating tumour site with visual function. The aim of this study is to correlate OPG anatomical site with visual outcome in 234 patients with OPG from a population-based pilot study of treatment.

Methods: The visual function of 234 children at diagnosis, 101 males, median age 4 years (range: 2 months–16 years), 89 with neurofibromatosis type 1, with tumours at optic nerve (38, 16.2%), chiasm (167, 71.4%) and hypothalamus (29, 12.4%) were studied. The protocol specified measurement of visual function at diagnosis, overall protocol compliance in this regard was 84%, being highest for measurement of visual acuity (VA 80%) and lowest for visual fields (VF 60%).

Results: 159 children had symptoms (reduced VA, reduced VF, nystagmus, diplopia or a cranial nerve palsy) with 19.5% (n = 31) of this group experiencing one symptom, 55.35% (n = 88) experiencing two symptoms and 25.16% (n = 40) experiencing more than two symptoms. 122 (52.1%) children had reduced VA, which was bilateral in 58.2%. 77 (32.9%) had VF defect, 51.9% of which were bilateral. Tumour site was associated with defects in VA ($p<0.001$) and VF ($p = 0.027$). Hypothalamic tumours were associated with normal VA and VF, chiasmal tumours demonstrated bilateral reduced VA and for optic nerve tumours there was a unilateral reduction in VA. Nystagmus was present in 55 children (23.5%), 52% of whom had normal VA. Cranial nerve palsies affecting the extraocular muscles affected 26 (11%), sixth nerve palsy being the most common (n = 14). 13 patients had diplopia, only three having a cranial nerve palsy.

Conclusions: Visual deficits at diagnosis were least common in hypothalamic tumours, bilateral in chiasmatic and unilateral in optic nerve. More detailed anatomical staging may assist with more detailed grading of visual function at diagnosis and predict for visual outcome after treatment.

G139 OTOTOXICITY FOLLOWING PLATINUM-BASED CHEMOTHERAPY FOR INTRACRANIAL PRIMITIVE NEUROECTODERMAL TUMOURS IN CHILDREN

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Background: Current management of intracranial primitive neuroectodermal tumours (PNETs) includes chemotherapy with platinum agents. Ototoxicity is a recognised side-effect of such chemotherapy and current trials ensure hearing is monitored throughout and after treatment, with pure tone audiometry. Two different scales are currently used to assess ototoxicity: the German HIT and the UK Brock criteria. A retrospective analysis of children treated for intracranial PNET was carried out to compare the HIT and Brock scales and establish whether they describe hearing loss in the same manner. Additionally, this study aimed to describe the natural history of hearing loss following platinum-based chemotherapy for intracranial PNET.

Methods: A retrospective analysis of hearing outcomes in 38 children treated for intracranial PNET between the years 2000 and 2008 was conducted at two UK tertiary centres. Pure tone audiograms conducted prior to each chemotherapy cycle and after completion of treatment were graded with both the HIT and Brock criteria. The cumulative doses of cisplatin and carboplatin patients received was recorded and compared with hearing deficits.

Results: The HIT and Brock criteria described ototoxicity during chemotherapy in different ways, with the Brock criteria being more suitable for the pattern of hearing loss seen with platinum agents. Platinum chemotherapy's ototoxic effects progressed throughout treatment and hearing deficits advanced even after treatment was stopped. Ototoxicity was seen to be dose dependent; however, interindividual variability was demonstrated.

Discussion: This study demonstrates that the HIT and Brock criteria are not interchangeable, and suggests that future trials should use the Brock criteria as the standard for describing ototoxicity. This study also highlights the importance of audiological monitoring both during platinum chemotherapy and after completion, to avoid overlooking the significant high-grade hearing loss that can develop with time.