Autism Spectrum Disorder (ASD) and Chronic Kidney Disease – The challenges of renal replacement therapy

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**Background**

Over the last 12 months we have discussed the management of four paediatric patients with chronic kidney disease and autism spectrum disorders (ASD).

We will present:

1. The prevalence of ASD within our CKD population
2. Case presentations for these 4 paediatric patients

**Aim**

To share our experience and learn from others experience to ultimately improve our approach to managing RRT for those with ASD
Autism Spectrum Disorders
Autism Spectrum Disorder

Diagnostic Criteria

A. Persistent deficits in social communication and social interaction *across multiple contexts, manifested by the following, currently or by history* (examples are illustrative not exhaustive; see text):
   1. Deficits in social-emotional reciprocity; ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
   2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
   3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends, to absence of interest in peers.

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B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).

2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals need to take same route or eat same food every day).

3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).

4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

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- Impairment in Social Interaction
- Qualitative impairment in communication
- Restricted repetitive and stereotyped patterns of behavior, interests, and activities

Deficits in social communication and social interaction

- Restricted, repetitive patterns of behavior, interests, or activities
DSM-5:

Autistic Disorder → Asperger’s Disorder → PDD-NOS → CDD

Autism Spectrum Disorder
Methodology

• In December 2014 we reviewed our paediatric CKD population (age 0-18 years) to assess the prevalence of ASD.

  • All paediatric patients with eGFR<50ml/min/1.73m² currently attending the CKD clinic, dialysis clinic or post kidney transplantation were included.

Our unit serves the South-East of England with a population of over 9 million.
Methodology

- Cases of ASD identified from patient clinical diagnosis list
- Clinical staff involved in the clinics also requested to list any patient with a suspected diagnosis due to features but yet to undergo a formal assessment.

- Information collected included:
  - Renal diagnosis
  - Co-morbidity
  - ASD diagnostic tools utilised
  - Any genetic testing performed (results pending)
Results

- ASD prevalence in CKD population = 24/224: 107 per 1000 children with CKD (95% CI 71-157)

- This is compared to South London population prevalence of: 11.6 per 1000 children (95% CI 9.0–14.2)

Z score = 12.36, p<0.001
Results

• 224 CKD patients with eGFR < 50ml/min/1.73m² were identified
• 24 (10.7%) had a diagnosis of ASD, 17 (7%) some features of ASD

<table>
<thead>
<tr>
<th></th>
<th>ASD (n=24)</th>
<th>Non-ASD (n=200)</th>
<th>Total (n=224)</th>
<th>ASD vs non-ASD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD</td>
<td>17 (71%)</td>
<td>106 (53%)</td>
<td>123 (55%)</td>
<td></td>
</tr>
<tr>
<td>Dialysis</td>
<td>1 (4%)</td>
<td>16 (8%)</td>
<td>17 (7.5%)</td>
<td>Chi Square= 2.776</td>
</tr>
<tr>
<td>Tx</td>
<td>6 (25%)</td>
<td>78 (39%)</td>
<td>84 (37.5%)</td>
<td>p-value= 0.25</td>
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</tbody>
</table>
Results for those with ASD

• Significant co-morbidity (29%)
  • Chromosomal abnormality (n=4)
  • Jakobson syndrome
  • Fragile X
  • Congenital hypothyroidism

• Primary renal diagnosis
  • Hypoplasia/dysplasia (46%, n=11)
  • ARPKD (n=3)
  • PUV (n=2)
  • Nephrotic syndrome (n=2)

No statistical difference between autism and non-autism group in terms of renal diagnosis
Autism Spectrum Disorder (ASD)

• ASD is highly hereditable
• ASD is complex and heterogeneous disease with no established biomarker
• Despite heterogeneity, patients present with characteristic impairments
  • Common pathways involved in synaptic development & signaling.
  • ASD could be syndromic (~2%) vs non-syndromic (>500 candidate genes)
  • Learning difficulties seen in around 50%.

UK paediatric prevalence of 1.1\%^{2}
Disease models of **syndromic ASD** which also affect kidneys include:

- Tuberous Sclerosis Complex (TSC1/2);
- Phelan-McDermid syndrome (SHANK3);
- PTEN syndrome;
- Jacobson Syndrome (11q terminal deletion);
- Smith-Lemli-Opitz syndrome (DHCR7);
- Fragile X

3-8
Chronic Kidney Disease and Autism Spectrum Disorders

Is there a non-syndromic genetic link?

- **16q24.2** identified as region of interest for autism spectrum disorder, intellectual disability and congenital renal malformation.  

- **17q12 deletion.** 3/53 children with autism and cystic/hyperechogenic kidneys with 17q12 region deletion encompassing hepatocyte nuclear factor -1beta HNF1B.  

- **17q12 microdeletion** syndrome involves 15 genes including HNF1B and is considered to confer high risk of neuropsychiatric disorders. 39 children with HNF1b deletion diagnosed secondary to renal abnormalities were found to have 17q12 microdeletion syndrome, however, only one found to have autism.
Case Presentations:

1. Should ALL children with severe autism be offered renal replacement therapy?

2. How should we prepare children with ASD for renal replacement therapy?

3. How should we prepare children with ASD for the unpredictability of transplantation?
Should ALL children with severe autism be offered renal replacement therapy?

Case 1

- 11 year old girl
  - Hypoxic ischaemic insult
  - Fragile X
  - Autism
  - Severe intellectual disability
  - Ulcerative colitis
  - Current eGFR 15ml/min/1.73m²
Should ALL children with severe autism be offered renal replacement therapy?

• Case 1

  No communication
  Severe learning disability
  Self injurious behaviours
  Extreme distress screaming and recoiling in flexed position in clinic – relaxes only when given a clock to look at
  Dependent upon tube feeding for nutrition and fluid requirements
  Recent flare up of Ulcerative Colitis requiring inpatient stay
Should ALL children with severe autism be offered renal replacement therapy?

• Case 1

  Mother fully informed regarding renal replacement therapy

  - Mother has declined RRT on the basis that her daughter would not tolerate regular medical intervention and does not see RRT would offer a good quality of life for her daughter.

  - Medical team in agreement with the mother’s decision

  To continue on the active conservative pathway and family linked to local children’s hospice with plan for involvement of hospital palliative care team when appropriate
How should we prepare children with ASD for renal replacement therapy?

• We have currently got two patients preparing to start haemodialysis.

• Is it right to be preparing for dialysis as the first step in their RRT pathway?

For both patients considerable discussion was had with the families and amongst the multidisciplinary team. Collectively the decision to prepare these young people for dialysis was made as dialysis is generally more predictable and follows a clear routine. It would also allow time for the multidisciplinary team to work the young person up for transplantation.
How should we prepare children with ASD for renal replacement therapy?

• Case 2
  • 4 year old girl
    • Jakobsen syndrome (deletion in Chromosome 11)
    • Left MCDK with right renal dysplasia
    • Perimembranous VSD
    • Thrombocytopenia
    • Intellectual impairment
    • Autism
    • Current eGFR 15ml/min/1.73m²
How should we prepare children with ASD for renal replacement therapy?

• Case 2

  • Only child, mother has had 7 miscarriages
  • Struggles to stay still, mother struggles to manage her behaviour
  • Dislikes blood tests
  • Previous attempts to manage her bladder with catheterisation abandoned due to extreme distress
  • Mother keen for ‘everything to be done’
  • Tolerated video-urodynamic investigation well with distraction
  • Discussed in multidisciplinary team meeting to offer haemodialysis
How should we prepare children with ASD for renal replacement therapy?

• Case 2
  • Early preparation for haemodialysis was started
  • Play therapy team are working intensively with her and her mother
  • Her mother is committed to engage in preparation process
How should we prepare children with ASD for renal replacement therapy?

• Case 2
  • School involved in the preparation process
  • Photographs from unit used to create story for use at school
  • School SENCO has attended preparation sessions
How should we prepare children with ASD for renal replacement therapy?

• Case 2

• Currently attends for weekly visits to ‘role play’ dialysis:
  • weight performed on arrival
  • sits in the dialysis chair with distraction
  • regular observations performed as they would for dialysis
  • commode used if needing to void

Over 3 month period has progressed from sitting for 5 minutes to achieving a full 2 hours

• If unwell, tired or if there is disruption at home this impacts upon whether she is able to sit
How should we prepare children with ASD for renal replacement therapy?

• Case 3

• 15 year old boy
• Bengali family with limited English. Father has mod/severe learning difficulties
• 1 of 5 children, 4 with polycystic kidney disease, 3 have learning difficulties and 3 autism
• Social problems – child protection plan
• Polycystic kidney disease
• Learning difficulties
• Autism - very limited communication, no communication tools used at home
How should we prepare children with ASD for renal replacement therapy?

• Case 3

• Requires a ‘fixed’ routine for hospital visits
  • Needs to be in the first clinic slot to reduce waiting time and duration in busy waiting area
  • Blood tests, blood pressure, clinic consultation must always be done in the same order
  • Consultations limited to small number of clinicians

Family and school believe transplantation is ‘possible’ if we just get him used to it....

• Multidisciplinary decision to attempt to prepare for haemodialysis.
How should we prepare children with ASD for renal replacement therapy?

• Case 3
  • School actively involved
    • using photos to make social stories for the hospital visits.
    • school do preparation work the day(s) before hospital visits to reduce anxiety.
  • Social services are involved with the family
    • working on parenting skills
    • getting communication tools used in the home setting
How should we prepare children with ASD for renal replacement therapy?

• Case 3

• Current hospital ‘Action Plan’
  
  • Weekly visits to the hospital clinic for 2 months.
  
  • School attended hospital taken photos of hospital, lift, waiting areas, dialysis unit, staff members to develop social stories
  
  • Visits gradually increased in length and each time areas closer to the dialysis unit were visited until the point of sitting in dialysis chair watching DVD achieved.
  
  • Blood tests and voiding into a bottle introduced

  After 4 months he will now happily go and sit on the dialysis unit. He knows where to go but insists on the same chair each visit.
How should we prepare children with ASD for the unpredictability of transplantation?

• Case 4
• 16 year old boy
• PUV
• CKD clinic: psychology involved to help with aggressive behaviour and needle phobia
• Commenced haemodialysis and started preparation for transplantation
How should we prepare children with ASD for the unpredictability of transplantation?

• Case 4 – On haemodialysis
  • Disliked change
  • Hypersensitive to sound, light and touch
  • Misinterpreting peoples emotions
  • Uncomfortable around people
  • Agitated and verbally aggressive to staff, parents and patients

Involvement of psychology – behavioural contract drawn up, ASD diagnosis explored.....

Asperger’s syndrome diagnosed

“What’s the point of all this? We are all going to die...”
How should we prepare children with ASD for the unpredictability of transplantation?

• Case 4 - The day of transplant

• Extremely anxious and fearful

• Disliked the anaesthetist plan to place a neck line, this was not what he was told would happen.

• He became increasingly distressed and angry that the anaesthetist hadn’t read his notes properly and that no-one was listening to him.

• He decided he didn’t know enough about the operation, the procedure and what was going to happen to him

He refused to go ahead with the transplant....
How should we prepare children with ASD for the unpredictability of transplantation?

• Case 4 - Back on haemodialysis

• Long multi-disciplinary discussions regarding how to re-prepare this young man for transplant

• Intensive preparation commenced with play specialist and medical team
  • Strict guidelines drawn up regarding behaviour
  • Clear documentation of each session with review at next session
  • Negotiations held regarding management
    • Agreement needed for certain medical procedures and TED stockings
    • Safe allowances where possible for no neck line, cubicle on the ward.
How should we prepare children with ASD for the unpredictability of transplantation?

• Case 4 - Preparation for transplant
  • His mother decided to put together his transplant plan.
  • Once agreed this became his transplant plan - ‘Important things about me’

He was successfully transplanted in October 2014.
How should we prepare children with ASD for the unpredictability of transplantation?

• Case 4 - Post transplantation – challenges continue..
  • Has to be seen first in clinic
  • Does not interact with the other patients
  • Refuses to leave urine samples
  • Refuses to go to alternate day steroids
  • Gets angry if he is told something or asked to do something he doesn’t agree with.
How should we prepare children with ASD for the unpredictability of transplantation?

• Case 4 - Post transplantation – challenges continue..

  “Mental health is neglected by the NHS”

  “Adult services kill people”

  “Adult services have ‘under qualified’ staff to manage me”

• His transplant function is stable and we are attempting to transition him to adult services.

  • However, he has decided he wants to remain in children’s services...
Summary

• Autism spectrum disorder is common in our CKD population

• All these young patients require a lot of clinical time from members of the multidisciplinary team

• How should we make the decision to start dialysis and/or transplant?

• How should we best prepare them for medical intervention?
Follow on

- Follow up for those not yet with diagnosis
- Benefit of diagnosis or recognition of communication difficulties
- Genetics of those diagnosed
Comments, questions and discussion.......
References

1. DSM-V (2013) APA.
11. Laffargue F et al Arch Dis Child 2015 Mar; 100(3):259-64