Appendix 6: Paediatric guidelines


This document gives guidance on the screening for Juvenile Idiopathic Arthritis associated Chronic Anterior Uveitis (JIA CAU), and the management of JIA CAU and idiopathic paediatric uveitis (IPU).

Very rarely uveitis occurs in children with other disease associations, such as Behcet’s disease, sarcoid, inflammatory bowel disease, and other rare causes. The management of these conditions is poorly evidence based, and is best done by experts with the greatest possible knowledge of these conditions, but it is expected the management should adhere to the principles of good uveitis and paediatric care and care pathways inherent in this document.

Rationale

Asymptomatic CAU associated with JIA has long been recognised as an important cause of visual loss in childhood (244,245) with high levels of complications compared to other forms of anterior uveitis. The incidence of bilateral disease is between 67-85% (246,247,248,249), and complications are reported in 20-40% of children at presentation and steadily accumulate over the first two decades of life, especially in those with persistently active disease (247,248,249,250,251,252). In order to reduce the ocular complications early, regular, screening by slit lamp examination has been recommended for many years, but the incidence of a poor visual outcome remains high (16-38%) (246,247,253,254). The current screening advice (255), albeit based on limited evidence is the basis for the current screening guidance in this document, and is in line with other guidance (256). It has not been possible to demonstrate unequivocally that screening programmes have reduced the frequency of either complications at presentation, or long-term visual loss (257,258,259), but it is becoming clearer that early diagnosis, and early immunosuppression with an aggressive approach to removal of inflammation are important (1, 246, 251, 253, 260, 261, 262, 263, 264, 265, 266). Some medication choices may be important risk factors for developing uveitis (61, 57, 134, 135, 136, 137, 138, 139, 140, 267, 268, 269, 270). Other risk factors are not yet clearly elucidated, poorly controlled uveitis and chronicity of inflammation themselves presents a significant risk of cataract and glaucoma in 10- 50% of patients in many series, and are increasingly common with longer follow-up (47, 251, 253, 261, 263).
Persistent ongoing application of topical steroid is also associated with cataract and glaucoma \(^{(246, 251, 253, 261, 263, 264, 265)}\). There is growing evidence for the value of early introduction of disease modifying anti-rheumatic therapies (DMARD), particularly methotrexate \(^{(276, 277)}\) and mycophenolate \(^{(278, 279, 280, 281)}\), and for early introduction of biologic therapies, namely infliximab \(^{(57, 74, 75, 76, 282, 283, 284)}\) or adalimumab \(^{(58, 59, 60, 62, 269)}\). The majority of children with uveitis have JIA, and paediatric rheumatology services in Scotland already manage and prescribe these drugs for the other organ manifestations of JIA. This includes access to specialist paediatric nurses with a remit to manage and educate about these drugs for children and parents.

These guidelines are based on an agreement between SPARN and the Uveitis Network that joint working between these teams is a useful way forward, and that paediatric rheumatology services are happy to support the use of these complex drugs in all children with uveitis, including those who do not have JIA, including providing paediatric nurse specialist support for ophthalmology services. Whilst the networks accept this guidance is not fully evidence based they are current best practise and are adopted by both networks until more definitive, evidence based guideline is developed.

**Core principles:**

**Communication**

In each region key personnel caring for paediatric uveitis and providing screening should be clearly identified through both SPARN and the uveitis network.

- For eye screening identified paediatric ophthalmologists would usually be the key lead for each region.

- The management of paediatric uveitis is expected to be undertaken by an ophthalmologist who has expertise in the management of uveitis, but who should be properly supported by paediatric services, including specialist paediatric nursing support in line with current standards of care \(^{(286, 287, 288)}\). This will usually be through the local paediatric rheumatology service. In some regions the same individuals may provide both screening and uveitis care. It is essential that all children are seen in an appropriate paediatric environment supported by appropriately trained paediatric staff, even where occasional component of care takes place unavoidably in an adult setting. In many regions paediatric
Ophthalmologists may do the screening, day to day uveitis care, liasing with uveitis experts as required.

- Rapid, consistent and complete two way communication between the ophthalmologist and the paediatric rheumatologist / paediatric rheumatology services is key to an effective screening service. Both services will need to have good knowledge of the screening guidelines, with awareness of decisions that alter the screening requirements for an individual patient.

- Uveitis care requires the same high level of communication.

- Planned transition to adult services aims to involve both adult rheumatology and ophthalmology services.

- The following is considered a core set of information to be included in all correspondence, or immediately accessible from shared clinical notes, from both ophthalmologists and rheumatologist includes:
  
  - Next planned appointment
  - All systemic and topical medication, whether or not given for eyes. Systemic treatment given for JIA or other systemic disease association should be recorded in the ophthalmology notes whether or not it is given for eye complications.
  - All changes in systemic and topical medication particularly cessation of treatments.
  - Ophthalmologists should record at each visit in the clinical notes, and where the clinical notes are not shared with the rheumatology team, communicate the following to the rheumatology team in numerical values, vague or descriptive terms should be avoided: visual acuity, the presence and absence of uveitis, and the severity of uveitis using the SUN criteria\(^{(289)}\) recording the actual number of cells using a 1mm circular beam set at 45 degrees, bright light and high magnification. Flare should be recorded. For the measurement of intraocular pressures proxymetacaine should be used and a gentle examination performed. Goldman is preferred\(^{(290)}\). This may be difficult in the very young and the failure to record pressures should be documented. The appearance of the optic disc, and the macular if the vision.
is reduced, should be recorded. If there is posterior involvement and macular oedema this should be highlighted as a red flag for aggressive treatment.

- Those providing screening should be able to provide rapid access to examination under anaesthetic where examination is difficult in line with current standards of care $^{(255)}$. To minimise the number of general anaesthetics ideally a shared general anaesthetic with rheumatology services providing joint injections wherever possible.

- Rheumatologists should urgently highlight to the ophthalmologist any changes in medication or diagnostic details that materially alter the screening programme required $^{(255)}$. The paediatric rheumatologist should be aware of the implication to the management of the eyes that changes in treatment for other aspects of JIA care will make, and where this is unclear should make this decision in conjunction with the ophthalmologist.

- It should be avoided that ophthalmologists and rheumatologists are both prescribing disease modifying drugs (DMARDS) or biologics for different aspects of JIA care. The lead clinician for prescribing should be formally identified, and should normally be the paediatric rheumatologist unless otherwise agreed in writing, and appropriate paediatric nursing support provided.

- All communication should be sent within two weeks of clinical review in line with current guidance.

**Uveitis Screening**

JIA CAU Screening guidelines have been produced jointly by BSPAR and the RCPOphth in 2006 $^{(255)}$ (appendix 7). Whilst these are not fully evidence based they are current best practise and are adopted by both networks until more definitive, evidence based guideline is developed. Both rheumatology and ophthalmology services should be aware of these guidelines, and ensure changes in diagnosis or management are effectively communicated to the other services to facilitate adherence to these guideline. In Scotland geographical issues are not an acceptable barrier to meeting screening needs. Where screening is provided by training ophthalmology doctors they should be aware of their responsibilities under the screening guidelines, and should not deviate from the screening guideline unless this is a consultant led decision and communicated to the paediatric rheumatology team.
Management of JIA CAU and IPU

The management of paediatric uveitis differs from adult uveitis in that an earlier and more aggressive approach to the introduction of DMARDS and biologics is found \(^{(47, 57, 58, 59, 60, 62, 74, 75, 76, 140, 259, 269, 271, 272, 273, 276, 277, 278, 280, 281, 282, 283, 284)} \). The algorithm demonstrates the key pathways agreed includes time lines for rapid progression through treatment regimes but acknowledges the lack of evidence base for this \(^{(1, 246, 251, 253, 261, 262, 263, 264, 265, 266, 271)} \). Key red flags for concern are considered to be:

- Persistent requirement of topical steroids after 4 months, with or without a DMARD
- Presence of macular oedema or posterior involvement.

**Detailed discussion points from the algorithm:**

Differences between the management of uveitis in adults and children include:

1) Steroids

   a. In children a very cautious approach to even low dose topical steroid is usually taken (because of the risk of glaucoma and cataract) \(^{(135, 246, 251, 253, 261, 263, 264, 291, 292)} \). In severe inflammation where high dose frequent application of topical prednisolone is required earlier introduction of DMARDS or more rapid progression through the algorithm is appropriate.

   b. Once control is achieved it is expected that low dose topical and systemic steroid will be withdrawn before weaning off the second line agent. The second line agents are usually given for a longer time period than is usual in adult uveitis, and may be required indefinitely.

2) Biologics: In children progress to a biologic agent is usual after the first second-line agent has failed.

**Paediatric Nursing Care**

Children receiving DMARDS or biologic agents are expected to have

- Access to identified trained paediatric nursing care with expertise in the management of these drugs including skills in education, monitoring and training of families appropriate for the care of children \(^{(286, 287, 288)} \).
The paediatric nurse has a key role in coordinating both the PR and ophthalmology teams. One team (usually paediatric rheumatology because of their role in prescribing immunosuppression for other organ involvement) is formally responsible for the monitoring and prescribing of these drugs.

Drug Monitoring

DMARDs and biologics are expected to be formally monitored. The BSPAR and RCN guidelines on the use of these drugs, including doses and monitoring guidelines, are appropriate guidance to follow for these patients (287, 288, 293).

Choice of DMARD

The usual choices of DMARD would be methotrexate or mycophenolate (259, 276, 277, 278, 279, 280, 281). The rationale for the choice may be influenced by the other features of JIA, such as joint involvement where methotrexate is usually the preferred choice, mycophenolate has poorer efficacy for synovitis (281), whereas where eye features predominate mycophenolate may be the preferred choice. Whichever is chosen first if the response to DMARD treatment is unacceptable a biologic would usually be the next choice rather than the other DMARD. Methotrexate is also used as the first choice in conjunction with the biologic agents infliximab and adalimumab to reduce allergic reactions, and may improve the efficacy of these drugs for JIA and uveitis (57, 61, 269) although adalimumab is licensed for use on its own.

Choice of Biologic

The current first choices for which there is evidence of efficacy are of an anti-TNF. The choice is between infliximab (75, 76, 282, 283, 284) or adalimumab (57, 58, 59, 60, 61, 62, 76, 269, 282, 283). There is a current lack of evidence base to guide choice between either of these, and practical or patient related issues around administration often influence the choice. The licences suggest these should be given with a DMARD, usually methotrexate. Where the response to one is inadequate or significant side-effects occur the other may be tried. The anti-TNF etanercept should be avoided in uveitis because of lack of efficacy and some suggestion that it might worsen inflammation in uveitis (57, 61, 135, 136, 137, 138, 139, 140, 252, 267, 268, 269, 270).

Macular oedema

The assessment of macular oedema is difficult in children. If the vision is reduced it is appropriate to assume that macular oedema is present, until proven otherwise. Initially oral steroid can be given, but in severe cases intravenous pulsed methylprednisolone may be
most appropriate. Concurrent commencement or escalation of DMARDS or biologics is appropriate.

**Time lines for moving through the algorithm**

These are the longest time periods felt acceptable before moving through the algorithm. Where severe disease persists, vision is threatened, glaucoma has developed, or unacceptable doses of topical or systemic steroids are required it is appropriate to move more rapidly to the next stage of the algorithm.
JIA associated chronic anterior uveitis or idiopathic paediatric uveitis

Introduce corticosteroid treatment

Anterior Chamber involvement only
Topical prednisolone

Wean topical prednisolone to zero over 4 months.
If activity recurs or is not controlled add DMARD

DMARD usually methotrexate or mycophenolate

Failure to wean topical or systemic corticosteroids to zero over 12 weeks despite optimisation of dose and route of DMARD progress to biologic therapies

BIOLOGICS usually adalimumab or infliximab

Macular oedema
start steroids and a DMARD +/- topical steroids

Communication between named personnel in rheumatology and ophthalmology services

DMARD and biologic use requires the support of a trained paediatric nurse

Uveitis NMCN Treatment Guidelines
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