

PARENTS' PERCEPTION OF THE ADVANTAGES/DISADVANTAGES OF SUSTAINED RELEASE AND IMMEDIATE RELEASE METHYLPHENIDATE

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Meena Agarwal is a consultant in Adolescent and Child Psychiatry based at the Longlands Child Development Centre, Lancaster. Her interests in the dynamics of the family have resulted in her undertaking an MSc in Family Therapy. This contribution to the Journal describes her experience of introducing a new formulation of a drug used for Attention Deficit Hyperactivity Disorder (ADHD).

Attention Deficit Hyperactivity Disorder (ADHD) is a neurobiological disorder characterised by a set of behavioural difficulties with attention, impulse control and activity regulation not consistent with the developmental level of a child or adolescent. It is the most common of the disruptive behaviour disorders of childhood with the prevalence rate ranging between 3%-5%⁽¹⁾. ADHD is defined by the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-IV)⁽²⁾, but the World Health Organisation International Classification of Diseases (ICD-10)⁽³⁾ uses the term hyperkinetic disorder (HKD) instead. ADHD and HKD are related conditions that differ in their severity and their precise clinical definition. HKD is a narrower category but it appears that nearly all cases of hyperkinetic disorder should be included within ADHD⁽¹⁾. The DSM-IV category of ADHD is more broadly defined and is a much commoner diagnosis.

There is overwhelming evidence for the use of stimulants for the treatment of ADHD. They have a long history of usage and one of the lowest profiles of adverse side effects⁽⁴⁾. Methylphenidate immediate release preparation (IRMP), ie Ritalin, has been the psychostimulant most commonly used as the recommended first choice treatment of ADHD⁽⁵⁾.

More recently, the multi-modal treatment of ADHD study⁽⁶⁾ also concluded that methylphenidate should be given three times daily and titrated to the dose that delivers maximum therapeutic efficacy. Dosing is required three or four times a day because ADHD impairs across the day and because methylphenidate's duration of action is about four hours.

Sustained release methylphenidate (SRMP), ie Concerta XL, an extended release, osmotic delivery formulation of methylphenidate, was licensed in the UK in 2002. It is taken once daily and it is said to provide symptom control for 12 hours. The American Academy of Child and Adolescent Psychiatry recognised that a gradually ascending methylphenidate plasma profile over the day produces equivalent improvements to three peaks obtained with immediate release methylphenidate, three times daily⁽⁷⁾.

In a recent study it was shown that SRMP can be successfully started in 96% of patients; independent of the initial treatment status (naïve or previously treated with methylphenidate or another drug for ADHD)⁽⁸⁾. It was also suggested that since SRMP improves attention and behaviour

throughout the day it eliminates the need for in and after school dosing.

Until SRMP was available, locally patients fulfilling diagnostic criteria for ADHD were managed with either immediate release methylphenidate or dexamphetamine. With the licensing of the sustained release preparation we were approached by many parents requesting the new medication, and we agreed to do so if certain criteria were fulfilled (Table 1).

Immediate release methylphenidate perceived to be ineffective
Child forgetting to take the three times daily dosage
Child worried about asking for lunchtime dose at school

Table 1 Clinical indication for switching to slow release preparation

We then carried out a study of the effectiveness of this medication switch by issuing the parent with a questionnaire (Figure 1).

QUESTIONNAIRE FOR A STUDY BY DR MEENA AGARWAL CHILD & ADOLESCENT PSYCHIATRIST PARENTS' PERCEPTION OF THE ADVANTAGES/DISADVANTAGES OF CONCERTA XL OVER RITALIN

Age of child:

Gender of child:

Date:

Please read the following questions carefully before answering them in your own words and/or ticking the YES/NO box.

1. Has your child been on Ritalin/Equasym before going on Concerta XL? Yes No
2. When your child was switched onto Concerta XL what was the daily dosage tried?
18mg Yes No
36mg Yes No
54mg Yes No
3. Has Concerta been (a) more useful/effective than Ritalin, (b) same, or (c) less useful/effective than Ritalin?
(a) more useful/effective Yes No
(b) same as Ritalin Yes No
(c) less useful/effective Yes No
4. If the answer to Question 3 is (a) please list the advantages of Concerta XL over Ritalin.
5. If the answer to Question 3 is (c) please list the disadvantages of Concerta over Ritalin.
6. Please write any other comments.

Figure 1 Parents' questionnaire

METHOD

All children and adolescents included in this study were already under the direct care of a consultant child & adolescent psychiatrist. All met the DSM-IV⁽²⁾ diagnostic criteria for ADHD (Table 2).

Six (or more) of the following symptoms of inattention or hyperactivity-impulsivity have persisted for at least six months, to a degree that is maladaptive and inconsistent with developmental level. Symptoms must be present before the age of seven years.

Symptoms of Inattention

1. Often fails to give close attention to details or makes careless mistakes in schoolwork, work or other activities
2. Often has difficulty sustaining attention in tasks or play activities
3. Often does not seem to listen when spoken to directly
4. Often does not follow through on instructions and fails to complete schoolwork, chores or duties in the workplace (not due to oppositional behaviour or failure to understand instructions)
5. Often has difficulty organising tasks and activities
6. Often avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)
7. Often loses things necessary for tasks or activities (eg toys, school assignments, pencils, books or tools)
8. Is often easily distracted by extraneous stimuli
9. Is often forgetful in daily activities

Symptoms of Hyperactivity-Impulsivity

Hyperactivity

1. Often fidgets with hands or feet or squirms in seat
2. Often leaves seat in classroom or in other situations in which remaining seated is expected
3. Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
4. Often unduly noisy in playing or has difficulty in engaging quietly in leisure activities (ICD-10)

OR

4. Often has difficulty playing or engaging in leisure activities quietly (DSM-IV)
5. Exhibits a persistent pattern of excessive motor activity that is not substantially modified by social context or demands (ICD-10)

OR

5. Is often 'on the go' or often acts as if 'driven by a motor' (DSM-IV)
6. Often talks excessively (DSM-IV)

Impulsivity

1. Often blurts out answers before questions have been completed
2. Often has difficulty awaiting turn
3. Often interrupts or intrudes on others (eg butts into conversations or games)
4. Often talks excessively without appropriate response to social constraints (ICD-10)

Table 2 DSM-IV criteria for the diagnosis of ADHD

The diagnosis was made by obtaining a relevant history and direct child observations within the clinical setting. Confirmation of the final diagnosis was based on the analysis of completed and returned Conners' Questionnaires (both the parent's and the teacher's versions)⁽⁹⁾. All ADHD children/adolescents were initially treated with IRMP in divided daily doses. This was stopped at the time of switching to SRMP.

SRMP is prescribed initially in the dosage of 18mg once daily and increased if necessary in steps of 18mg according to response, to the maximum of 54mg once daily⁽¹⁰⁾. All children were initially started on SRMP 18mg once daily dosage in this study. This dose was gradually titrated to 36mg and the maximum of 54mg once daily, depending on the needs of each individual child.

Since this study aimed to focus on the parental perceptions, a questionnaire was specifically designed to

obtain the parents' views (Figure 1). This questionnaire was given to the parents at least after three months of starting their child on SRMP as it has been suggested that it may take two to three months of titration until the optimal dose is reached. This questionnaire was given to all consecutive parents between August 2003 and May 2004. The parents were fully informed and given the choice to participate in this study if they wished. None of the parents who were requested to give their views refused to participate in this study. The data collected in this way was analysed subsequently.

The aim of the study was to evaluate the claimed benefits of slow release compared with immediate release methylphenidate in our population of patients under the direct clinical supervision of a consultant psychiatrist.

The objective of this study was to analyse the overall impact of introducing a newly licensed long-acting formulation of methylphenidate on the children with ADHD, as perceived by their parents. It is a common practice in clinical child psychiatry to ask the parents of the child being treated to feed back on the effectiveness and side effects of any psychoactive medication the child is on. In the present study this process of information gathering was further extended by the means of a semi-structured parent reported questionnaire. All parents were adults in the general population. They were not patients themselves and they were happy to give their feedback as required for the purposes of this study.

This was not a randomised double blind control clinical drug trial in an experimental setting putting children at risk of having potentially serious side effects, and these children were not directly involved in this study without the involvement and permission of their parents. This is why it was not considered necessary to seek the approval of the Ethics Committee.

This study could be seen simply as an extension of a day-to-day clinical practice, put in a more structured form to examine, evaluate and expand one's own clinical practice. This study was not done at the request of any drug company and no grant/funding was received from any source to complete it.

RESULTS

Table 3 shows the demographic details of the study. The age range of 11 to 16 gives a mean age of 12.7 years.

Total Number of Children n = 29		
Age	Range = 11 years to 16 years	
Gender	Males	Females
	25 (86%)	4 (14%)

Table 3 Demographic details

Table 4 summarises the parents' responses to the study. None of the total of 29 said that Concerta XL was equally effective as Ritalin.

n = 29		
	Concerta XL More effective	Concerta XL Less effective
Number (%) of parents who responded to this question	18 (62%)	11 (38%)

Table 4 Parents' responses to the effectiveness/usefulness of Concerta XL over Ritalin

Table 5 shows the breakdown of the parents' responses by dosage.

	Concerta XL More Effective n = 18	Concerta XL Less Effective n = 11
Dosage of Concerta XL	Number (%) of Parents	Number (%) of Parents
18mg once daily	4 (22%)	2 (18%)
36mg once daily	7 (39%)	5 (45%)
54mg once daily	7 (39%)	4 (36%)

Table 5 Dose related parents' response to the effectiveness of Concerta XL

In addition, the parents were also requested to list their own reasons for saying whether Concerta XL was more or less useful/effective than Ritalin or another immediate release preparation. In response, a number of themes emerged. Table 6(a) summarises the responses of parents who stated that Concerta XL was more useful/effective and Table 6(b) summarises the main responses of parents who did not find Concerta XL useful/effective.

<ul style="list-style-type: none"> ● Can forget about any more pills – used to be on 4 a day ● Likes only having one tablet to take ● Easier to remember to take as he only has one in the morning ● Once a day tablet, no forgotten tablets ● No need to go and ask for it at 11.00am/lunchtime at school. Doesn't have to be picked out ● No bad consequences of forgetting the lunchtime dose at school ● Can go to different places without having to take medication during the day ● Continual improvement all day – more stable ● Concerta lasts longer – smooth action ● Works without highs and lows – when he was on Ritalin, when its effects wore off he had to be given another tablet soon ● More even day, no peaks and troughs – perhaps because it comes down more gently ● Concerta maintains the child to a more manageable level, less edgy, less fidgety ● He is not as angry as he was on Ritalin ● His mood swings are less, a lot happier on Concerta ● Less facial tics, less nail biting ● Appetite has not been affected, does not cause nausea, not noticed any weight loss, improved appetite ● Sleeps better

Table 6(a) Main themes – advantages of Concerta XL

<ul style="list-style-type: none"> ● Child has been less attentive and unable to sit still while taking Concerta XL ● He has more behaviour problems, particularly at school ● He has been more 'hyper', it seems he has not taken any medication ● Was more aggressive and confrontational on Concerta ● Concerta did not last very long. Ritalin had a better and longer effect. Concerta did not last long enough to get him through the school day. Lasted only between 7 and 9 hours, not 12 hours ● His 'habits' have become worse ● He does not sleep

Table 6(b) Main themes – disadvantages of Concerta XL

The parents of these children were also given the opportunity to make any other comment(s) if they wished and Table 7 summarises these comments.

DISCUSSION

This is an examination of the introduction of a slow-release preparation of a well-known drug, licensed for a specific indication in a series of patients under the care of a single consultant. The numbers studied were small and there is no

- The size of 36mg Concerta tablet is much bigger than Ritalin
- It's a funny shape, but not too difficult to take
- Concerta is easier to swallow
- Concerta is more convenient
- Overall, Concerta's effects were not as good as Ritalin
- The effects of Concerta seem to be the same as Ritalin
- Ritalin wore off a lot quicker
- As with other drugs, one has to accept that what suits one person may not be suitable for another
- Concerta has been much more helpful to us as a family because with school and other places that our child goes it means we don't always have to explain about a 'top up dose' throughout the day. We have not experienced any side effects
- At school there are no times when he feels more agitated. These were the times other children would wind him up. Since starting Concerta he has a much smoother day, therefore, children don't have the opportunity to wind him up

Table 7 Main themes – other comments

control population. The patients were recruited from a population of patients who might be expected to respond in a positive way to the introduction of a new preparation with perceived advantages in terms of dose frequency and reduction of side effects, and who in many cases requested the introduction of the new preparation. Our conclusions throw some light on the work that has previously been undertaken.

Of particular note is our apparently high failure rate. This may be dose related, but we were interested that at a dose of 36mg 45% of patients/parents were not reporting benefit.

It was a cross-sectional study of children with ADHD who were switched from IRMP to SRMP. All these cases were thoroughly assessed aiming to reach a more accurate diagnosis and the choice of treatment which was more individually tailored for each child. The gender differences in this sample reflect the overall preponderance of boys over girls who receive the diagnosis of ADHD.

One study in 2003 concluded that in their recent randomised open-label trial, SRMP was associated with superior symptom control when compared to usual clinical care with IRMP in children with ADHD⁽¹¹⁾. This same study also reported that 76% of parents whose children received SRMP were completely satisfied or somewhat satisfied with treatment vs 59% of parents with children who received usual care treatment with IRMP (P = 0.003). Although in this study the overall trend was in support of this finding, it was surprising to find that up to 38% of parents perceived SRMP less effective than IRMP.

This raised the question whether or not the parents' response has any linkage with the dose of SRMP prescribed to their child. Relatively fewer parents could comment upon the effectiveness, or otherwise, of SRMP at the initial dose of 18mg once daily. Comparing the proportion of parents who perceived SRMP more useful with those who perceived it less useful at different doses of 18mg, 36mg and 54mg once daily, the overall pattern appears to be almost the same in both groups. The more striking difference seems to be in relation to the dose of 36mg daily where 39% of parents found it useful, but a higher proportion (45%) found SRMP less useful/effective than IRMP.

The reasons for these findings do not seem to be clear. One suggestion is that if SRMP is going to be useful it will be so regardless of any specified dose provided it is adequately titrated in order to achieve an optimal dose for an individual child. However, there may be a sub-group of children who may not respond to SRMP even when titrated to a 36mg or 54mg once daily dose.

As suggested in 1988⁽¹²⁾, depending on the study, only about 70%-90% of children respond to the treatment with stimulants. So this sub-group of children with ADHD might have been the group that does not respond to methylphenidate in any form. It could be that these children had specific clinical characteristics that made them methylphenidate non-responders. However, it was not the objective of this study to analyse the specific characteristics of this sub-group of children who did not respond to SRMP more favourably.

Instead, a more obvious question was posed as to whether this sub-group of children could be tried on even higher than 54mg once daily dosage bearing in mind that 54mg once daily dosage is the upper limit recommended in the BNF⁽¹⁰⁾. This is asked because the 15mg of standard release formulation of methylphenidate is equivalent to SRMP 18mg once daily; and 30mg is equivalent to 36mg of SRMP once daily; but only 45mg of standard release methylphenidate is equivalent to 54mg of SRMP once daily. According to the BNF, the maximum daily dosage of IRMP is 60mg in divided doses. Therefore, the equivalent SRMP dose should be higher than the maximum recommended dose of 54mg once daily.

The qualitative analysis of parents' responses perceiving SRMP more useful/effective revealed that the vast majority found it more convenient because of its once daily dosage. This was not an unexpected finding because there are clear advantages of taking the medication only once instead of two or three times daily. In addition, parents also reported positively on its longer lasting action and providing symptom control without any peaks and troughs during the day.

Some parents commented on SRMP's better side effect profile, but a more robust evidence for this seems to be lacking. On the contrary, a 2001 study has reported that SRMP has a similar side effect profile to IRMP three times daily⁽¹³⁾.

Qualitative analysis of parents' responses perceiving SRMP less effective revealed that these parents found that the effects of SRMP did not last long enough to get their child through the school day. Some parents commented on the size and shape of 36mg SRMP, but did not say that it was difficult to swallow.

It was surprising to note that although none of the parents ticked the boxes in response to question 3(b) in the questionnaire, one parent reported Concerta's effects seemingly the same as Ritalin under the heading 'any other comments' (question 6).

Since the effects of IRMP last only for a short duration of each dose, the tablets have to be given during the school day. Administration of medication at school is a source of stigmatisation and relatively few schools have the flexibility/efficiency to manage three times daily dosing. On the point of local interest, the use of long-acting preparation of methylphenidate instead may be perceived more convenient by the schools, head teachers, teacher unions and the governors. The prospect of not having potentially dangerous/addictive drugs stored in teachers' cupboards must be useful to many parties.

CONCLUSION

Despite the methodological limitations, this study provides useful information about the parents' (of children with ADHD) perceptions of the usefulness/effectiveness of SRMP over IRMP. When a new form of treatment for a long term

condition is made available, it is only natural for the parents to request a trial of that treatment hoping that it may prove superior to the older form of treatment. However, the advantages/disadvantages of such treatments may only become apparent after trial of the medication for a considerable time period and the nature of individual clinical characteristics of the child.

Although this study found that a higher proportion of parents perceived SRMP more useful, just over a third of the total number who participated in this study perceived it less useful/effective than IRMP. The reason(s) for this finding were unclear.

However, as one possibility it was questioned whether these children could have further benefited with a higher than 54mg once daily dose of SRMP. Future research into this area may prove helpful in deciding whether or not a 72mg once daily dosage could be tried for a sub-group of children with ADHD with more favourable results.

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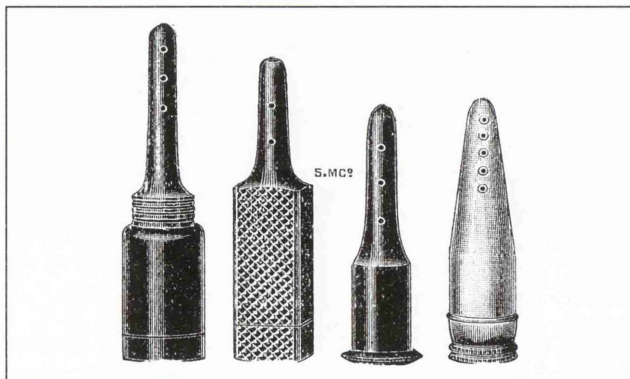
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QUID EST HOC

We didn't have any replies to the last quiz. The object is a rectal ointment introducer. These illustrations show the different designs available in a 1930s catalogue.



Rectal Instruments—*continued*

No.	2149 Sc. 3	£ s. d.
2149—Rectal Ointment Introducer, Canny Ryall's, slide action, boxwood	each	0 4 0
2150—Ditto vulcanite	each	0 7 0

This is of simple construction and very easily used. Remove the cap, and place the ointment in the cylinder; replace the cap, introduce the pipe into the rectum, press gently as illustrated, and the ointment will exude through the perforations.