A taste-testing study in healthy volunteers (children) to investigate children's preference for ibuprofen or placebo suspension

S Reader[1], H Shaw[1], S Hails[2]

[1]*Boots Healthcare International, Nottingham, UK*

[2]*Reading Scientific Services Ltd, Reading, UK*

Corresponding author

Sandie Reader, Boots Healthcare International, Nottingham, UK. Email: sandie.reader@ntlworld.com

Objective: **To assess the influence of the "ibuprofen taste" on children's preference for ibuprofen or placebo suspension.**

Methods: **151 children aged 4–7 years tasted two suspension samples: ibuprofen 5 mg/ml and matched placebo, in a randomised order. After tasting each sample, children indicated how much they liked that sample on a 10 cm visual analogue scale (VAS) depicted with a "sad face" at the beginning of the scale and a "happy face" at the end, and described what they liked or disliked about the sample. After tasting both samples, children were asked whether they could distinguish between the samples and, if so, which they preferred and why.**

Results: **Mean (SD) VAS scores, measured from the "sad face" end, were 6.78 (3.49) and 7.13 (3.42) for ibuprofen and placebo, respectively ($P = 0.38$). 84% of children could distinguish between the samples and, of these children, 58% preferred placebo and 42% preferred ibuprofen ($P = 0.07$). Preference for the placebo was driven by a perception of sweetness compared with the ibuprofen suspension. There were no significant differences between ibuprofen and placebo in any parameter assessed.**

Conclusions: **The formulation effectively masks the taste of raw ibuprofen. The "peppery" taste characteristic does not appear to be a significant factor in driving taste preference.**

Paed Perinat Drug Ther 2006; 7: 54–58

Keywords: ibuprofen – taste – child – placebo – comparative study

Introduction

Ibuprofen (100 mg/5 ml) is widely available over the counter (OTC) throughout Europe for a number of non-serious, self-limiting conditions involving mild to moderate fever and pain[1]. Ibuprofen suspensions are sometimes associated with a "peppery" taste. This potential association sometimes leads to reluctance on the part of healthcare professionals and parents to administer ibuprofen to children, who are therefore denied the benefits of this effective analgesic and antipyretic. However, it is known that the chemical sensory perception of children is different from that of adults, as evidenced by their heightened preferences for sweet and sour tasting foods[2]. A taste-testing study was sponsored by Boots Healthcare International (BHI) in order to identify the extent to which their paediatric ibuprofen suspension, Nurofen® for

Children, is associated with a "peppery" taste and to measure the influence of the taste characteristic on child preference in comparison with placebo.

Methods

Study design

This was a single-centre, single-dose, single-blind, two way cross-over study in which each volunteer tasted two suspensions (ibuprofen and placebo) in a randomised order. The study was conducted in the Reading University Science and Technology Centre by Reading Scientific Services Limited (RSSL) in June 2004. The study was approved by RSSL Independent Ethics Committee before any study-specific procedures took place.

Subjects

Subjects' parents were members of the public who had expressed an interest in taking part in consumer research studies and whose details were held on RSSL's database of local households. Subjects were aged 4–7 years (yr) and had previously taken an analgesic containing ibuprofen. Before any study-specific procedures were performed, the parents signed an informed consent form. Children gave assent by signing a simplified version of the consent documentation if they were considered capable of doing so by the parent and RSSL interviewer.

Dispensing

Ibuprofen (Nurofen® for Children, white, sugar-free, orange-flavoured) and placebo suspensions were provided by BHI, Nottingham. Placebo suspension was formulated as for the active, minus ibuprofen, and was visually indistinguishable from the ibuprofen suspension. Trained dispensers (unblinded but with no other study involvement) dispensed each test sample, using a disposable plastic syringe, onto a pre-coded white plastic spoon according to a predetermined randomisation schedule. Children aged 4–6 years received 7.5 ml and children aged 7 yr received 10 ml of both the ibuprofen and placebo samples in accordance with the recommended OTC dose of Nurofen® for Children.

Taste testing

The child remained with the parent during the taste testing in order to minimise anxiety. Parents were instructed not to prompt their child during the interview. This was reinforced by the interviewer. The child cleansed the palate with water biscuits and bottled water before tasting the first sample. The first plastic spoon was handed to the parent who administered the sample to the child. The child was instructed to take the whole sample into the mouth and to taste and swallow it.

The interviewer recorded whether the child took the sample and, if not, whether it was spat out or refused. The interviewer recorded whether the child had a positive, negative, or no particular reaction and, if a negative reaction, whether this manifested itself as a cough, clearing of the throat, pulling a face or swallowing water. The child was then asked to record how much he/she liked the sample by putting a mark on a 100 mm visual analogue scale (VAS) with a happy face at one end and a sad face at the other. The child was asked to comment on anything liked or disliked about the sample and whether he/she would take the medicine again if unwell. Approximately two minutes after tasting the sample, the child was asked whether he/she could still taste the medicine and, if so, to describe the taste.

The child cleansed the palate with biscuits and bottled water between samples. At least five minutes elapsed between samples. After answering the same questions on the second sample, the child was asked whether the medicines were different and, if so, to describe the difference. The child was then asked which medicine was preferred and the reason for the preference. If the preferred sample, as stated by the child, had not been given the higher VAS score, the discrepancy was not questioned.

Data analysis

The study data were analysed using the market research software package QPS (Market Research Software Ltd, Wallingford, Oxon). Mean scores and distributions of responses were calculated for each question. Comparison of means was undertaken using paired *t*-tests to determine the significance level between the two products. Results were presented overall and split into two main age groups: 4–5 yr and 6–7 yr. In order to determine whether there was an order effect, the mean VAS scores obtained when either product was tried first were compared with the scores when the product was the second sample.

Results

One hundred and fifty one children (78 females) entered the study. The number of children aged 4, 5, 6 and 7 yr was 21, 36, 48 and 46, respectively. None of the children directly refused to take either medicine. However, two children spat it out. One child spat out both samples and one spat out only ibuprofen. Table 1 summarises the spontaneous reactions according to age group.

Table 1 Spontaneous reactions after tasting each medicine

Reaction	Age 4–5 yr				Age 6–7 yr			
	Ibuprofen		Placebo		Ibuprofen		Placebo	
	n	%	*n*	%	*n*	%	*n*	%
Positive	25	45	24	42	34	37	45	48
None	22	40	29	51	40	43	32	34
Negative	8	15	4	7	19	20	16	17
Total	55	100	57	100	93	100	93	100

There were few negative reactions recorded following tasting of either medicine. However, there were slightly more on tasting ibuprofen than on tasting placebo. The older children were more likely to express a negative reaction to both products than the younger children. The majority of negative reactions constituted the child pulling a face.

The placebo received a slightly higher VAS rating (mean ± SD, 7.18 ± 3.40) than the active product (6.90 ± 3.38). However, this difference was not statistically significant (P=0.54). Table 2 gives the mean score according to age group. This suggests that the younger children were driving up the rating for the placebo, although this difference was also not statistically significant. Older children tended to down-rate the taste of both medicines in comparison with their younger counterparts.

The placebo was considered to be "sweet" by slightly more children (25%) than ibuprofen (19%). In addition, the flavour of both products was identified by a similar proportion of children as being "orange" (17% placebo, 19% ibuprofen). However, a number of children did mention a range of disparate flavours, some more closely related (lemon) than others (raspberry, blackberry, cherry, banana, strawberry and apple). The older children were more likely to describe the flavour of the two suspensions as "orange" (22% ibuprofen and placebo) than the younger children (11% ibuprofen, 16% placebo) and were, not surprisingly, more capable of ascribing a flavour to the products. The majority of comments made by the children concerned the flavour of the medicine, while a small number of comments were made on the texture, relating to smoothness and cooling. Six children, however, did make comments on the ibuprofen sample that were pertinent to the research objectives, describing the samples as "spicy", "sour", or "causing a tickle in the throat and tongue". Six children made similar comments about the placebo sample.

Table 2 VAS response according to age

VAS score	Age 4–5 yr		Age 6–7 yr	
	Ibuprofen	Placebo	Ibuprofen	Placebo
Mean ± SD	7.08 ± 3.49	7.76 ± 3.44	6.78 ± 3.33	6.75 ± 3.34
P value	0.30		0.95	

The majority of children did not dislike either product (58% ibuprofen, 66% placebo). A small number of children, however, made negative comments (Table 3).

Over 70% of all children reported still being able to taste the medicine after approximately two minutes (Table 4). Slightly more of the younger children reported an aftertaste following consumption of the placebo than ibuprofen, while slightly more of the older children reported that ibuprofen delivered an aftertaste compared with placebo.

The placebo aftertaste was described as "sweet" by twice as many children compared with that of ibuprofen. Spontaneously mentioned negative comments on the aftertaste are summarised in Table 3.

Table 3 Negative comments and aftertaste

Comment	Number of children			
	What do you dislike? about this medicine		What did it taste like? (referring to the aftertaste)	
	Ibuprofen (*n* = 148)	Placebo (*n* = 149)	Ibuprofen (*n* = 110)	Placebo (*n* = 107)
Too sour	7	4	3	0
Soreness in back of throat/burning in throat	4	0	1	0
Left tickle in back of throat/throat irritating	3	1	6	4
Dislike aftertaste	3	0	-	-
Too spicy	1	1	2	1
Has a tang	1	1	-	-
Too bitter	1	1	1	0
Horrible	0	0	4	2
Not strong / mild / less flavour	0	0	2	6
Powdery	0	0	1	0
Needed a drink after	0	0	0	1

Table 4 Response to question "Can you taste the medicine now?"

	Age 4–5 yr				Age 6–7 yr			
	Ibuprofen		Placebo		Ibuprofen		Placebo	
	n	%	*n*	%	*n*	%	*n*	%
Yes	37	66	44	77	73	78	63	68
No	19	34	13	23	20	22	30	32
Total	56	100	57	100	93	100	93	100

The older children again exhibited a wider range of vocabulary. More of the older than the younger children commented on the sweetness of the placebo compared with ibuprofen.

When asked whether they thought the two medicines were different from each other, 84% of children could differentiate the two medicines from each other (75% of 4–5 yr olds and 89% of 6–7 yr olds). More of the older children than younger children thought there was a difference. Of those who did detect a difference, just over half thought they were "only a little bit different from one another". When asked to describe how the medicines were different, the reason given by the greatest number of children was that one was sweeter than the other (21%). Others (17%) stated simply that the two medicines were different, while others (10%) stated that one was "orange flavour". The majority of comments were made on the specific flavour that the medicines were perceived to be (orange, banana, apple etc). It was not possible to attribute the comments to either ibuprofen or placebo since the child did not identify the product to which they were referring (Table 5).

When asked whether they liked one medicine more than the other, 84% of children (77% of 4–5 yr olds and 88% of 6–7 yr olds) said that they did. Older children were more likely to have a preference than younger children. When asked which medicine they preferred, 58% preferred placebo and 42% preferred ibuprofen. This difference was not statistically significant ($P = 0.07$) (Table 6).

Table 5 Comments pertinent to research objectives made in response to the question "Can you tell me how they were different from each other?"

Comment	Number
One was sour	7
One was too strong	6
One was nasty	4
One was burning	3
One not so strong	2
One made throat sore	2
One was spicy	2
Less medicine taste	1
One had more flavour	1
Flavour didn't linger	1
One was less sour	1
One was bitter	1
One was tangy	1
One was less tangy	1

The preference for placebo was consistent among the older and younger children. When asked why they preferred the chosen medicine, the comment made by the largest number of children to explain their preference was that one of the medicines was "yummy" or "nice tasting". More children gave "sweetness/tasted like sugar" as a reason for preferring placebo (25%) than as a reason for preferring ibuprofen. In addition, there was a suggestion that preference for the placebo was also driven by a delivery of a superior orange flavour, with nine children giving "one was orange flavour/like orange" as a reason for preferring the placebo compared with none for the ibuprofen.

In order to investigate the robustness of the preference assigned by the children, the VAS scores in response to the question "how much do you like this medicine?" were compared with the results of the question asking which medicine was preferred. For 71% of children, the medicine that scored the higher VAS score was also the one preferred. Of those children who said they did not prefer one medicine to the other, 60% had also rated them the same on the VAS. Of those children who did express a preference, only 5% rated them as being the same on the VAS. Of those children whose preference was inconsistent with the VAS scores, 48% scored ibuprofen higher than placebo and 52% scored placebo higher than ibuprofen on the VAS, indicating that the inconsistency was unrelated to the medicine preferred.

Over 75% of children stated that they would be prepared for their parents to give them either medicine if they were unwell. The younger children indicated a more positive willingness to receive both medicines than the older children. The majority of parents stated that they would give either medicine to their child if unwell (85% ibuprofen, 91% placebo). Those parents who would not do so said this was because it was clear the child did not like it.

Adverse events

One adverse event was reported. One subject experienced vomiting and fever which started eight and a half hours after tasting the test medications and lasted for two days. The supervising GP determined that a relationship with the study medication was unlikely.

Table 6 Preferences of those children who preferred one medicine to the other

	Age 4–5 yr				Age 6–7 yr			
	Ibuprofen		Placebo		Ibuprofen		Placebo	
	n	%	*n*	%	*n*	%	*n*	%
	17	40	26	60	35	43	47	57
P value	0.22				0.22			

Discussion

There were no significant differences between the ibuprofen and placebo in any of the parameters tested. There was little evidence to suggest that a "peppery" taste could be attributed to the inclusion of ibuprofen in the active sample, or that ibuprofen causes the suspension to be less acceptable to children aged 4–7 yr.

The results demonstrated that the placebo suspension was considered to be sweeter than the active product. That this was the predominant reason given for more children preferring the placebo to ibuprofen is not surprising since it is known that preferences for sweet tastes remain heightened during infancy and childhood[2].

It was evident that the older children (6 and 7 yr) were able to describe their perceptions of the product more effectively than the younger children (4 and 5 yr). Although not always correct in their assertions, the older children were more willing to ascribe a flavour to the products and tended to be more descriptive. Younger children were less likely to discriminate between the two samples and less likely to describe ibuprofen in terms that could be associated with a "peppery" taste.

Although the two medicines were clearly perceived to be different from one another, any "peppery" taste associated with ibuprofen was noticed and mentioned by only a small proportion of the more articulate older children and the comments tended to be "one-off" in nature. Moreover, in terms of acceptability, the older children gave the two suspensions an almost identical score. In addition, it appears that it was the younger children who were driving any difference between the overall ratings of the two suspensions.

The high level of consistency between two methods of expressing preference (VAS and the response to being asked which medicine was preferred) suggests that the children in this study were capable of detecting a difference and expressing a reproducible preference. A study compared the ability of young adults, 5 yr old children and 4 yr old children to discriminate between different concentrations of sucrose in orangeade[3]. Young adults and 5 yr old children were able to discriminate between the solutions and showed a high consistency between discriminatory ability (>76% consistency) and preference (>71% consistency). In contrast, 4 yr olds detected differences in sweetness during the preference tests but failed to distinguish sweetness intensities during the discriminatory ability tests. It was concluded that the dissimilarity between 4 and 5 yr olds was due to a difference in their cognitive skills rather than their sensory perceptual differences. Although a high degree of consistency was seen in the BHI taste testing study, 4 yr old children accounted for only 14% of participants.

In summary, the results indicated that there was a difference, albeit non-significant, between the two suspensions. This difference was greatest in terms of the delivery of superior sweetness and a recognisable orange flavour by the placebo. While these factors suggest that the inclusion of ibuprofen does indeed impact upon perception of the product and, ultimately, on product preference, the anticipated accompanying level of mouth and throat irritation caused by the active ingredient was not manifested. Therefore, the inclusion of ibuprofen within the formulation base does not detract from the product's high degree of acceptability.

References

1. Davies NM. Clinical pharmacokinetics of ibuprofen: the first 30 years. Clin Pharmacokinet 1998;34:101-154.
2. Liem DG, Mennella JA. Heightened sour preferences during childhood. Chem Senses 2003;28:173-180.
3. Liem DG, Mars M, de Graaf C. Consistency of sensory testing with 4 and 5 year old children. Food Quality Preference 2004;15:541-548.

CrossRefs are available in the online published version of this paper:
http://www.librapharm.com
Paper PPDT-0151_4, *Accepted for publication*: 2 March 2006
Published Online: 26 May 2006
doi:10.1185/146300906X105087