# Treatment of Children's Asthma with a Lipid Extract of the New Zealand Green Lipped Mussel *(Perna canaliculus) (Lyprinol)*

A Double Blind, Randomised Controlled Trial in Children with Moderate to Severe Chronic Obstructive Asthma


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## Introduction and Aims of Study

Oily fish and shellfish are rich in the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The potential anti-inflammatory effect of fish oil is that these long chain polyunsaturated fatty acids (PUFAs) competitively inhibit the formation of leukotrienes and prostaglandins from arachidonic acid this may reduce airway inflammation and bronchoconstriction. An oral standardised lipid extract of the New Zealand green lipped mussel (Perna canaliculus) marketed as Lyprinol® contains a characteristic fatty acid and sterol composition with a high concentration of EPA and DHA and is virtually free of fish protein.

Few controlled trials have examined Lyprinol in asthma and to our knowledge no trials have examined the use of Lyprinol in children with moderate asthma.

### Aim:

To investigate the safety of Lyprinol in children with moderate chronic persistent asthma taking regular inhaled corticosteroid (ICS) and to assess any impact on:

1. the ability to wean ICS dose
2. the frequency of asthma exacerbations, requirement for symptom reliever medication, quality of life measures

## Study Design and Methods

- 16 week prospective double blind randomized parallel-group controlled trial.
- Primary outcome measure - inhaled corticosteroid dose reduction
- Secondary outcome measures: asthma exacerbation rate, asthma symptom score, - Juniper quality of life score, use of short acting beta agonist (SABA).
- Children 6-13 years old meeting inclusion and exclusion criteria screened
- Diagnosis of asthma audited by two clinicians independent of study team
- 2 two weekly run in (stabilisation) visits, randomisation visit (visit 3), monthly medication and review (visits 4-7) and follow up visit (visit 8)
- independently audited datasets analyzed by a biostatistician not involved in the conduct of the study.

## Analysis

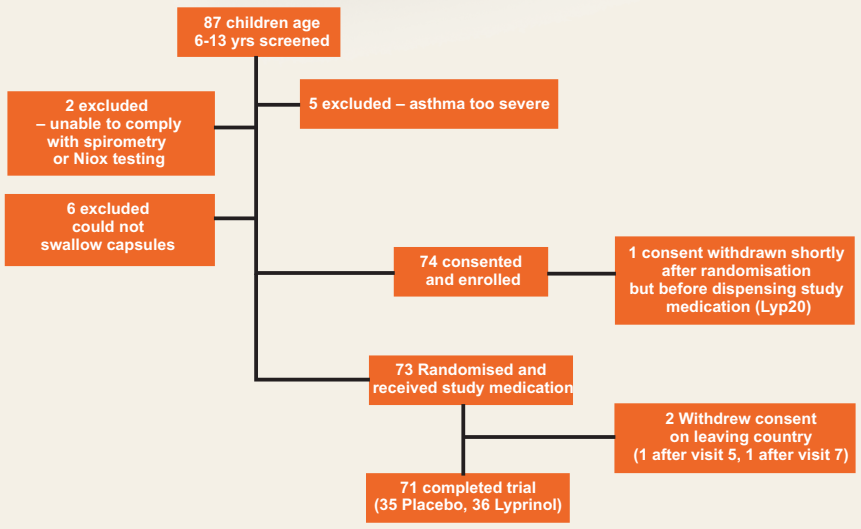
- general linear mixed model for repeated measures was used to investigate whether the changes in the endpoint of interest over the 4 months of treatment differed between the Lyprinol and placebo groups. Unstructured covariance used. The baseline value of endpoint (ICS dose, SABA use, Juniper score etc.) was included as a covariate in the model together with the treatment group, visit and the interaction between visit and treatment group which was effect of interest.

## Study medication

- Lyprinol® capsule contains 50 mg of omega-3 polyunsaturated fatty acids dissolved in 100 mg olive oil.
- Placebo capsule contains 150 mg olive oil. Both Lyprinol and placebo capsules formulated to have identical taste and smell.
- Dose two capsules orally twice daily. Compliance check at each study visit with any returned capsules and recorded dose of all other medication
- Any other asthma medication (other than SABA) excluded subjects from the trial, although antihistamines, or nasal sprays were permitted for co-existing allergic conditions.

## Safety Assessments

Adverse experiences (spontaneously provided or elicited through interviews) results of respiratory function testing, and findings on physical examination, NiOx testing was included in the protocol (children were not weaned from ICS if a NiOx reading had increased by 20 parts per billion in the previous month).




## Results

Figure 1 shows disposition of patients through the trial. Baseline asthma and demographic characteristics were similar between groups (Table 1). ICS dose used was converted to fluticasone equivalent dose in the ratio of 1: 2: 2 fluticasone: beclomethasone: budesonide). The SABAs noted in the study were predominantly salbutamol.

Mean fluticasone dose at baseline was 177 mcg / day for Lyprinol and 173 mcg/ day for placebo. Baseline FEV1 and other spirometric values were comparable.

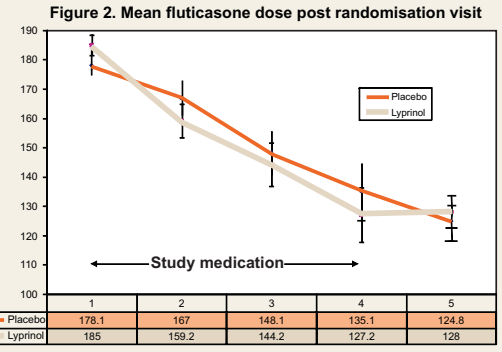
### 1. Inhaled corticosteroid dose reduction over treatment period.

Both groups were able to decrease inhaled steroids over time (mean reduction fluticasone 43 mcg/day for control group and 58 mcg/day for Lyprinol group see Figure 2) This difference was not significant. (p=0.27)

**Table 1 Demographic and Clinical characteristics at baseline**

| | Lyprinol n= 36 | Placebo n= 35 |
|---|---|---|
| Male (%) | 21(58%) | 19(54%) |
| Age at diagnosis Mean (std. dev) | 3.8 yrs (2.4) | 3.6 yrs (2.0) |
| Inhaled corticosteroid dose at study entry (fluticasone equivalent mcg/ day) Mean (std. dev) | 177 (56) | 173 (59) |
| Ethnicity Maori or Pacific Islander | 11(31%) | 7(20%) |

**Figure 2. Mean fluticasone dose post randomisation visit**




### 2. Asthma Symptoms, Quality of Life measures, and exacerbations.

**a.Quality of life score**

There was evidence that the pattern of change was different for the two groups over time (p=0.057) with similar levels of QOL initially with the Lyprinol group reporting fewer problems at visit 6. (Table 2.)

**b. Symptom diary scores**

Most participants had few symptoms as measured on the symptom score. No significant differences were found in the pattern of breathlessness, the pattern of cough, wheeze, chest tightness during the day or the pattern of sleep loss between the Lyprinol and placebo groups.

**c. Asthma exacerbations**

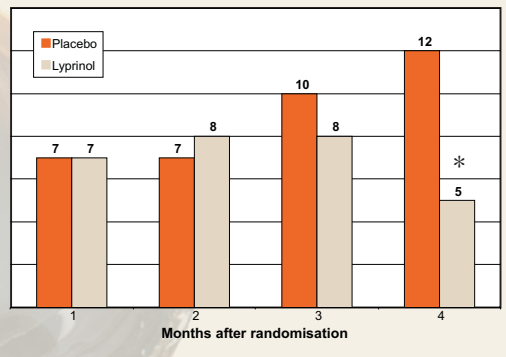
Mild and moderate asthma exacerbations during the study were common. Most of these were mild. 64 mild and moderate exacerbations recorded and 28 children recorded with no exacerbations during the study period. There were 48 mild exacerbations recorded (26 in the placebo group, 22 in the Lyprinol group). There were 16 moderate exacerbations (10 in the placebo group and 6 in the Lyprinol group). There were no severe exacerbations while on study medication. See Figure 3. The numbers were small and the zero cells mean that the logistic regressions were not appropriate.

**Table 2**

| Visit | Placebo | | Lyprinol | |
|---|---|---|---|---|
| | % with none or hardly any problems | 95% confidence intervals | % with none or hardly any problems | 95% confidence intervals |
| 4 | **86.1** | 60.1,96.2 | **76.8** | 50.5,91.5 |
| 5 | **76.1** | 46.3,92.2 | **66.5** | 37.9,86.6 |
| 6 | **75.8** | 45.7,92.1 | **96.8*** | 87.1,99.3 |
| 7 | **90.2** | 67.9,97.6 | **85.2** | 62.4,95.3 |

* p= 0.057

**Figure 3.Number of mild or moderate exacerbations**




Overall there was an annualized rate of moderate exacerbation (moderate exacerbations per patient per year) of 0.86 in the placebo group compared to 0.5 in the Lyprinol group. This rate difference bordered on significance (p=0.067).*

## Safety

- no adverse events led to withdrawal of children from the study.
- 1 severe exacerbation recorded, randomized to placebo group) two weeks before visit 8 (off study medication)
- Considered related to study medication -Generalised itching (1, Lyp), exacerbation of eczema (1, Pl), urticaria (2, both pl.)
- Lyprinol was considered well tolerated.

## Conclusion

In this study Lyprinol appears to be a safe nutritional supplement when taken by children with moderate asthma for 4 months. We cannot say from our data that use of Lyprinol resulted in greater weaning from ICS. There were however trends noted to improved quality of life (Juniper scale measure) and a decreased rate of moderate asthma exacerbations in those children randomised to Lyprinol. We recommend that larger prospective controlled studies be performed to further assess the use of Lyprinol as an adjunct to conventional treatment.


### Acknowledgments

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