



Title	Effectiveness and safety of oral immunotherapy for severe food allergy
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論文内容の要旨

Synopsis of Thesis

氏 名 Name	Yuri Takaoka
論文題名 Title	Effectiveness and safety of oral immunotherapy for severe food allergy (重症食物アレルギーにおける経口免疫療法の有効性と安全性)
1. Effectiveness and Safety of Double-Blind, Placebo-Controlled, Low-Dose Oral Immunotherapy with Low Allergen Egg-Containing Cookies for Severe Hen' s Egg Allergy: A Single-Center Analysis (Abstract) [Introduction] To evaluate the efficacy and safety of OIT with low allergen cookies (LACs) containing a low dose of hen' s egg. [Methods] Thirty-three patients with severe hen' s egg allergy were randomly administered either OIT with LACs ($n = 21$) or placebo ($n = 12$). Two patients in the LACs group withdrew before completing OIT. The primary endpoint was the number of good responders (G-R), patients with negative results in the oral food challenge (OFC) with a final dose of 2 g hardboiled egg whites after 4 months of OIT, in each group. Total OFC Aichi score for anaphylaxis/cumulative protein dose (TS/Pro) as the marker of severity of food allergy was also compared. Adverse events during OIT were evaluated using patients' diaries. [Results] The proportion of G-R in the LACs group was higher than in the placebo group (7/19 [37%] vs. 1/12 [8%], χ^2 test; $p = 0.077$). The TS/Pro after OIT in the LACs group was lower than in the placebo group (median score, 44.2 vs. 104.1, $p = 0.059$; Mann-Whitney U test). The threshold and TS/Pro before and after OIT significantly improved in the LACs group ($p = 0.015$, $p = 0.027$, respectively; Wilcoxon signed-rank test). There were 99 recorded incidences of symptoms of 1,938 intake events in the LACs group during OIT. Of these, 90 were mild; no severe symptoms occurred. [Conclusion] OIT with LACs potentially increases the OFC threshold and decreases allergy severity and is a relatively safe treatment modality. 2. Single-Center Noninferiority Randomized Trial on the Efficacy and Safety of Low- and High-Dose Rush Oral Milk Immunotherapy for Severe Milk Allergy (Abstract) [Introduction] Oral immunotherapy (OIT) has been reported to be effective but associated with a risk of severe symptoms. Thus, an OIT method with decreased risk is required. [Purpose] We aimed to evaluate the efficacy and safety of low- and high-dose OIT regimens in children with severe milk allergy. [Methods] Overall, 33 participants (median age, 9 years; median final dose of the milk oral food challenge [OFC], 2 mL) were included. The participants were randomly assigned to groups that received either a low (20 mL; $n = 19$) or high (100 mL; $n = 14$) maintenance target dose of OIT. The dose was gradually increased to the target dose in the rush escalation phase and was then maintained daily at home. The primary endpoint was the final OFC dose at 6 months of OIT. Adverse events during OIT were evaluated. [Results] The final OFC dose after OIT was significantly higher than that before OIT in both groups (low-dose, $p = 0.000$; high-dose, $p = 0.006$), but there was no significant difference in the final OFC dose between the 2 groups ($p = 0.767$). In the maintenance phase, the high-dose group had significantly more severe symptoms than did the low-dose group (0.5%, 11/2,355 total intake events vs. 0.1%, 4/3,230 total intake events; $p = 0.018$). [Conclusion] An equally increased dose effect was observed for maintenance OIT doses of 20 and 100 mL in children with severe milk allergy. The risk of severe symptoms in the maintenance phase was lower in the low-dose group. A low-dose OIT regimen is recommended for severe milk allergy.	

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨 重症食物アレルギーにおける低用量の経口免疫療法の有効性と安全性について評価した論文である。主論文1では、重症鶏卵アレルギーに加熱卵1g相当を含むボーロを使用して経口免疫療法を行いプラセボと比較した。治療後の固ゆで卵白経口負荷試験の最終負荷量2gが陰性となった割合は、治療群37% (7/19) プラセボ群8% (1/12) と治療群の方が高い傾向がみられた($p=0.077$)。両群ともに自宅摂取で重症の症状はみられなかった。主論文2では、重症牛乳アレルギーの急速経口免疫療法の目標維持量を20mlとし目標維持量100mlとの比較検討を行った。治療後の牛乳経口負荷試験陽性の最終負荷量は両群に有意差はみられず、維持期の重度の症状は100ml群で多かった。以上より低用量の経口免疫療法は閾値上昇効果がみられ安全性も高用量と比較して高く、重症食物アレルギーの治療の新たな選択肢となる可能性がある。さらに治療による免疫学的変化の解明、長期経過の報告に期待したい。論文博士(医学)の学位授与に値すると考える。			