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Research paper

Age-related periodontitis and alveolar bone loss in rice rats

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ABSTRACT

Objective: To characterize in rice rats: (a) periodontitis (PD) progress with feeding of standard laboratory rat chow (STD) during ages 4–80 weeks; and (b) PD progress with feeding of a high sucrose-casein (H-SC) diet during young adulthood.
Methods: One group (N = 12) was euthanized at age 4 weeks (Baseline). Four groups (N = 8-16) consumed a STD diet from baseline and were necropsied at ages 22, 30, 52, and 80 weeks. Three groups (N = 10-16) consumed an H-SC diet from baseline. Two were necropsied at ages 22 and 30 weeks, respectively. The third switched to the STD diet at age 22 weeks and was necropsied at age 30 weeks. All mandibles/maxillae were assessed by histometry for degree of periodontal inflammation (PD Score), alveolar crest height (ACH, mm), and horizontal alveolar bone height (hABH, mm^2).
Results: In STD diet rats aged ≥30 weeks, all endpoints were worse ($P < 0.05$) than at Baseline. In H-SC diet rats aged ≥22 weeks, all endpoints were worse than at Baseline ($P < 0.05$). At age 22 weeks, all endpoints were worse in the H-SC group than in the STD group ($P < 0.05$). By age 30 weeks, the STD and H-SC groups did not differ.
Conclusions: 1) STD diet fed rice rats develop moderate/severe PD by age 30 weeks; 2) an H-SC diet accelerates moderate/severe PD development; and 3) switching to a STD diet does not halt/reverse PD that was accelerated by an H-SC diet. These data further clarify use of the rice rat as a PD model.

1. Introduction

Tissue level characteristics of human periodontitis (PD) that illustrate its severity are well known (Loe, 1983; Page, 1986; Tonetti & Mombelli, 1999). The thoroughness and specificity of epidemiologic evaluation of human PD has increased during the past decade, with a new emphasis on detecting individuals with severe PD (SP), that now afflicts 11% of the world's population (Kassebaum et al., 2014). In fact, the US National Health and Nutrition Examination Survey (NHANES) III 1988–1994, that screened two quadrants and two sites/tooth per patient, had revealed an overall PD prevalence of only 16.1% in people over age 20 (Borrell & Talih, 2012). NHANES 2009–2010's most recent evaluation of US PD prevalence not only focused on people over age 30 and screened four quadrants and six sites/tooth per patient, but also categorized PD as mild, moderate, or severe. It reported their respective US prevalence as 8.7%, 30.0% and 8.5% (Thornton-Evans, Eke, & Wei, 2013). Given the current US population, this translates into approximately 15 million cases of SP, indicating sufficient prevalence to warrant investigation of small animal models that specifically address SP.

Though several well-standardized, highly-respected laboratory rat models for study of both induction processes and early and intermediate phase human PD now exist (Oz & Puleo, 2011; Graves, Kang, Andriankaja, & Wada, 2012; Struillou, Boutigny, Soueidan, & Layrolle, 2010), a recent review summarizes the current status of the field as follows: "A simple and reproducible model that truly mimics human pathogenesis of periodontal disease has yet to be discovered" (Oz & Puleo, 2011). This statement implies that additional preclinical models, that ultimately comprise a group that together faithfully mimics all severities of human PD at the tissue level, could enable experiments that test phase-specific

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therapeutic approaches that are as yet, neither ethical nor proven safe in humans.

Existing laboratory rat models for mild and moderate human PD (Oz & Puleo, 2011; Graves et al., 2012; Struillou et al., 2010) include ligature-induced localized PD (Cesar Neto, de Souza, Barbieri, & Sallum, 2004; Lohinai, Benedek, & Feher, 1998), LPS-injection-induced localized PD (Dumitrescu, Abd-El-Aleem, Morales-Aza, & Donaldson, 2004; Nakamura, Ukai, & Yoshimura, 2010), and bacterial-inoculation-induced PD (Li et al., 2010; Lohinai et al., 1998; Okada, Hamada, & Kim, 2010). Each, with a known initiation date and requirement for ongoing maintenance or injection/inoculation, causes development of either localized or generalized tissue level PD similar to moderate PD in humans and permits studies of both the induction phase itself, and of preventive or remedial treatments of 2–8 weeks duration. The rice rat (*Oryzomys palustris*), is now known to be susceptible to induction of progressive SP by feeding of a powdered diet high in sucrose and casein (H-SC) with no requirement for mechanical manipulation to initiate/maintain the condition (Gupta & Shaw, 1956; Ryder, 1980; Aguirre, Akhter, & Kimmel, 2012a). As in human PD itself and the other small animal PD models, marginal gingivitis is the initial pathologic finding (Leonard, 1979), followed by widespread plaque accumulation and gingival ulceration. Unlike experimental PD models that focus on mild and moderate PD, substantial soft tissue destruction and alveolar bone loss with loss of functional tooth support routinely occur in rice rats following the moderate PD phase (Gupta & Shaw, 1956; Gotcher and Jee, 1981). However, unlike SP in humans that classically progresses over many years, rice rat SP develops within 12–18 weeks of starting the H-SC diet (Leonard, 1979).

We recently confirmed that rice rats consuming a pelleted H-SC diet develop PD, including worsening of both alveolar crest height (ACH) and horizontal (h) alveolar bone height (ABH) (Aguirre et al., 2012a). Though this study (Aguirre et al., 2012a) also disclosed a trend for rice rats consuming a pelleted standard (STD) diet to develop tissue level PD, there are currently no long-term studies of PD in STD diet-fed rice rats because of the perceived requirement to feed a H-SC diet to induce PD in rice rats. The STD diet-fed rice rat may have potential as a pre-clinical model that, without dietary intervention, not only complements existing rat models of mild and moderate PD, but also evolves continuously into SP in a sufficiently-compressed timeframe to enable practical studies that address human SP.

We report here an experiment that investigates three new topics: a) ACH and hABH from STD diet-fed rice rats that includes the first evaluation of their periodontal condition at ages 4 weeks, 52 weeks, and 80 weeks (Gupta & Shaw, 1956; Aguirre et al., 2012a; Gotcher & Jee, 1981); b) systemic metabolic condition of rice rats that consumed a H-SC diet for 26 weeks; and c) a method to reverse H-SC-diet-induced PD. We hypothesize that rice rats fed a: a) STD diet from weaning develop durable SP by age 30 weeks; b) H-SC diet from weaning develop SP more rapidly than STD diet rats; c) H-SC diet from weaning for 26 weeks have abnormal serum glucose, insulin, and cholesterol; and d) H-SC diet long enough from weaning to develop moderate PD and then switched to a STD diet, experience stabilization or healing of PD.

2. Materials and methods

2.1. Animals, diets and experimental groups

Ninety-two male rice rats were physically examined and weighed immediately after weaning (age 4 weeks). Clinically normal, healthy rats (body weight (BW) ≥30 g and body condition

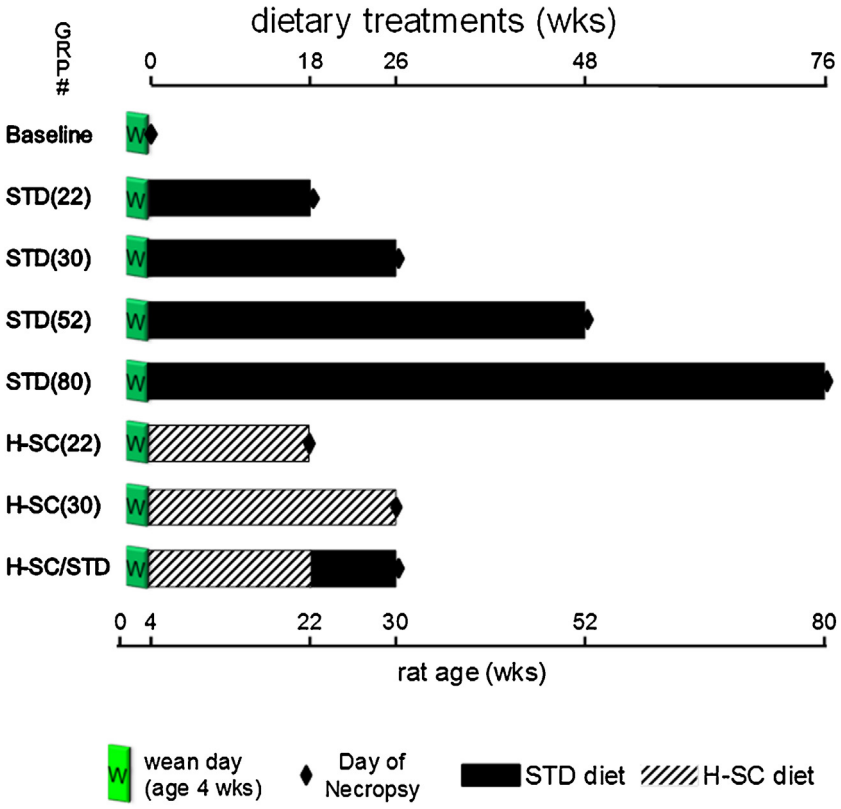

Fig. 1. Experimental Design. One group was necropsied at age four weeks (Baseline). Four groups (STD [22], STD [30], STD [52], and STD [80]), were fed standard laboratory chow, starting at age four weeks and necropsied at ages 22, 30, 52, and 80 weeks. Three groups were fed the H-SC diet starting at age four weeks. Two of those groups (H-SC [22] and H-SC [30]) were necropsied after 18 or 26 weeks. The third group (H-SC/STD) switched from H-SC to STD diet at age 22wks and was necropsied at age 30 weeks.