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Full Length Research Paper

Comparison of the tissue biocompatibility of Resilon and gutta-percha cones

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The aim of this study was to evaluate the tissue biocompatibility of Resilon compared to gutta-percha cones. Three subcutaneous pockets were made in the back of 36 rats weighing between 200 to 250g. Subcutaneous pockets were left unfilled (control, 1 pocket) or filled with Resilon (1 pocket) or gutta-percha (1 pocket). At 3, 10, 30 and 90 days after implantation, 9 rats were killed and the materials were removed with their surrounding tissues. Histological samples were prepared, stained with hematoxylin-eosin (H&E), and observed under light microscopy, and intensity of tissue inflammatory response was assessed. Chi-square and Fisher's exact tests were used for statistical analysis, with significance defined at the *P*<0.05 level. No significant differences were seen between the three groups at 3 or 10 days. There were significant differences in tissue reaction between the experimental groups and control group at 30 and 90 days. However, tissue reactions for Resilon and gutta-percha were similar at 30 and 90 days. Within the limits of this study, Resilon had similar tissue compatibility to gutta-percha on rat connective tissue.

Key words: Gutta-percha, Resilon, subcutaneous implantation, tissue-compatibility.

INTRODUCTION

Biocompatibility is an important property of root canal filling materials, because in clinical practice, these materials may accidently enters into and remains in the periapical tissue for a prolonged period (Hauman and Love, 2003; St.John, 2007; Zmener, 2004). Gutta-percha is a solid filling material that is most commonly used in endodontics. It is highly biocompatible (Hauman and Love, 2003) but exhibits poor sealing properties (Magura et al., 1991; Swanson and Madison, 1987). Resilon, a thermoplastic synthetic root-canal filling material comprising of bifunctional methacrylate resin, bioactive glass, and radio-opaque fillers (Donadio et al., 2008), is a new alternative for gutta-percha. Resilon might improve treatment outcomes by creating a superior seal within the root canal system (Jack and Goodell, 2008). Resilon looks and handles like gutta-percha, and is therefore called resin-percha (Pawin'ska et al., 2006). It is available in standardized points, various tapers, and pellets for use with the Obtura II delivery system (Donadio et al., 2008).

Many recent studies have evaluated the biological properties of Resilon. These studies have revealed controversial results, with *in vitro* studies reporting toxic (Brackett et al., 2008; Economides et al., 2008) and non-toxic (Susini et al., 2006; Key et al., 2006; Merdad et al., 2007) properties. Only a few studies have examined the tissue compatibility of Resilon (Onay et al., 2007; Bodrumlu et al., 2008; Garcia et al., 2010). Therefore, the aim of this study was to evaluate the tissue compatibility of Resilon cones compared to gutta-percha.

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MATERIALS AND METHODS

All ethical and humane criteria contained in the Helsinki declaration

Table 1. Distribution of inflammation intensity.

Day	Resilon					Gutta-percha					Control					*P*
	N	Mi	Mo	S		N	Mi	Mo	S		N	Mi	Mo	S		
3	-	-	-	9		-	-	-	9		-	-	-	9		-
10	-	-	3	6		-	-	2	7		-	3	6	-		0.226
30	-	4	5	-		-	3	6	-		9	-	-	-		0.000
90	4	5	-	-		4	5	-	-		9	-	-	-		0.024

P, P-value compared to control using chi-square test; N, no reaction; Mi, mild reaction; Mo, moderate reaction; S, severe reaction

and all recommendations of the Institutional Animal Care and Use Committee (IACUC) for the care and use of laboratory animals were observed in all stages of this project.

Thirty-six (36) male Wistar albino rats (200 to 250 g) were anesthetized intraperitoneally with ketamine HCL 60 mg/kg and xylazine 6 mg/kg (Alfasan, Netherlands). The dorsal skin of animals was shaved and disinfected with a 10% iodine solution (Behsadin, Iran). Longitudinal sections of ~10 mm were cut with a surgical blade (Meheco, China) at three sides of the dorsum (two at the scapula and one at the pelvic). Three separate pockets were created by blunt dissection to implant the test materials in the subcutaneous tissue at a depth of ~15 mm. To prevent interactions between materials, the pockets were placed at least 2 cm away from each other.

Ultraviolet (UV) sterilized segments of 10 mm cut from the tip of #40, 0.02 taper Resilon (Pentron, USA) and gutta-percha (Gapadent, China) cones were placed directly into two separate pockets. The skin was closed with 3/0 silk sutures. In each animal, one pocket (control) was treated similar to the pockets for the experimental materials, except that no test material was implanted in it. The implant location of the materials and control group were rotated in each animal.

Evaluations were made at 3, 10, 30 and 90 days after surgical implantation. At each time-point, 9 animals were sacrificed by anesthetic overdose. The dorsal skin was shaved, and the test materials and surrounding tissues were removed and fixed in buffered 10% formalin (Merck, Germany) for 48 h. For cross-sectioning, the blocks were placed parallel to the long axis of the test materials. The sections were cut to a thickness of 4 µm and stained with hematoxylin and eosin (H&E; Merck, Germany).

Histological sections were analyzed at different magnifications under a light microscope (Zeiss, Germany) by a blinded observer. Tissue reaction parameters, such as the inflammation intensity, type of inflammatory cells, presence of foreign body giant cells, necrosis and fibrous capsule formation, were evaluated and recorded. The inflammation intensity was estimated by summing the means of the different types of inflammatory cells in 10 separate fields at 400× magnification, according to the following criteria: no inflammation (no observed inflammatory cells), mild ($n<25$ cells), moderate ($25 \leq n < 125$ cells) and severe ($n \geq 125$ cells).

The inflammation intensity was statistically analyzed using the Chi-square and Fisher's exact tests, with statistical significance defined at the $P < 0.05$ level.

RESULTS

Microscopic evaluation in the study phases did not reveal any inflammation and/or infection on the surgical sites prepared to receive the implants (Table 1).

Initial stages (3 to 10 days)

Severe inflammation was seen in all groups at 3 days, characterized by an intense infiltration of acute inflammatory cells, particularly neutrophils. Some infiltrated plasmocytes and lymphocytes were also seen. No foreign-body multinucleated giant cells or fibrous capsules were observed, although small necrotic areas were sometimes seen (Figure 1A and B). By 10 days, the tissue was infiltrated with macrophages, plasmocytes, lymphocytes and a few neutrophils. Foreign body giant cells were sometimes present, but no necrotic areas were observed. The tissues exhibited an initial organization state, with few fibroblasts and diffuse collagenous fibers; a clear fibrous capsule had not yet completely formed (Figure 1C and D). The inflammatory reactions were mild to moderate (control) or moderate to severe (experimental groups) at 10 days. No significant differences were seen between the three groups at 3 or 10 days (Table 1).

Late stages (30 and 90 days)

No inflammation was seen at 30 or 90 days in the control group. This was significantly different from the experimental groups, which exhibited mild to moderate inflammation at 30 days and no mild to inflammation at 90 days ($P > 0.05$ between experimental groups for 30 and 90 days; Table 1). At 30 days, the experimental group tissues were more organized than previously, and were characterized by chronic inflammatory cells, the absence of necrotic areas and giant cells, and a well-formed fibrous capsule (Figure 1E and F). At 90 days, minimal plasmocytes and lymphocytes were seen in some specimens, the fibrous capsule appeared more mature, and no giant cells or necrotic areas were observed (Figure 1G and H).

DISCUSSION

Subcutaneous implantation of materials in the body of

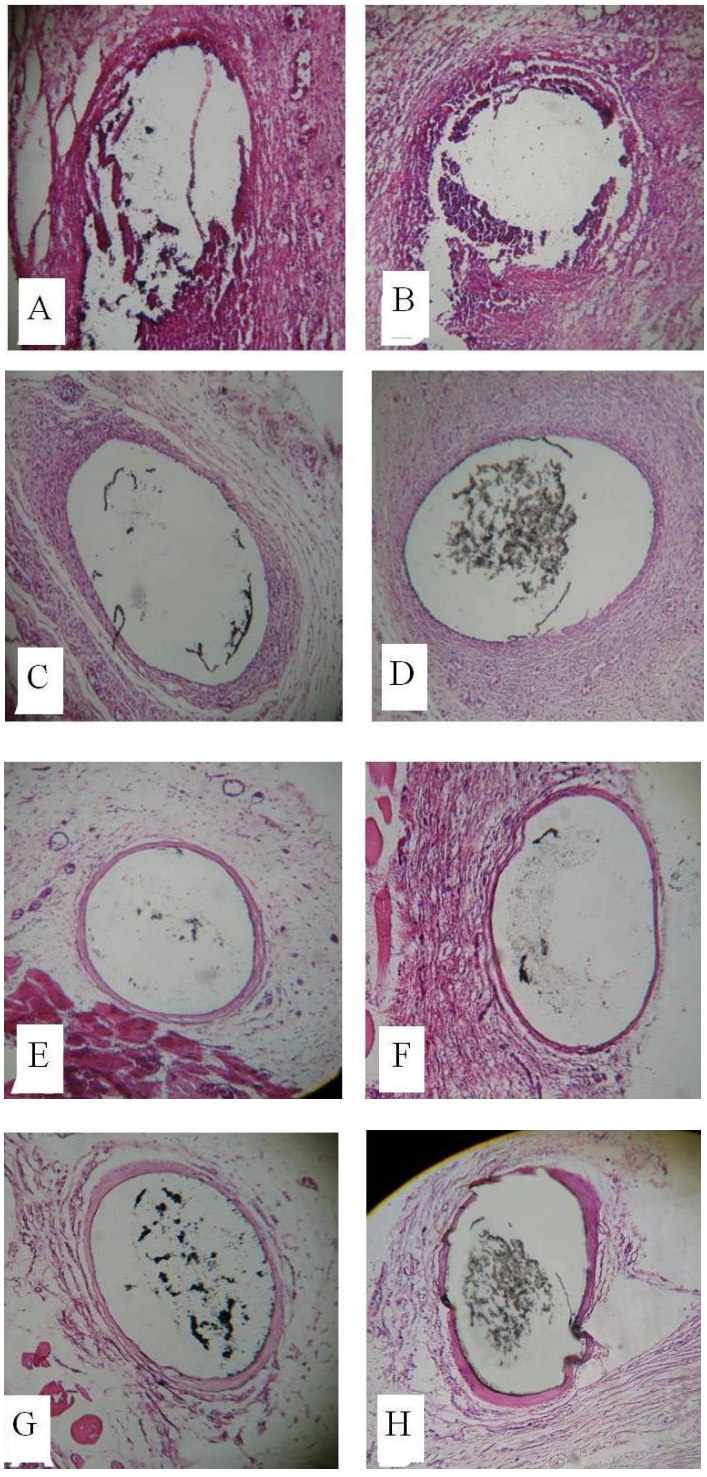

Figure 1. Stages of microscopic evaluation. After 3 days, severe inflammation and necrotic tissue were noted in connective tissue adjacent to (A) implanted Resilon (B) gutta-percha (H&E,×100). After 10 days, severe to moderate inflammation and numerous giant cells were in direct contact with the (C) implanted Resilon (D) gutta-percha (H&E, ×100). After 30 days, moderate to mild inflammation and a complete fibrous capsule were observed around the (E) implanted Resilon (F) gutta-percha (H&E, ×100). After 90 days, mild to no inflammation and a thick fibrous capsule were observed around the (G) implanted Resilon (H) gutta-percha (H&E, ×100).

animals is a common method for evaluating the biocompatibility of dental materials (Hauman and Love, 2003; St. John, 2007). This method allows complex systemic interactions, provides a more comprehensive result than *in vitro* tests and generates results that are more relevant to the clinical situation. When assessing the biocompatibility of a material, the delayed harmful effects are considered more important than initial effects (Bodrumlu et al., 2008; Zafalon et al., 2007). In the present study, we observed that tissue reactions to Resilon and gutta-percha were similar at all time-points tested (3, 10, 30 and 90 days post-implantation).

Various factors determine the biocompatibility of a material, particularly the amount and nature of its soluble components (Onay et al., 2007). Resilon is mainly composed of poly-caprolactone (Donadio et al., 2008), and has been safely used for tissue engineering and biomedical applications (Serrano et al., 2004; Ng et al., 2001). However, Resilon also contains barium sulfate, bismuth oxychloride, calcium phosphate and coloring pigments, which could be released and thereby adversely affect the biocompatibility (Brackett et al., 2008). Because gutta-percha has acceptable biocompatibility and is the material of choice for root canal filling (Hauman and Love, 2003), this material was selected as the standard for comparison with Resilon.

We observed similar tissue reactions caused by Resilon and gutta-percha cones at all phases, with no significant difference between these materials. Nearly all reported bioimplanted materials initially induce a severe tissue response, which eventually subsides over time (Onay et al., 2007; Bodrumlu et al., 2008; de Campos-Pinto et al., 2008). In this study, all of the implanted materials promoted a severe inflammatory reaction by 3 days, possibly due to surgical trauma rather than to material toxicity. This inflammation decreased over time, and the materials became surrounded by a fibrous capsule. This result indicates that both Resilon and gutta-percha were well-tolerated by the tissues. The inflammatory reaction at 10, 30 and 90 days could be attributed to the release of barium (Resilon) or zinc (Resilon or gutta-percha), which decreased with time.

The results of this study are consistent with those of previous studies (Onay et al., 2007; Bodrumlu et al., 2008) showing that inflammatory responses caused by Resilon in rat connective tissue were similar to gutta-percha and acceptable at 60 days. Another study demonstrated that dentin tubes filled with the Resilon-epiphany system created a satisfactory tissue reaction in rat connective tissue (Garcia et al., 2010). Our results also confirmed the previous finding that the cytotoxicities of Resilon and gutta-percha are similar at acceptable levels (Susini et al., 2006, Key et al., 2006; Merdad et al., 2007). Contradictory *in vitro* findings (Donadio et al., 2008; Brackett et al., 2008; Economides et al., 2008; Zhu et al., 2006) might be due to differences in measurement methods, studied cell types or sample preparation techniques.

Conclusion

Within the limitations of this study, the tissue compatibility of Resilon was acceptable and similar to that of gutta-percha at 90 days after implantation. Since the connective tissues of rat and human are not identical, further studies are needed.

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