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CLINICAL RESEARCH

Cardiovascular Effects and Efficacy of a Hemostatic Agent in Periradicular Surgery

Christina Hong Vy, DMD, J. Craig Baumgartner, DDS, PhD, J. Gordon Marshall, DMD

The purpose of this study was to evaluate the hemostatic efficacy and systemic cardiovascular effects of CollaCote™ collagen sponges saturated with 2.25% racemic epinephrine during endodontic surgery. A total of 48 patients participated in the study. Patients received CollaCote-saline or CollaCote-epinephrine placed in the bony crypt, after which hemostatic efficacy was evaluated. Blood pressure and pulse rate was recorded before and after administration of the local anesthetic, after the application of the test solutions, and before the patient's dismissal. Results showed no significant difference in blood pressure or pulse rate between the experimental and control groups. In the CollaCote-saline group, five of six cases failed to achieve hemorrhage control. In the CollaCote-epinephrine group, 1 of 42 cases had no hemorrhage control. Two patients had slight but apparent intermittent bleeding. Complete hemostasis was achieved in 39 of 42 cases. In conclusion, the results suggest that CollaCote collagen sponges saturated with 2.25% racemic epinephrine provide excellent hemostasis with no evident changes in blood pressure or pulse rate.

One concern during endodontic surgery is the need to achieve hemostasis in the surgical crypt. Adequate hemostasis is essential to achieve a surgically dry field, which improves vision, minimizes surgical time, and allows the proper environment for placement of a moisture-sensitive, root-end filling material (1–4).

Many topical hemostatic agents have been advocated as being effective in obtaining hemostasis. These include bone wax, ferric sulfate, thrombin, resorbable agents such as Gelfoam and Surgicel, and vasoconstrictors (1, 4). Bone wax has been advocated for hemostasis and debris control within the bony crypt. It has been shown to produce a foreign-body reaction and retard bone healing and is no longer recommended for periradicular surgery (2, 4). Ferric sulfate, with its ability to coagulate blood, has been found to be an effective hemostatic agent; however, prolonged application and failure to remove ferric sulfate from the surgical site can result in severe inflammation and impaired healing (5). Thrombin is a dry powder that intrinsically produces a fibrin clot. The main disadvantage of thrombin is that it is difficult to handle and deliver to the bleeding site (6). Gelfoam and Surgicel are effective in forming clots but become soft on contact with blood (1). Vasoconstrictor agents, such as epinephrine, have been used to control hemorrhage during surgery. Grossman (7) suggested the use of a cotton-roll saturated with 1:100 epinephrine or Racellets (Pascal Co., Bellevue, WA). Racellets are cotton pellets containing 1.5% racemic epinephrine hydrochloride that have been recommended to control bleeding. Epinephrine causes vasoconstriction by activating alpha-adrenergic receptors. The application of racemic epinephrine-impregnated cord to an exposed vascular bed may increase pulse rate and blood pressure (8). In addition, the use of vasoconstrictors for local hemorrhage control during periradicular surgery may produce a systemic cardiovascular response (9).

Vickers et al. (10) compared the hemostatic efficacy and cardiovascular effects of ferric sulfate and #3 Racellets. The results from that study showed very good hemostasis with both agents with no evident cardiovascular changes. One concern with the use of epinephrine-impregnated cotton pellets is the potential to leave cotton fibers in the surgical site, which may produce inflammation and retard healing (11).

CollaCote™ (Integra LifeSciences Corporation, Plainsboro, NJ) is a collagen wound dressing that is biocompatible and resorbable. Collagen dressings are highly absorbent, can retain their structural integrity even when wet, and have no fibers.

The purpose of this study was to evaluate the hemostatic efficacy of CollaCote saturated with 2.25% racemic epinephrine during periradicular surgery and determine whether there was any significant change in blood pressure or pulse rate.

MATERIALS AND METHODS

Patients in this study were treated using a protocol approved by the institutional review board at Oregon Health & Science University. Patients presenting to the School of Dentistry requiring endodontic surgery that included root-end filling were considered

for the study. Written informed consent was obtained from all participating patients. Second-year, postgraduate, endodontic students performed all surgical procedures.

The patients were assigned to one of two groups. In group 1 (control), patients received CollaCote saturated with saline. In group 2 (experimental), patients received CollaCote saturated with 10 drops of 2.25% racepinephrine inhalation solution for bronchodilators. Each drop of the 2.25% racemic epinephrine solution from a tuberculin syringe (27-gauge needle) contains approximately 0.21 to 0.25 mg of racemic epinephrine, of which one-half is the pharmacologically active L-form. Each package contains a single, 0.5-ml, sterile vial (Nephron Pharmaceutical Corp., Orlando, FL). The patients and endodontic postgraduate students performing the surgery were blinded as to what was dispensed. A digital blood pressure monitor (Omron, Vernon Hills, IL) was placed on the left wrist of each patient according to manufacturer's instructions. Preoperative blood pressure and pulse rate was recorded. Once profound local anesthesia was achieved after using conventional nerve block or infiltration, blood pressure and pulse rate were recorded again. Access was gained to the periradicular area, and the operator proceeded with the indicated endodontic surgery. After root-end resection, the operator determined the need for hemostasis. If hemostasis was needed, a 1-cm × 2-cm CollaCote dressing saturated with epinephrine or saline was placed into the bony crypt. Additional dry CollaCote or Telfa pads were placed over the first sponge. Pressure was applied on these sponges, and all but the bottom sponge was removed after 3 to 4 min. The patient's blood pressure and pulse rate was recorded again (surgical reading). If hemostasis was inadequate, a second application of the saturated CollaCote was placed in each bony crypt. If hemostasis were inadequate after a second application, racemic-epinephrine cotton pellets (Racellet #3, Pascal Company, Inc., Bellevue, WA) were placed. After the surgical procedure, the last collagen sponge or cotton pellet was removed and the bony crypt examined with an operating microscope for any loose debris. The surgical site was gently irrigated with sterile saline to remove any loose debris before suturing.

The adequacy of hemostasis was determined by the surgical operator using the following scores:

0 = No hemorrhage control—continuous bleeding that compromised vision at the surgical site.
1 = Slight but apparent intermittent bleeding that persisted after the application of the sponges.
2 = Complete hemorrhage control, providing a "dry" surgical field.

A final blood pressure and pulse rate was obtained before the patient's dismissal. An analysis of variance ($p < 0.05$) was used to evaluate any differences in blood pressure or pulse rate between the experimental and control groups. Within the individual groups, the Tukey post-hoc analysis was used to compare differences between preoperative and postoperative readings, readings taken after anesthesia, and surgical readings.

RESULTS

A total of 48 patients participated in the study, of which 6 patients received CollaCote-saline as controls and the remaining 42 patients received CollaCote-epinephrine. An analysis of variance of the data showed no significant difference in blood pressure or pulse rate at any time period between the experimental (epinephrine) and control (saline) groups. The p values were 0.753, 0.337, and 0.062 for systolic blood pressure, diastolic blood pressure, and pulse rate, respectively. The mean and standard error of the mean (SEM) for blood pressure and pulse rate for both groups studied is presented in Table 1.

TABLE 1. Mean and standard error for blood pressure and pulse for both groups studied

Group	N*	Mean	Standard Error
Systolic blood pressure			
Saline	24	131	5.3
Epinephrine	168	130	1.3
Diastolic blood pressure			
Saline	24	80	3
Epinephrine	168	77	0.8
Pulse			
Saline	24	76	2.2
Epinephrine	168	72	0.9

* N = Mean for 48 patients (6 saline and 42 epinephrine) each with four blood pressure and pulse readings.
Unit for mean blood pressure = mm Hg.
Unit for mean pulse rate = beats per minute.

In group 1 (CollaCote-saline), hemorrhage control was not achieved in five of six cases. In five patients, continuous bleeding that compromised vision at the surgical site occurred. In these cases, Racellet #3 pellets were used to obtain hemostasis. In one case, CollaCote-saline provided adequate hemostasis. In group 2 (CollaCote-epinephrine), complete hemorrhage control was achieved in 39 of 42 cases. Two patients had slight but apparent intermittent bleeding that persisted after the application of the sponges. In these patients, #3 Racellets were not needed because the slight bleeding did not compromise the surgical procedure. The remaining one case had no hemorrhage control even with the application of #3 Racellets.

The range of epinephrine used was 2.1 to 7.5 mg. All the patients in the CollaCote-epinephrine group received 10 drops of racemic epinephrine (approximately 2.1–2.5 mg). Two patients required a second application of the CollaCote-epinephrine to achieve adequate hemostasis. One patient had three bony crypts, so three separate sponges were used in each crypt (a total of 30 drops of racemic epinephrine approximating 7.5 mg). For patients in whom Racellet pellets were used, the results were similar to those given CollaCote-epinephrine.

Figure 1 shows the mean systolic blood pressure at different time periods throughout the surgery for both the saline and epinephrine groups. On average, the systolic blood pressure decreased after the administration of the anesthetic and test solutions compared with the preoperative readings. However, the Tukey's multiple comparison test showed no significant difference among the means at any time periods ($p = 0.378$).

The mean diastolic blood pressure at different time periods is shown in Figure 2. The average postoperative diastolic pressure was approximately 6 mm Hg higher than the pressure during the administration of the anesthetic. This was statistically significant at $p = 0.014$. There was no significant difference between the other time periods.

Figure 3 shows the mean pulse rate at different time periods throughout the surgery. On average, the mean pulse rate was 9 and 8 beats per minute higher after the administration of the anesthetic than it was during the surgical procedure and postoperatively, respectively ($p = 0.002$).

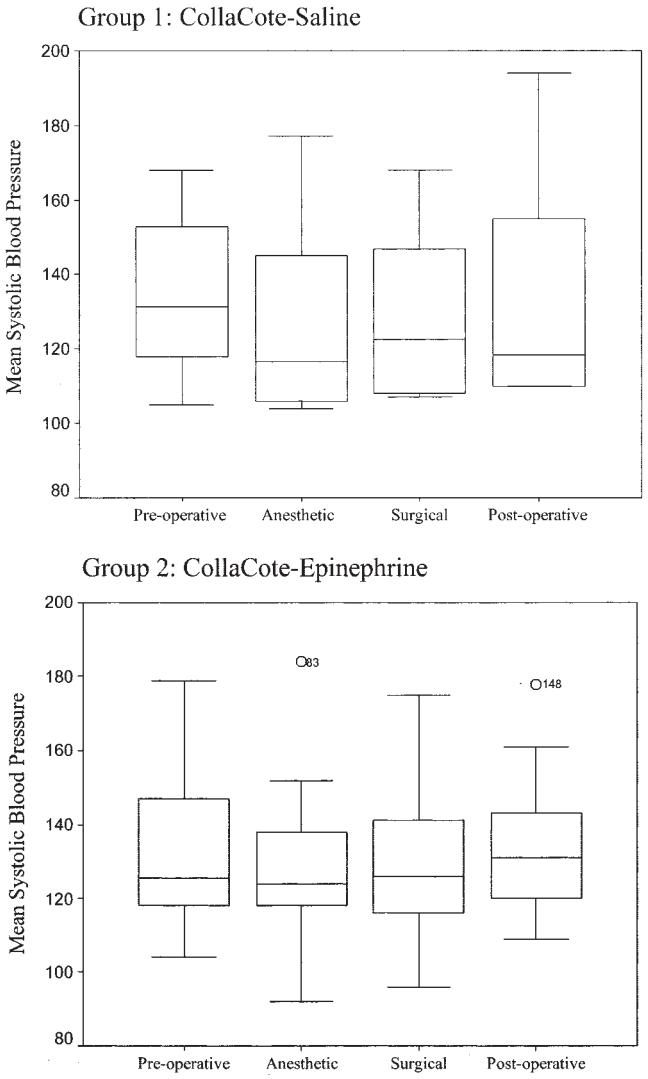

FIG 1. Mean systolic blood pressure of CollaCote-saline and CollaCote-epinephrine.

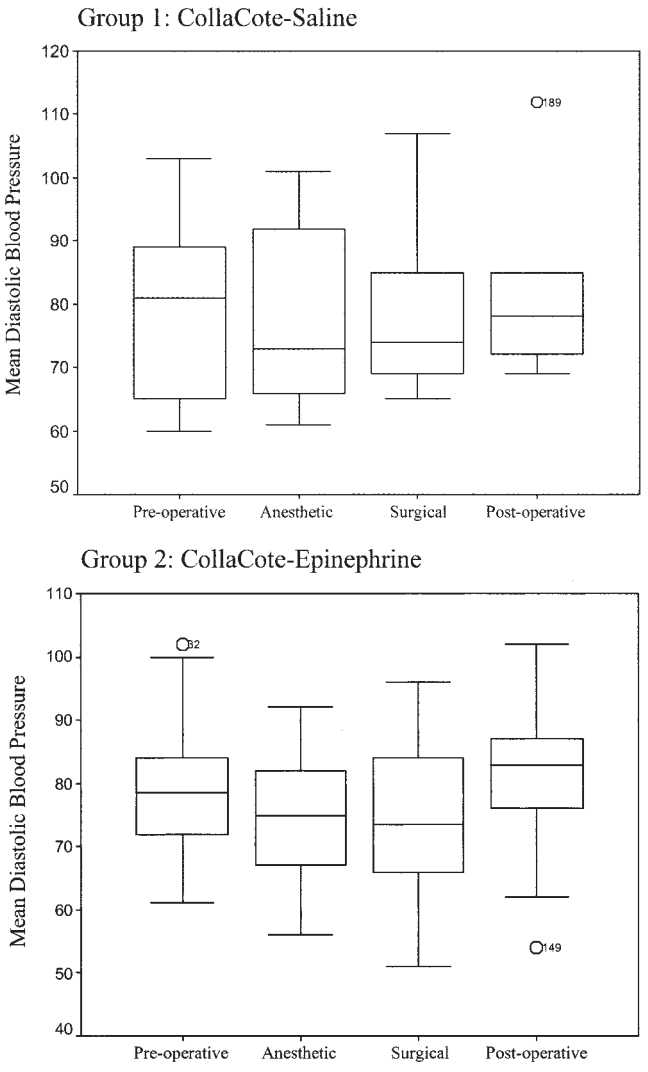

FIG 2. Mean diastolic blood pressure of CollaCote-saline and CollaCote-epinephrine.

DISCUSSION

Hemostasis during endodontic surgical procedures is essential for successful case management. Sympathomimetic-amine vasoconstrictors, such as epinephrine, norepinephrine, and phenylephrine, have been recommended as topical agents for hemorrhage control during periradicular surgery (1, 12). These vasoconstrictors exert their effects by binding to and interacting with adrenergic receptors that are located in various tissues throughout the body (13, 14). Of these agents, epinephrine has been shown to be the most effective. Epinephrine is a powerful agonist of both alpha- and beta-adrenergic receptors. The alpha-adrenergic receptors predominate in tissues, such as oral mucosa, submucosa, bone, and periodontium. When bound to these alpha-adrenergic receptors, epinephrine produces vasoconstriction. Beta-adrenergic receptors, however, predominate in skeletal muscles. When bound to these beta-adrenergic receptors, epinephrine may increase heart rate, cardiac output, and vasodilation (1, 12, 15).

Intraosseous injection allows placement of a local anesthetic solution directly into the cancellous bone. Intraosseous injection of 36 mg of lidocaine with 0.018 mg of epinephrine has been shown to produce a transient (4-min) period of tachycardia with an average increase in heart rate of 28 beats per minute (16). In our study, as many as three bony crypts were prepared in one patient. CollaCote sponges saturated with as much as 7.5 mg (range, 2.1–7.5 mg) of 2.25% racemic epinephrine were placed directly into the cancellous bony crypt(s). The results showed excellent hemostasis with no evidence of cardiovascular changes compared with the control group. One possible explanation is that the topically applied epinephrine causes immediate local vasoconstriction of the capillaries with little absorption into the systemic circulation, and thus little systemic effect. The vasoconstrictive effects of the local anesthetic, in addition to the pressure on the tissues, may act conjointly with these agents to constrict capillaries and prevent further uptake of epinephrine (1).

Cotton or gauze impregnated or injected with solutions of 1:100 to 1:10,000 epinephrine has been advocated for years to achieve local hemostasis (1, 11, 17–18). Grossman first suggested the use of cotton pellets saturated with 1:100 epinephrine or Racellets containing 1.5% racemic epinephrine hydrochloride to control bleeding in a surgical bony crypt (7). Ingle (18) recommended packing the bony cavity with 2% racemic epinephrine (Surgistat)

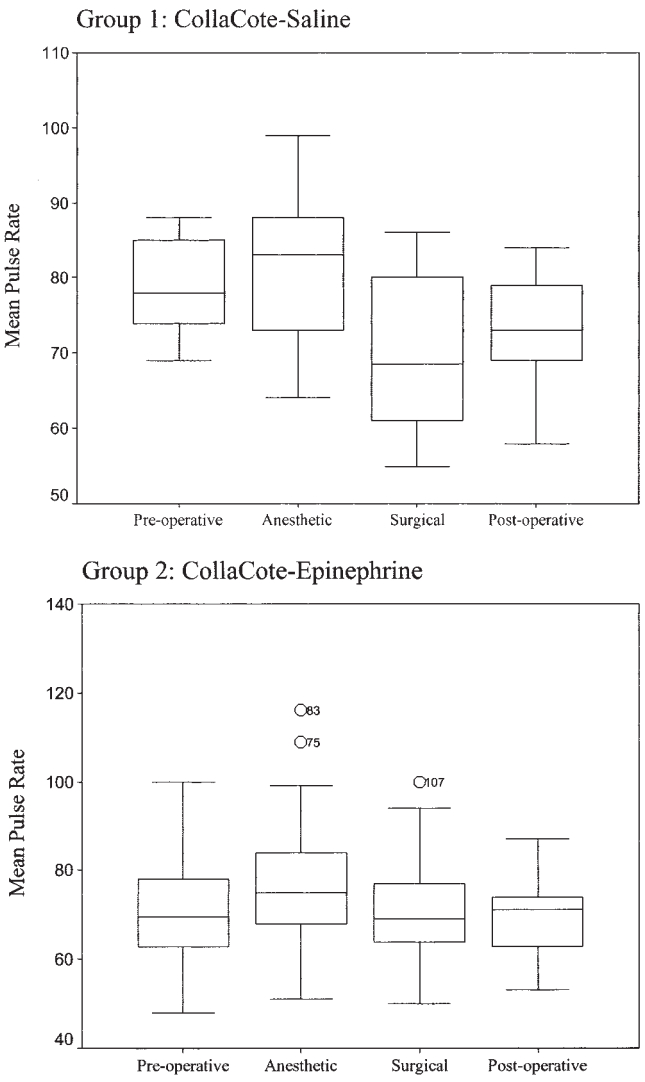

FIG 3. Mean pulse rate of CollaCote-saline and CollaCote-epinephrine.

for 4 min. Sommer et al. (17) recommended vasoconstrictors such as epinephrine 1:500 or 1:1000, phenylephrine 1:100, or nordefrin 1:200 on saturated gauze packs. Although the use of cotton or gauze with vasoconstrictor may be effective, there is potential for leaving fibers in the surgical site. Fibers that are left at the surgical site may impair root-end seal by being trapped along the margins of the root-end filling material or serve as foreign bodies in the surgical site and result in impaired wound healing. Therefore, cotton pellets and gauze products containing cotton should be considered a less desirable material for root-end isolation or hemostasis (11).

Absorbable collagen, such as CollaCote, CollaTape, or CollaPlug, contains no fibers and could be considered as a more desirable material for root-end isolation or hemostasis. These wound dressings are soft, white, pliable, nonfriable sponges that retain their structural integrity even when wet. These sponges are highly absorbent; more than 90% of the dressings consist of open pores, which can fill with fluid. Collagen is known to aggregate platelets, which release coagulation factors. Those factors, with plasma factors, help form fibrin and subsequently a clot (1). In our study, CollaCote was cut it into three pieces; each piece was saturated with 10 drops of fluid from a tuberculin syringe.

Each drop of the 2.25% racemic epinephrine solution from a tuberculin syringe contains approximately 0.21 to 0.25 mg of racemic epinephrine, of which one-half is the pharmacologically active L-form. Ten drops of this solution is equivalent to three to four Racellet #3 pellets. According to the manufacturer, each vial is intended for single use and must be protected from light. Long-term exposure to light turns the solution brown from oxidation. Each vial costs approximately $1.00.

Maintaining strict hemostasis during endodontic surgery enhances visibility and may minimize surgical time (1, 11). Our findings with regards to blood pressure and pulse agree with those of Vickers et al. (10). Kim and Rethnam (1) stated that the epinephrine-cotton pellet technique is the most efficient for hemostasis in the bony crypt. In a pilot study, we used CollaCote alone in the bony crypt. Adequate hemostasis was not achieved in any of the cases. Racellet #3 pellets were used in these patients to control bleeding. Hemorrhage control was adequate; however, some bleeding persisted in the crypt in all cases. In contrast, the majority of cases in the CollaCote-epinephrine group had excellent hemostasis. In two cases, slight but apparent intermittent bleeding persisted after the application of the CollaCote-epinephrine sponges. However, the slight bleeding did not compromise the surgical procedure, therefore, Racellet #3 pellets were not used. In the remaining case, continuous bleeding occurred, despite using both the experimental technique and #3 Racellet pellets. Continuous suctioning was required to maintain dryness in the bony crypt. In reviewing the patient's medical and dental history, no apparent explanation could be provided for this lack of hemostasis.

One major concern with cotton pellets with vasoconstrictors is the potential to leave fibers in the surgical site, which could produce inflammation and retard healing (11). With microscopic inspection, it appeared that CollaCote did not leave any debris in the surgical site. The CollaCote with epinephrine lined the bony crypt and could be left in place during retrofilling to catch debris and prevent filling materials from getting lodged in the crypt. This was particularly useful in cases in which the bony crypt was too small to accommodate bulky cotton pellets. Unlike cotton pellets, CollaCote is biocompatible and can be resorbed by the body within 10 to 14 days if left *in situ* (www.calcitek.com/rg_colla.asp).

In conclusion, our results suggest that CollaCote saturated with 2.25% racemic epinephrine provides excellent hemostasis with no evident changes in blood pressure or pulse rate.

Dr. Vy is a former resident, Department of Endodontology, Oregon Health & Science University, School of Dentistry, and is presently in private practice in Portland, OR. Dr. Marshall is associate professor, and Dr. Baumgartner is professor and chairman, Department of Endodontology, Oregon Health & Science University, School of Dentistry, Portland, OR.

Address requests for reprints to Dr. J. Craig Baumgartner, Department of Endodontology, School of Dentistry, OHSU, 611 SW Campus Drive, Portland, OR 97239. E-mail: baumgarc@ohsu.edu.

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