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Procjena djelovanja formokrezola u odnosu na agregat mineralnog trioksida kod mliječnih kutnjaka liječenih pulpotomijom: meta-analiza

Evaluation of Formocresol Versus Mineral Trioxide Aggregate in Primary Molar Pulpotomy: Meta-Analysis

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Sažetak

Svrha: Ovim se radom željelo predstaviti sustavan pregled učinaka formokrezola (FC-a) i agregata mineral-trioksida (MTA) kao lijekova u terapiji pulpotomije mliječnih kutnjaka. **Materijal i metode:** Metotologija istraživanja sastojala se od pretraživanja MEDLINE-a, PubMed-a, SCI-a i sveučilišne knjižnice Marmara. Ukupno je bilo obrađeno 165 radova u kojima je bilo riječi o kontroliranim randomiziranim kliničkim istraživanjima. Kod svih se radilo o mliječnim kutnjacima kod kojih se otvorila vitalna pulpa zbog karijesa ili traume, a terapija se sastojala od pulpotomije i postavljanja MTA ili FC-a te minimalno šestomjesečnog kontrolnog razdoblja i radiološkog dokaza. Bila je obavljena i meta-analiza u programskom paketu Comprehensive Meta-Analysis, Version 2,0 (2005.). Rabio se i fiksni učinak za agregaciju podataka. **Rezultati:** Istraživači su se koristili sa šest istraživanja koja su zadovoljavala sve uključne uvjete. Ukupno je MTA-om bilo tretirano 195 zuba, a FC-om 203. Radiološki uvjet kod obje terapije bio je u rasponu od 72 do 100 posto. Podaci su neovisno uzeti iz istraživanja te uneseni u bazu podataka. Razlike su riješene raspravom. Opći omjer vjerojatnosti bio je 1,146. Bila je pronađena i homogenost među istraživanjima (Q-vrijednost= 9,865, df=5, p=0,079). **Zaključak:** Dentalna medicina temeljena na dokazima sve je češće osnova za sintezu, procjenu i objašnjavanje istraživanja, kako bi se prihvatile kliničke smjernice i zaključci. Krajnji rezultati, promatrani radiološki, pokazuju da nakon korištenja MTA pulpotomija mliječnih kutnjaka s otvorenom vitalnom pulpom nije ništa bolja od one tretirane FC-om.

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Ključne riječi
formokrezol; agregat mineral-trioksida; meta-analiza; denticija; mliječni kutnjak; pulpotomija

Uvod

Pulpotomija je terapijski postupak koji se sastoji od kirurške amputacije koronarne pulpe otvorene zbog karijesa ili traume, dok radikularni dio ostaje zdrav (1, 2). Ako karijesni proces prodre duboko u dentin, pulpa reagira upalnom reakcijom privremeno ograničenom na područje blizu lezije. Progresijom te karijesne lezije upalni se proces širi po cijeloj koronarnoj pulpi. Kod pulpotomije se uklanja cijeli koronarni dio pulpe. Smisao pulpotomije je u pretpostavki da je upala ograničena na koronarnu pulpu. Budući da je teško, ako ne i nemoguće, klinički odrediti histološki status pulpe, operater se treba pouzdati u subjektivni kriterij te procijenti je li i radikularni dio pulpe zahvaćen ili nije. Prema tome, vrijeme krvarenja radikularnog dijela pulpe nakon amputacije, boja krvi te konzistencija tkiva, subjektivni su kriteriji koji mogu rezultirati pogrešakama u dijagnosticiranju. Kronično upaljena pulpa, ako je pogreškom dijagnosticirana kao neupalna

Introduction

Pulpotomy is a therapeutic procedure which consists of the surgical amputation of coronal pulp infected by caries or traumatized, while the radicular pulp remains healthy (1,2). When the carious process advances deep into the dentin, the pulp reacts by producing an inflammation that is temporarily limited to the area close to the caries lesion. With the progression of the lesion, the inflammatory process spreads throughout the coronal pulp. When pulpotomy is performed, the complete coronal pulp is removed. The rationale for pulpotomy is based on the assumption that the inflammation is limited to the coronal pulp. As it is difficult, though not impossible, to determine clinically the histological status of the pulp, operator has to rely on somewhat subjective criteria to determine whether the radicular pulp is not affected. Thus, the bleeding time of the radicular stump after the amputation, color of the blood, and consistency of the tissue

i neinficirana, jedan je od glavnih mogućih uzroka neuspješne pulpotomije mliječnih kutnjaka (3).

Oštećena i ranjena površina radikularne pulpe tretira se lijekom ili zavojem, kako bi se omogućilo cijeljenje, ili se fiksira preostalo tkivo. Pritom je cilj zadržati vitalitet.

Za postupak pulpotomije preporučuju se različiti materijali: formokrezol (FC), mineral-trioksid agregat (MTA), bioaktivno staklo (BAG), feritni sulfat(FS), cink-oksidni eugenol, polikarbonatni cement i kalcijev hidroksid (1).

Formokrezol (FC) uobičajeni je medikament kojim se liječnici koriste u slučaju pulpotomije mliječnih zuba (4). Smatra se "zlatnim standardom", a prvi ga je upotrijebio Sweet godine 1930. i to s 97-postotnim uspjehom (5).

Formokrezol u susjednom pulpnom tkivu stvara područje učinkom fiksacije koja slabi prema apikalno. Apikalna trećina pulpe nije zahvaćena i dugo ostaje vitalna (5). Formokrezol (FC) je popularan lijek za pulpotomiju kod mliječnih zuba te se u posljednjih 60 godina smatra najraširenijim i najomiljenijim u terapiji zubne pulpe mliječnih zuba (2, 6, 7). Svojedobno su se pojavile i određene sumnje u toksičnost te moguće kancerogeno djelovanje FC-a, pa su bile predložene alternative kako bi se zadržao vitalitet preostale pulpe. Alternative uključuju:
1. elektrokirurgiju; 2. laser; 3. glutaraldehid; 4.feritni sulfat; 5. smrznutu suhu kost; 6. koštano-morfogenetski protein i 7. osteogeni protein (3).

U proteklom desetljeću proizveden je još jedan materijal za terapiju zubne pulpe, a to je mineral-trioksid agregat (MTA). To je prah koji se sastoji od sitnih hidrofilnih čestica trikalcijeva silikata, trikalcijeva aluminata, trikalcijeva oksida i silikatnog oksida. Sadržava i male količine drugih mineralnih oksida koji djeluju na njegova kemijska i fizikalna svojstva. MTA se pokazao sposobnim inducirati stvaranje tvrdog tkiva unutar pulpe te poticati rast stanica *in vitro* (1). U nekoliko istraživanja *in vivo* i *in vitro* dokazano je da sprječava mikrocurenje i da je biokompatibilan, te da potiče regeneraciju prvotnoga tkiva kada se položi tako da dotiče zubnu pulpu ili periradikularno tkivo (3).

Randomizirana klinička istraživanja (RCT) u kojima su sudionici nasumce nazočni određenim terapijskim postupcima, smatraju se "zlatnim standardom" u eksperimentalnom postupku (5).

Unatoč tome u nekim studijama isti terapijski postupci pokazuju veći učinak od ostalih, ili ih čak nema. Zato možemo reći da terapijski postupak među pojedincima može varirati, ali isto tako i u različitim istraživanjima. Potreba za dogovorom o učinku terapije pokazala se u literaturi i više nego potrebnom, tako da se ovaj problem može riješiti pomoću meta-analize kombiniranjem podataka iz različitih istraživanja (8). Kratko objašnjenje meta-analize jest da je to zbroj statističkih tehnika za kombiniranje informacija iz različitih istraživanja, kako bi se dobila ukupna procjena učinka terapijskog postupka.

Svrha ovog istraživanja bila je predstaviti sustavan pregled učinka FC-a i MTA kada se upotrebljavaju kao medikamenti kod pulpotomije mliječnih molara. Iz tog se razloga najveći dio informacija može dobiti iz dokazom potkrijepljenih pristupa u dentalnoj medicini (EBD-u) korištenjem određe-

are all subjective criteria that might lead to diagnosis error. A chronically inflamed radicular pulp erroneously diagnosed as noninflamed and noninfected is one of the major factor possibly causing pulpotomy failure in primary molars (3).

The wounded surface of the radicular pulp is treated with a medicament or dressing agent to promote healing or to cause fixation of the underlying tissue. The objective is to maintain vitality of the radicular pulp.

Various materials have been recommended for pulpotomy, and these are formocresol (FC), mineral trioxide aggregate (MTA), bioactive glass (BAG), ferric sulphate (FS), zinc oxide eugenol, polycarboxylate cement, and calcium hidroxide (1).

Formocresol (FC) is a commonly-used primary tooth pulpotomy medicament (4). Formocresol is regarded as the 'gold standard' and was first used for pulpotomy by Sweet(1930) with a 97% success rate (5).

Formocresol produces an area of necrosis in the adjacent pulp tissue with the fixative effect diminishing as it progresses apically. The apical third of the pulp is unaffected, and retains its vitality for an extended time (5). Formocresol (FC) has been a popular pulpotomy medicament in the primary dentition for the past 60 years, and is considered as the most universally taught and preferred pulp therapy for primary teeth (2, 6, 7). Concerns have been raised about the toxicity and potential carcinogenity of FC in humans, and alternatives have been proposed to maintain the radicular pulp's vitality. These include: 1- electrosurgery, 2- laser, 3- gluteraldehyde, 4- ferric sulphate, 5- freeze-dried bone, 6- bone morphogenetic protein and 7- osteogenic protein (3).

In the past decade, an alternative material called mineral trioxide aggregate (MTA) became available for use in pulpal procedures. MTA (mineral trioxide aggregate) is a powder consisting of fine hydrophilic particles of tricalcium silicate, tricalcium aluminate, tricalcium oxide and silicate oxide. It also contains small amounts of other mineral oxides which modify its chemical and physical properties. MTA has demonstrated the ability to induce hard-tissue formation in pulpal tissues, and it promotes rapid cell growth in vitro (1). In several vitro and in vivo studies, it has shown that MTA prevents microleakage, it is biocompatible, and promotes regeneration of original tissues when it is placed in contact with the dental pulp or periradicular tissues (3).

Randomized clinical trials (RCTs) in which participants are randomly assigned to treatment and control groups, are considered as the gold standard of experimental design (5).

However, some studies show a greater effect of a treatment while some show a lesser effect of the same treatment or do not. Therefore, the response to a treatment will vary among individuals and it will also vary among studies. The consensus need on the treatment effectiveness becomes important in the literature, so with Meta Analysis it can be found a solution to this problem with combining data from different studies (8). The brief definition of the Meta Analysis becomes as a set of statistical techniques for combining information from different studies to derive an overall estimate of a treatment's effect.

The aim of the study is to present a systematic review of the effects of formocresol (FC) and mineral trioxide aggre-

nih kriterija za odabir literature, kako bi se ispitala relativna učinkovitost FC-a i MTA kao lijekova u slučaju pulpotomije mliječnih zuba.

Izjava PICOT korištena u ovom istraživanju glasi (8):

1. (P) - određuje problem (humani mliječni kutnjaci pogođeni karijesom i reverzibilnim koronarnim pulpitisom);
2. (I) - je li pulpotomija obavljena MTA-om;
3. (C) - usporediti s formokrezolom;
4. (O) - rezultati potvrđeni radiološki;
5. (T) - u određenim vremenskim razmacima do ispadanja.

Kriteriji radiološkog uspjeha:

1. zub je ostao asimptomatičan do ispadanja;
2. zub nasljednik nije bio izvrgnut oštećenjima;
3. nije bilo periapikalne patologije ili interne resorpcije;
4. zubi nisu ispali prerano.

Materijal i metode

Relevantna literatura identificirana je pretraživanjem četiriju baza podataka: MEDLINE (od srpnja do studenoga 2007.), PubMed, SCI i sveučilišne knjižnice Marmara.

Svi uključeni članci ispunjavali su sljedeće uvjete:

1) ispitivanja o FC-u ili MTA-u;
2) povezanost s pulpotomijom i
3) mliječne zube.

Ispitivanja su morala biti u kategoriji randomiziranih kliničkih ispitivanja na mliječnim zubima kod kojih je zubna pulpa bila otvorena zbog karijesa ili traume, a tretirani su korištenjem FC-a ili MTA s najmanjim razdobljem kontrole od šest mjeseci i radiološkim dokazom uspješnosti (šest istraživanja) (Tablica 1.).

gate (MTA) when used as medicaments in primary molar pulpotomy. Therefore, maximum information must be obtained by an evidence-based approach in dentistry (EBD), using defined criteria for literature selection, in order to examine the relative efficacy of FC and MTA as pulpotomy agent in primary teeth.

PICOT statement used for the study was (8);

1. (P) defines problem (in human carious molars with reversible coronal pulpitis)
2. (I) does a pulpotomy performed with MTA
3. (C) compared with formocresol
4. (O) results in radiographical success
5. (T) in time periods up to exfoliation

The criteria for radiographical success were;

1. tooth remained asymptotic until normal exfoliation,
2. successor tooth was uneffected,
3. no periapical pathology or internal resorption,
4. tooth did not exfoliate prematurely.

Material and methods

Relevant literature was identified using 4 search engines as; MEDLINE(Jun-Nov 2007) PubMed, SCI and Marmara University Library.

Inclusion criteria

Firstly, all papers were conducted by fulfilling the following criteria:

1) studies on FC or MTA
2) related to pulpotomy
3) primary teeth.

Secondly, studies of interest were randomized controlled trials of primary molar teeth where there was exposure of vital pulp caused by caries or trauma, treated by using MTA or FC pulpotomy, with at least 6 months follow-up, and radiographic evidence (6 studies) (Table 1).

Tablica 1. Raspodjela papira za svaki sistemski pregledni proces te rezultati za procjenu istraživanja na temelju dokaza za formokrezol i MTA kao lijekove u slučaju pulpotomije mliječnih kutnjaka
Table 1 Distrubition of papers at each systematic review process and the results of evidence based assessment of Formocresol and MTA as primary molar medicaments.

	Tijek pretraživanja literature • Search History	Rezultat pretrage • Results of search and sieving
1	Prekrivanje zubne pulpe • Dental pulp capping	1693
2	Pulpotomija • Pulpotomy	1140
3	Devitalizacija zubne pulpe • Dental pulp devitalization	385
4	Otvaranje zubne pulpe • Dental pulp exposure	1085
5	Terapija pulpe • Pulp therapy	8180
6	Mliječni kutnjak • Primary molar	2770
7	Formokrezol • Formocresol	380
8	Mineral trioksid agregat • Mineral trioxide aggregate	472
9	MTA-FC-pulpotomija • MTA-FC-Pulpotomy	32
10	MTA-FC	28
11	9 + randomizirani • 9 + randomized	8
12	11 + 6(šest) mjesteci radiološki kontrolni pregled • 11 + 6(six) months radiographic follow up	6

Meta –analiza

Ukupni rezultati svakog kliničkog ispitivanja uneseni su u program za analizu. Primarni učinak određen je kao omjer vjerojatnosti (OR) između MTA i FC-a. Vrijednost koja bi prelazila 1 za omjer vjerojatnosti značila bi da je testirani MTA znatno bolji od kontrolnog medikamenta FC-a. Standardna pogreška za OR računala se prema tome razlikuje li se statistički značajno od jedan, s intervalom od 95 posto granice pouzdanosti (CI).

Ispitana je bila i heterogenost među istraživanjima. Kada je potvrđena homogenost među opažanjima, izračunati su predviđanje OR-a i 95-postotni CI na osnovi pretpostavljenog modela fiksnog učinka (Peto Method) (9). Meta-analiza obavljena je korištenjem Comprehensive Meta-Analysis, Version 2,0 (2005.).

Rezultati

Sva istraživanja, a bilo ih je ukupno šest, bila su randomizirana klinička istraživanja (RCT) te su iskorištena u meta-analizi.

Meta-analiza

Meta-analiza uspoređuje MTA i FC. Šest RCT-a (ukupno 398 kutnjaka:195 MTA-om i 203 FC-om) analizirani su meta-analizom.

Tablica 2. pokazuje distribuciju istraživanja (u kronološkom slijedu) s obzirom na vrstu istraživanja, radiološke podatke, lijekove, broj promatranih zuba, kontrolno razdoblje, neuspješnost i postotak uspješnosti. Podaci su neovisno izva-

Meta -analysis

Summary results of each clinical trials of the study were tabulated for the analysis. The estimate of the principal effect was defined as odds ratio (OR) between MTA and FC. The value exceeding 1 for the general OR implies that the test medicament (MTA) is significantly successful than the control medicament (FC).The standard error for the general OR is computed to assess if it differs significantly from 1, with 95% Confidence Interval (CI).

The heterogeneity test between studies was assessed. When the homogeneity between observations of the studies was found, estimates of OR and 95% CI were calculated with model based on fixed effects assumption (Peto Method) (9).

The Meta Analysis was performed using by Comprehensive Meta-Analysis, Version 2.0 (2005).

Results

Study Selection and data summary

All of the six studies were randomized controlled trials (RCT) and were used in the Meta-Analysis.

Meta-Analysis

Meta- analysis comparing MTA and FC. 6 RCTs (total 398 molars:195 MTA and 203 FC) were analyzed by meta-analysis.

Table 2; shows distribution of studies (in chronological order) with respect to type of trial, radiographic data, medicament, number of teeth studied, follow-up period, failure and percent success.

Tablica 2. Pregled rezultata kod svih kliničkih ispitivanja za meta-analizu radiološkog uspjeha MTA i FC-a kao lijekova u slučaju pulpotomije mliječnih kutnjaka
Table 2 Summary results of each clinical trials for the Meta-Analysis of radiographic success of MTA and FC on primary molar pulpotomy medicament

Istraživanja • Studies	MTA			Formokrezol • Formocresol			Razdoblje kontrole • Follow up period
	N	neuspjeh • failure	uspjeh • success	N	neuspjeh • failure	uspjeh • success	
Jabbarifar SE. (2004) [10].	32	n=1	90%	32	n=3	89%	6 mjeseci • months
Naik S. (2005) [11].	25	n=1	96%	15	n=1	92%	6 mjeseci • months
Eidelman E. (2001) [12].	17	n=0	100%	15	n=1	93%	30 mjeseci • months
Holan G. (2005) [3].	33	n=2	97%	29	n=2	83%	38 mjeseci • months
Neamatollahi H. (2006) [13].	45	n=12	72%	45	n=3	93%	6 mjeseci • months
Aeinehchi H. (2007) [14].	43	n=0	100%	57	n=6	89%	6 mjeseci • months
Ukupno • Total	195	16	91.7%	203	16	91.1%	

Tablica 3. Meta-analiza sažetka podataka o radiološkoj procjeni MTA i FC-a u slučaju pulpotomije mliječnih kutnjaka.
Table 3 Meta-analysis data summary of radiographic assesment of MTA and FC on primary molar pulpotomy medicament.

Model		Učinak veličine i 95%-tni interval • Effect size and 95% interval			Test 0 hipoteze (2 kraja) • Test of null (2-tail)			Heterogenost • Heterogenecity	
Model	Broj istraživanja • Number studies	Točka procjene • Point estimate	Donja granica • Lower limit	Gornja granica • Upper limit	Z vrijednost • Z-value	P vrijednost • P-value	Q vrijednost • Q-value	df (Q)	P vrijednost • P-value
Fixed	6	1.146	0.479	2.738	0.306	0.760	9.865	5	0.079

đeni iz svih istraživanja te uvršteni u bazu podataka. Radiološki uspjeh terapije u šest istraženih studija kretao se, za obavljene uz pomoć MTA, od 72 do 100 posto, a uz pomoć FC-a od 89 do 93 posto (Tablica 2.).

Nije bilo heterogenosti u istraživanjima (Q-vrijednost= 9,865, df=5, p=0,079). (Tablica 3.).

Tablični prikaz upućuje na to da na samo jedno istraživanje statistički znatno utječe korištenje MTA i FC-a kod pulpotomije mliječnih kutnjaka (p= 0,018). Meta-analiza šest promatranih istraživanja nije otkrila statistički značajnu razliku između dvaju lijekova za pulpotomiju mliječnih kutnjaka s općim OR=1,146 i 95 posto za CI, uključujući 1 (0,479, 2,738). Dijagram pokazuje OR i CI za radiološki uspjeh MTA i FC-a u šest istraživanja.

Rasprava

Dentalna medicina (EBD) temeljena na dokazima sve se češće koristi kao sredstvo sinteze, procjene i tumačenja istraživanja kako bi se prihvatile kliničke smjernice i zaključci. Korištenje načela EBD-a posebice je relevantno u postavljanju novih kliničkih preporuka za lijekove u slučaju pulpotomije mliječnih kutnjaka na temelju podataka iz trenutačno dostupne literature (8). U ovom je istraživanju samo šest randomiziranih kontroliranih kliničkih istraživanja preostalo na kraju postupka procjene i stupnjevanja.

Premda su u RCT-u bili kvalitetni članci, većina nije pratila preporuke CONSORT-a, osobito u randomizaciji, postupku "slijepog pokusa" i vrijednosti analize. Takva situacija može utjecati na vrijednost meta-analize (5).

Vrijednost ovog istraživanja je u korištenju meta-analize kao sofisticirane statističke analize, no rijetko se upotrebljava u istraživanjima dentalne medicine iako se na taj način može dobiti maksimalna količina informacija o usporedbi FC-a i MTA s dokazima potkrijepljenima pristupom u dentalnoj medicini.

Meta-analiza prikupljenih podataka pokazuje da kod mliječnih kutnjaka s otvorenom pulpnom komorom zbog karijesa ili traume pulpotomija obavljena MTA-om , radiološki promatrano, nije omogućila bolje rezultate nego što su oni s FC-om. Na temelju toga, na dokazima utemeljenog zaključka, može se tvrditi da se kod humanih mliječnih zuba s reverzibilnim koronarnim pulpitisom kod pulpotomije liječene FC-om i MTA-om najvjerojatnije mogu očekivati slični radiološki uspjesi (10-14). Ng FK i L.B. Messer raščlanili su 5RCT izravnom meta-analizom i došli do zaključka kako ne postoji statistički značajna razlika u kliničkom i radiološkom uspjehu, ali je direktna meta-analiza prikupljenih podataka pokazala da su klinički i radiološki uspjeh MTA statistički mnogo viši od FC-a (12, 15,16) .

Klasificirana metamorfoza i interna resorpcija najčešći su radiološki nalazi kod primjene FC-a. Fuks i suradnici dobili su 1997. iste radiološke nalaze (17). Radiološko ispitivanje nije otkrilo dentinski mostić kod bilo kojeg zuba nakon pulpotomije FC-om. Cleaton-Jones P. Markovic istaknuo je da ne postoje statistički značajne razlike između reakcijske učestalosti kod pulpotomije FC-om (18, 19, 20). N. Innes tvrdi da je MTA nadmoćan u odnosu prema FC –u kod pulpo-

Data which were extracted from each study independently, entered into a database.

The radiographic success rate of treatment with MTA and FC in the 6 studies ranged from 72% to 100% and 89% to 93% respectively. (Table 2)

There was no heterogeneity among the studies (Q-value= 9.865, df=5, p=0.079). (Table 3) Funnel Plot shows only one research statistically significantly effects of MTA and FC on primary molar pulpotomy (p= 0.018). The Meta-Analysis result concerning the six studies did not reveal statistical differences between the two medicaments in pulpotomized primary molars with the general OR=1.146 and 95% of CI including 1 (0.479, 2.738). The plot shows the ORs and Cl for the radiographic success of MTA and FC in the 6 studies.

Discussion

Evidence based dentistry is being used increasingly as a tool to synthesize, evaluate, and interpret research to produce clinical guidelines and conclusions. Use of the principles of EBD is particularly relevant in establishing new clinical recommendations for pulpotomy medicaments for primary teeth based on data currently available from the literature (8).

In the selection of studies, only 6 randomized controlled trials were available at the end of appraisal and ranking process in the present study. However RCTs were high quality articles, most of the RCTs failed to follow the CONSORT guidelines, especially in the randomization method, blinding process and the power analysis. This situation may affect the Meta-Analysis power (5).

The strength of this study is the use of Meta-Analysis which is sophisticated statistical analysis and rarely used in dentistry researches, therefore maximum information can be obtained about the comparison FC and MTA by an evidence-based approach in dentistry.

The Meta analysis of the pooled data demonstrate that in primary molar teeth with vital pulp exposure caused by caries or trauma, a pulpotomy performed with MTA results not better than FC radiographically observed outcomes. Based on this evidence-based assessment concludes that, in human carious primary molars with reversible coronal pulpitis, a pulpotomy performed with either formocresol or mineral trioxide aggregate is likely to have a similar radiographic success. (10-14).

Ng FK and Messer LB analysed 5 RCT's with Direct Meta Analysis and showed no statistically significant differences in clinical and radigraphic successes but Direct Meta Analysis of the pooled data showed the clinical and radiographic successes for MTA were significantly higher than for FC (12, 15,16) .

Calsific metamorphosis and internal resorption were the most common radiographic findings for FC. Fuks et al 1997 showed the same radiographic findings (17). Radiographic examination did not reveal the presence of a dentin bride for any of the teeth treated with FC pulpotomy. Markovic Cleaton-Jones P showed no statistically significant differences between reaction frequencies in FC pulpotomy. (18, 19, 20).

tomije te da ima manju stopu neuspješnosti (21). Nedavno su postignuti znatno bolji rezultati s MTA-om (7). Radiološki neuspjesi kod kutnjaka tretiranih MTA-om opisani su kao obliteracija pulpnog kanala. Meta-analiza je pokazala da je radiografski neuspjeh (p= 0,018) za MTA bio statistički mnogo viši od FC-a, možda zato što širi pulpni kanali kod mlađih zuba mogu olakšati prijenos stimulativnih čimbenika (13). U nedavnom kratkom izvještaju Nadina i suradnika u EBD-u o ovoj temi tvrdi se kako "ne postoji pouzdan dokaz o nadmoćnosti bilo kojeg lijeka u pulpotomiji mliječnih kutnjaka" (11).

U istraživanjima je istaknuta različita stopa kliničke i radiološke uspješnosti (od 59 do 100%) (22, 11). Bolja stopa uspješnosti bila je u skupini s FC-om (22). Dean i njegovi kolege ustanovili su da je za FC stopa kliničke uspješnosti 100 posto, a radiološke 92 posto. Radiološku uspješnost drugi su autori ocijenili kao 94,6-postotnu (23, 24, 25). FC je jako ubrzao ispadanje mliječnih kutnjaka (26) i postao sporan lijek u slučaju pulpotomije. Međunarodna zdravstvena organizacija i njezin ogranak - Međunarodna agencija za istraživanje karcinoma (2004.), ustanovile su da formaldehid uzrokuje nazofaringealni rak te su ga ponovno klasificirale kao humani kancerogen. Dovedena je u pitanje i sigurnost uporabe formokrezola jer je poznato da može uzrokovati toksične i imunosne poremećaje te mutagene i kromosomske aberacije. Zato liječnici dentalne medicine ne bi smjeli zanemariti rizik kad je riječ o FC-u, te bi morali shvatiti kako je njegova uporaba u dječjoj dentalnoj medicini nepoželjna (6, 13, 27, 28).

Premda je potrebno da mliječni kutnjaci ostanu u funkciji ponekad i devet godina prije ispadanja, dužina kontrolnog razdoblja u ovom istraživanju iznosila je šest do 38 mjeseci.

Potrebna su daljnja istraživanja, primjerice o duljem kontrolnom razdoblju, ali i veći broj tretiranih zuba FC-om i MTA-om, kako bi se odredio dugoročni utjecaj na mliječne zube. U ovom istraživanju nije bila provedena kontrola kvalitete. Obrađivanje istraživanja bolje i lošije kvalitete također može smanjiti vrijednost nalaza meta-analize.

PICOT-postavke bile su: (P) definiranje problema (ljudski karijesni kutnjaci s reverzibilnim koronarnim pulpitisom); (I) korištenje MTA; (C) usporedba s FC-om; (O) rezultatski MTA nije bolji od FC-a radiografski i (T) kontrolno vrijeme je šest mjeseci.

Zaključak

MTA se može preporučiti kao odgovarajuća zamjena za formokrezol nakon što se provedu buduća prospektivna RCT-istraživanja. Dodajemo - slažemo se sa značenjem ovog istraživanja zbog rijetko korištene meta-analize u studijama dentalne medicine te dobivenog dodatnog iskustva u pretraživanju podataka. Zato je potrebno obaviti daljnja randomizirana klinička istraživanja i meta-analize kako bi se potvrdila uspješnost lijekova za pulpotomiju.

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Innes N suggested that MTA was superior to FC in pulpotomy, resulting in a lower failure rate (21). Most resently considerable better results have been obtained with MTA. (7).

Radiograhic failures of MTA molars were reported as pulp canal obliteration. Meta- analysis showed the radigraphic failure (p= 0.018) for MTA were significantly higher than for FC perhaps reflecting the wider pulp canals in younger teeth which can facilitate the transfer of stimulatory factors (13).

Recent brief EBD report on this subject by Nadin et al who stated that 'there is no reliable evidence supporting the superiority of one particular treatment method for pulpally involved primary molars (11).

Various clinical and radiographic success rates (59-100%) have been reported (22, 11) Better radiographic success was found in FC group (22). Dean et al observed that the clinical and radiographic success rates for FC, 100% and 92% respectivelyRadiograhic success rate in FC group was found 94.6% (23, 24, 25).

FC significantly hastened the exfoliation of pulpotomized primary molars (26). Formocresol has become a controversial pulpotomy medicament. The International Agency for Research on Cancer (2004) of the World Health Organization determined that formaldehyde cause nasopharyngeal cancer and reclassified formaldehyde as known human carcinogen. The safety of formocresol has also been questioned, as it was known to cause a toxic, immune sensitization, mutogenic and chromosomal aberrations. Therefore, dentists should not ignore the risks of FC, but realize its use in pediatric dentistry unwarranted (6, 13, 27, 28).

Although primary molars may be required to function for up to 9 years before exfoliation, the length of follow up period for molars included in this study were 6 to 38 months.

There is a need for further study, for example, longer follow up period and great numbers of teeth treated with FC and MTA to determine the long term effects on primary teeth.

Quality assessment were not performed in this study. The pooling of both high and low quality studies may also reduce the strength of the Meta analysis findings**.**

PICOT statement was (P) define problem (in human carious molars with reversible coronal pulpitis), (I) the use of MTA, (C) compared with FC, (O) resulted MTA not better than FC radiographically. (T) in time periods up to 6 months.

Conclusion

MTA may be recommended as a suitable replacement for formocresol after conducted further prospective RCTs. In addition, we agree with the importance of this study because of rarely using Meta-analysis in dentistry researches and requiring extra practice with widely data searching. Therefore, a further randomized clinical trials and meta analysis are needed to confirm the success of the pulpotomy medicaments.

Award winner at the_3rd International Meeting Methodological Issues in Oral Health Research- Clinical Trials and Evidence Based Dentistry, 16-18 April, 2008, Milan, Italy.

Abstract

Aim: The aim of this study is to present a systematic review of the effects of formocresol (FC) and mineral trioxide aggregate (MTA) when used as medicaments in pulpotomized primary teeth. **Methods:** Methodology of the study list was obtained by using MEDLINE, PubMed, SCI and Marmara University Library. Totally 165 studies were performed. Studies of interest were randomized controlled trials of primary molar teeth where there was exposure of vital pulp caused by caries or trauma, treated by using MTA or FC pulpotomy, with at least 6 months follow-up, and radiographic evidence. Meta - analysis was performed using Comprehensive Meta-Analysis, Version 2.0 (2005). Fixed effect model was applied to aggregate data. **Results:** Six studies that include criteria were used. Totally 195 teeth treated by MTA and 203 teeth treated by FC. The radiographic success for treatment with MTA or FC in the 6 studies ranged from 72% to 100%. Data were extracted from each study independently and entered into a database. Differences were resolved by discussion. The general odds-ratio was found 1.146. There was a homogeneity among the studies (Q-value= 9.865, df=5, p=0.079). **Conclusions:** Evidence based dentistry is being used increasingly as a tool to synthesize, evaluate, and interpret research to produce clinical guidelines and conclusions. The results demonstrate that in primary molar teeth with vital pulp exposure caused by caries or trauma, a pulpotomy performed with MTA results is not better than FC radiographically observed outcomes.

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Key words
Formocresol; Mineral Trioxide Aggregate; Meta-analysis; Dentition; Primary; Pulpotomy.

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