臺北市立萬芳醫院 - 委託財團法人臺北醫學大學辦理

Topical application of honey in the management of chemo/radiotherapy induced oral mucositis: A systematic review and network meta-analysis

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Journal Club

引言人:王錦雲

2019年06月11日

International Journal of Nursing Studies 89 (2019) 80–87

改善口腔黏膜炎-現況

方案一: 營養品~速養療
480g+280g/組 7020元

方案二:口腔凝膠
每盒21包，1590元/週

方案三:口內膏、或局部麻醉劑

方案四:生理食鹽水漱口

方案五:口腔清潔

前言-1

- 40%–76% patients with cancer undergoing chemo/radiotherapy develop mucositis which manifests itself as intense erythema in the treated areas and patients suffer from difficulties with swallowing.
- As oral mucositis is severely debilitating oral Pain and be more susceptible to infection which may result in the demise of the patient due to infections and compromising the cancer treatment.
- the incidence of moderate to severe (grades ≥3) mucositis is typically 30%–40% for conventional radiotherapy over 6–7 weeks, but double this when chemotherapy is added or an accelerated fractionation is used (Biswal et al., 2003; Kostler et al., 2001).

前言-2

- Several treatments have been used to prevent or reduce the moderate-severity of oral mucositis but outcomes are inconsistent.
- Honey main components are the sugars glucose and fructose. (van der Weyden, 2003; Molan and Moore, 2001; Vardi et al., 1998).
- Honey has found a place in the treatment of burns, infected wounds and skin ulcers. (Al-Waili and Saloom, 1999).
- The impaired mucosal barrier often permits the development of superadded bacterial and fungal infections (Nicolatou-Galitis et al., 2001; Dale et al., 2018).
- Honey has antibacterial properties and enhances epithelization, there by improving wound healing (Al-Waili and Saloom, 1999).

mechanism of action of honey

- The suggested mechanism of action of honey in chemo/radiotherapy- induced oral mucositis may be through its positive effect on cell epithelialization and regrowth, thereby encouraging rapid recovery of cell loss (Dorr et al., 2001).
- Although the mechanism of action of honey is not clear, it is likely that factors like osmolality, phenol (苯酚)content, flavanoid (類黃酮) levels, acidity, and the release of hydrogen peroxide (過氧化氫)are thought to be the most important factors for its activity (Almasaudi et al., 2016).
- Moreover, honey, because of their high permeability, honey may stimulate saliva production.

mechanism of action of honey

- Honey effectiveness may be related to its high permeability, anti-foaming properties and antioxidant properties (Ghashm et al., 2010; Yarom et al., 2013).
- Honey is known for its antioxidant and anti-inflammatory activity and increased nitric oxide(NO) in the lesion (Almasaudi et al., 2016; Raeessi et al., 2014).
- Honey can accelerate the repair and healing of chemo/radiotherapy-induced oral mucosal damage and reduce the related stimulation.

癌症病人口腔黏膜炎臨床照護指引

周繡玲　謝嘉芬　李佳諭　江孟冠　紀雯真

劑，一天使用4至8次，每次15c.c.，口含15分鐘，證實能有意義的減少接受放射線治療之頭頸癌病人口腔黏膜炎之發生。[7,12-13,28-30]（建議等級A）

(2) 頭頸癌病人接受放射線治療時可使用aloe vera（蘆薈）、蜂蜜或是抗生素口內膏（polymixin/tobramycin/amphotericin, PTA），以預防口腔黏膜炎。[17,21,25,30]（建議等級A）

2011年

建立癌症病人口腔照護之臨床照護指引

2013年

盧淑芬 / 台北榮民總醫院副護理長
林小玲 / 台北榮民總醫院護理督導長
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廖家惠 / 台北榮民總醫院護理師
陳玉枝 / 台北榮民總醫院護理部顧問

至於蘆薈、蜂蜜預防口腔黏膜炎之效果，Worthington 等 (2011) 行整合分析後，因樣本數少 (僅 2~3 篇隨機對照試驗)，雖達顯著，作者表訴此預防效果侷限，未來仍需更多大樣本研究的整合分析才能使證據等級與結果品質更強化。

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Topical application of honey in the management of chemo/radiotherapy-induced oral mucositis: A systematic review and network meta-analysis

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步驟 1:系統性文獻回顧探討的問題為何?

蜂蜜對於癌症病人之口腔黏膜炎是否有效?

研究族群 (population)	patients with chemo/radiotherapy-induced oral mucositis
介入措施 (Intervention)	any type of Honey
比較措施 (Comparison)	(1) efficacy outcome was chemo/radiotherapy-induced moderate-severe oral mucositis. (2) efficacy outcomes were treatment completed (3) onset time of mucositis (4)swallowing diary (5)fungal colonization (6)bacterial colonisation (7)analgesic

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Keywords:
Honey
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Oral mucositis
Network meta-analysis

ABSTRACT

Background: Mucositis is an inflammatory response of mucosal epithelial cells to the cytotoxic effects of chemotherapy and radiation therapy. To assess the comparative efficacy of honey for patients with cancer undergoing chemo/radiotherapy-induced oral mucositis through a systematic review and network meta-analysis.

Methods: A network meta-analysis was used to identify evidence from relevant randomized controlled trials (RCTs). We searched PubMed, Embase, and the Cochrane Library for publications up to November 2017. The prespecified primary efficacy outcome was the treatment effect of moderate-severe oral mucositis with honey. We performed subgroup analyses and meta-regressions according to the age group, cancer type, mucositis cause, honey type, control arm and type of assessment scale. Moreover, secondary efficacy outcomes were treatment completed, onset time of mucositis, swallowing diary, fungal colonization, bacterial colonisation and analgesic use. And, we did standardize meta-analyses using the random-effects model, later completing the random-effects network meta-analyses by different treatment/control arms.

Results: A total of 17 RCTs were eligible (22 analyses), involving 1265 patients and 13 arms. Honey treatment arm significantly increased the therapeutic effect of chemo/radiotherapy-induced moderate-severe oral mucositis (0.25, 0.14–0.46); significant efficacy was observed in a large proportion of subgroups. The meta-regression may have identified the causes of heterogeneity as the honey type ($P = 0.038$). Therefore, we need to perform

- Aim: **To compare and rank honey treatment arms and no-honey control arms for patients with cancer undergoing chemo/radiotherapy-induced oral mucositis.**

步驟2:系統性文獻回顧的品質如何?(FAITH)

F-研究是否找到所有的相關證據?

搜尋3個資料庫

- We considered large-scale RCTs of patients with chemo/radiotherapy-induced oral mucositis, searched PubMed, EMBase, and the Cochrane Library for eligible trials form the very beginning of the databases to November 2017, comparing any of the following treatments: treatment of chemo/radiotherapy-induced oral mucositis in cancer patients with any type of honey .

able S1 Search strategies for Pubmed, EMBASE and the Cochrane Library database.

Search strategies for PubMed

#1.("honey"[MeSH Terms] OR "honey"[All Fields]) AND ("mucositis"[MeSH Terms] OR "mucositis"[All Fields]) AND ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields])

Search strategies for EMbase

#1 'honey'/exp OR honey AND ('mucositis'/exp OR mucositis) AND ('cancer'/exp OR cancer)

Search strategies for Cochrane library

#1.honey, mucositis and cancer
#2. MeSH descriptor

步驟2:系統性文獻回顧的品質如何?(FAITH)

F-研究是否找到所有的相關證據?

不限英語、有說明是否用MESH Terms 及一般檢索詞彙

- **Inclusion criteria :**RCTs of patents with any type of cancer (such as head and neck cancer, nasopharyngeal cancer, etc.); patients of any age, gender, tumor stage, and histological grade; either smoking or not; and either using pure natural honey, manuka honey or local honey for treatment.
- **Excluded trials** published only as abstract (with no additional data available from other sources). No language restrictions were applied. We then screened reference lists of all obtained articles to avoid missing relevant.

評讀結果:☑是 ☐否 ☐不清楚

步驟2:系統性文獻回顧的品質如何?(FAITH)

A-文獻是否經過嚴格評讀 (Appraisal)?

- The risk of bias of the randomized controlled trials was assessed using the Cochrane risk of bias tool (Higgins et al., 2011).
- We assessed the following 7 items of risk of bias:
- random sequence (selection bias),
- allocation concealment (selection bias),
- blinding of participants personnel (performance bias),
- blinding of outcome assessment (detection bias),
- incomplete outcome data (attrition bias),
- selective reporting (reporting bias), and other bias.
- Low risk, high risk, and unclear risk were classified in all studies.

The quality assessment indicated that all included trials were of acceptable quality.

Table S4 Risk of Bias Assessment using the Newcastle-Ottawa Scale for Case-control Studies

Table S4 Risk of Bias Assessment using the Newcastle-Ottawa Scale for Case-control Studies

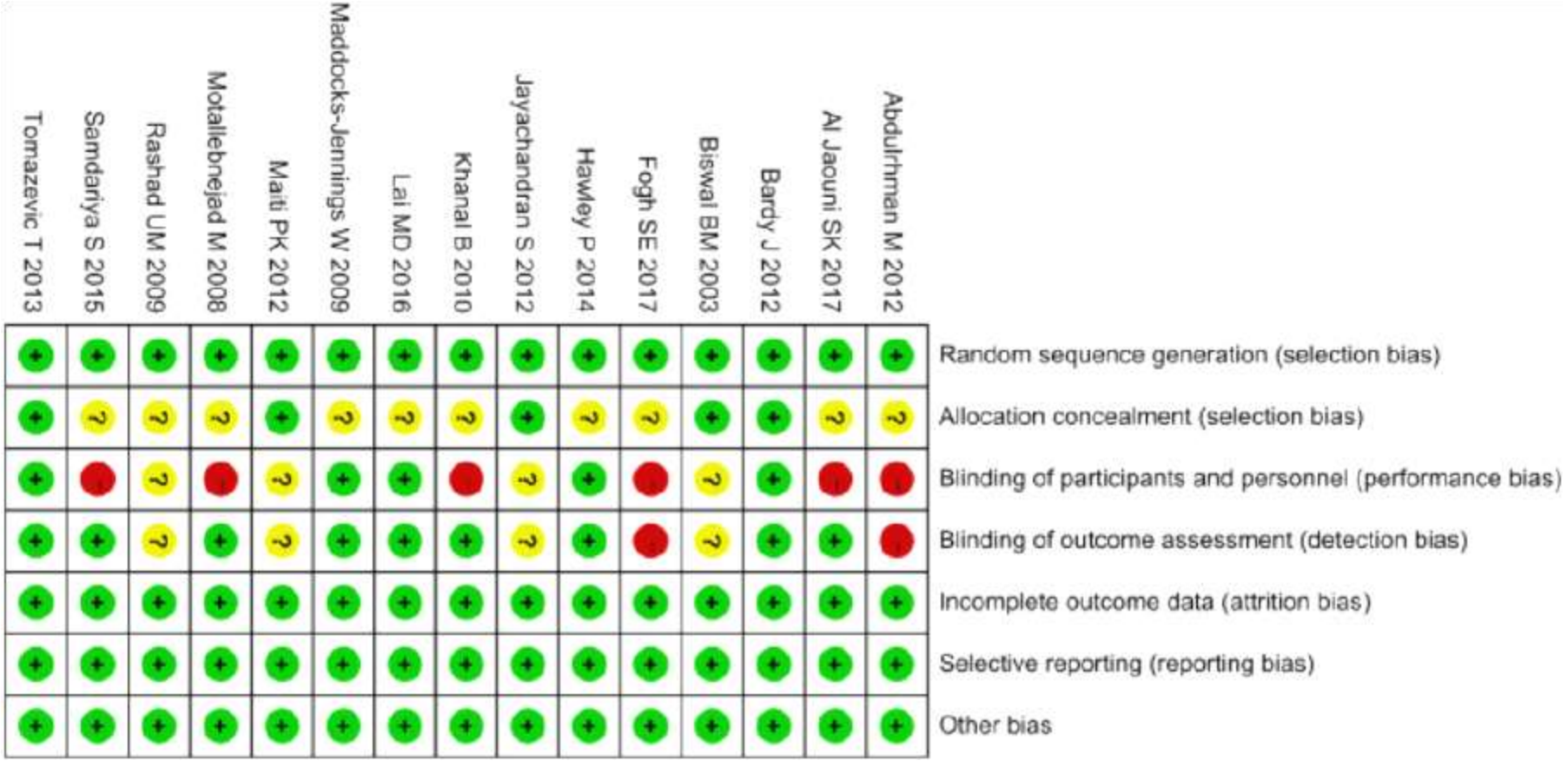
Publication(year)	Is the case definition adequate	Representativeness of the cases	Selection of Controls	Definition of Controls	Comparability of cases and controls (/2)	Ascertainment of exposure(/2)	Same method of ascertainment for cases and controls	Non-Response rate	Overall rating and TOTAL SCORE / 10
Kobya Bulut H,Turkey[3]	1	1	0	1	2	1	1	1	8
Bahramnezhad F, 2015,Iran[6]	1	1	0	1	2	2	1	1	9

Quality of evidence

- In addition, the quality of evidence for the primary outcomes was assessed based on the GRADE system using GRADEpro GDT (Balshem
- et al., 2011; Guyatt et al., 2008).
- The GRADE system assesses risk of bias (study limitations), imprecision, inconsistency, indirectness of study results, and publication bias (classifying each as high, moderate, low, or very low) across the body of evidence to derive an overall summary of the quality of evidence.(Table 2)

步驟2:系統性文獻回顧的品質如何?(FAITH)

I- 是否只納入(included)具有良好效度的文章?



評讀結果:☑是 ☐否 ☐不清楚

步驟2:系統性文獻回顧的品質如何?(FAITH)

T- 作者是否以圖表及表格總結試驗結果?

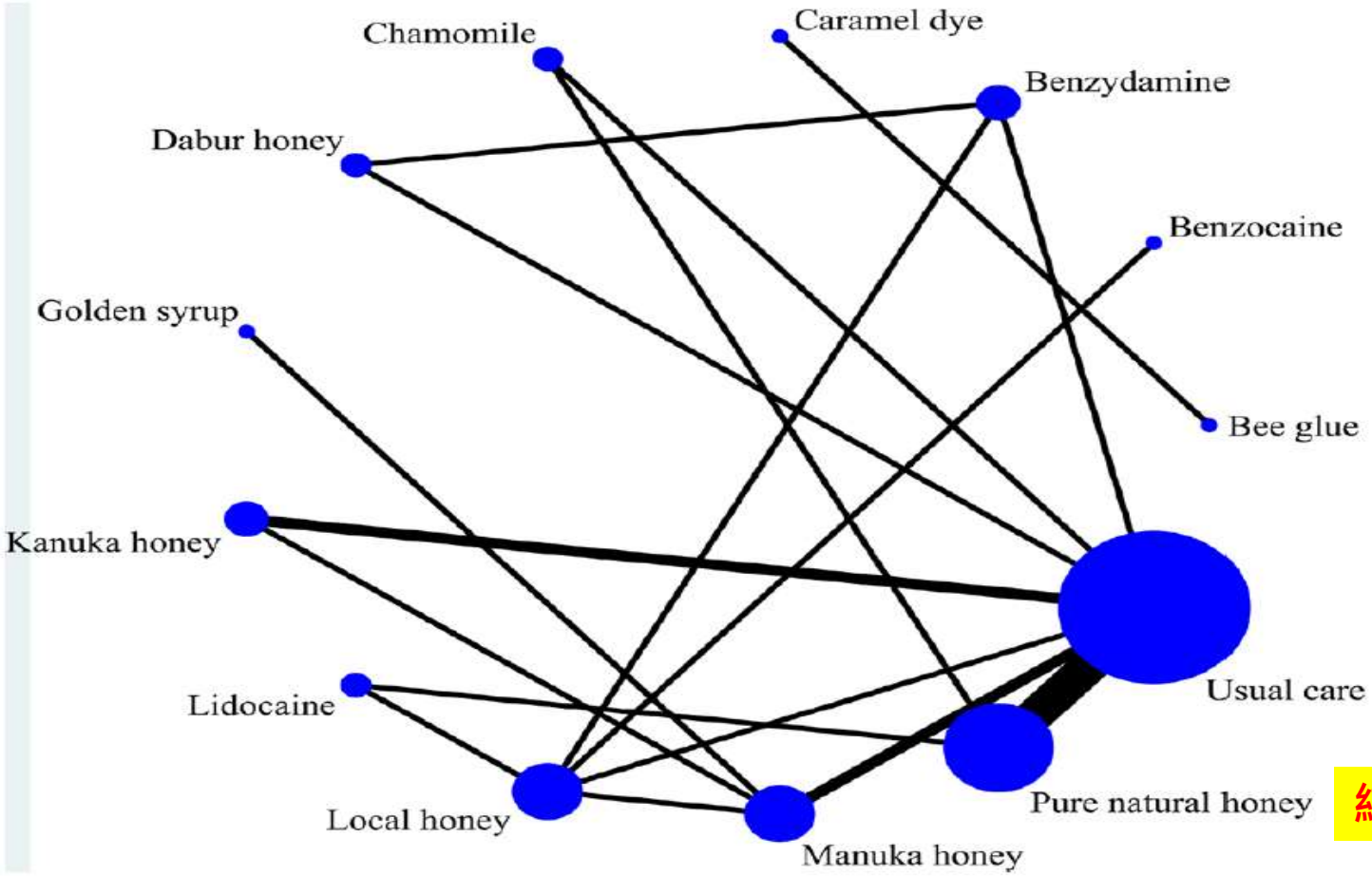


Fig. 2. Network of eligible comparisons for incidence of moderate-severe oral mucositis.

純天然蜂蜜

評讀結果:☑是 □否 □不清楚

Characteristics of baseline in patients associated with honey treatment arm vs control arm.

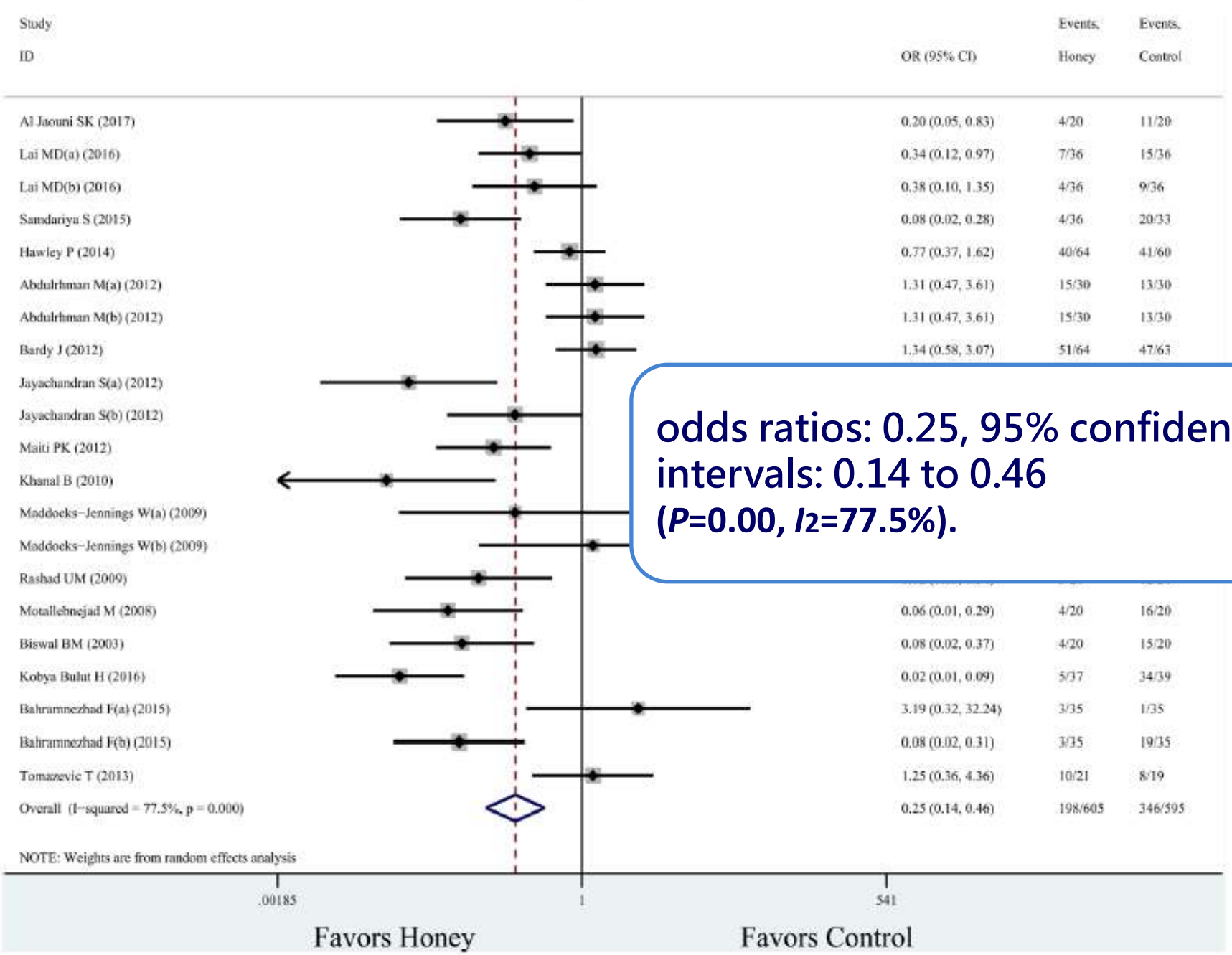
Table 1

Characteristics of baseline in patients associated with honey treatment arm vs control arm.

	Treatment vs control (OR, 95%CI)	Heterogeneity
Age (year)	−0.07 (−0.36, 0.21)[a]	$P = 0.975$, $I^2 = 0.0\%$
Male	1.13 (0.85, 1.51)	$P = 0.815$, $I^2 = 0.0\%$
Tumor stage (I–II/ III–IV)	1.31 (0.68, 2.54)	$P = 0.832$, $I^2 = 0.0\%$
Smoking	1.03 (0.59, 1.81)	$P = 0.356$, $I^2 = 3.3\%$

[a] Standardized mean difference.

Table S3 Study Characteristics.



odds ratios: 0.25, 95% confidence intervals: 0.14 to 0.46 (*P*=0.00, I^2=77.5%).

Fig. 1. Overall incidence of honey treatment arm versus control arm on chemo/radiotherapy-induced moderate-severe oral mucositis.

Subgroup analyses and meta-regressions

Table 2
Meta-analysis, meta-regression and quality of evidence for the moderate-severe oral mucositis between honey treatment arm vs. control arm.

Outcomes and subgroups	Participants (T/C)	OR (95%CI)	Heterogeneity (P, I^2)	Meta-regression (P)	Quality of evidence	Publication bias	
						Begg's (P)	Egger's (P)
Total (n = 21)	605/595	0.25 (0.14, 0.46)[a]	$P = 0.000$, $I^2 = 77.5\%$[b]		Moderate	$P = 0.121$	$P = 0.014$[d]
Age group							
Teenager (n = 5)	138/138	0.41 (0.09, 1.83)	$P = 0.000$, $I^2 = 87.3\%$[b]	$P = 0.414$	Moderate	$P = 0.086$	$P = 0.169$
Adult (n = 16)	467/457	0.21 (0.11,0.41)[a]	$P = 0.000$, $I^2 = 72.3\%$[b]		Moderate	$P = 0.207$	$P = 0.046$[d]
Cancer type							
Head and neck cancer (n = 13)	375/365	0.22 (0.10, 0.47)[a]	$P = 0.000$, $I^2 = 74.9\%$[b]	$P = 0.633$	Moderate	$P = 0.625$	$P = 0.128$
Other cancer (n = 8)	230/230	0.30 (0.10, 0.87)[a]	$P = 0.000$, $I^2 = 82.6\%$[b]		Moderate	$P = 0.019$[d]	$P = 0.057$[d]
Mucositis cause							
Chemo/radiotherapy-induced (n = 2)	40/40	0.16 (0.06, 0.44)[a]	$P = 0.600$, $I^2 = 0.0\%$	$P = 0.364$	Moderate	$P = 0.317$	$P = 1.000$
Radiation-induced (n = 15)	447/437	0.22 (0.11, 0.44)[a]	$P = 0.000$, $I^2 = 73.4\%$[b]		Moderate	$P = 0.216$	$P = 0.062$
Chemotherapy-induced (n = 4)	118/118	0.49 (0.08, 2.91)	$P = 0.000$, $I^2 = 89.8\%$[b]		Moderate	$P = 0.090$	$P = 0.260$
Honey type							
Pure natural honey (n = 10)	255/256	0.11 (0.06, 0.22)[a]	$P = 0.025$, $I^2 = 52.7\%$[b]	$P = 0.038$[c]	Moderate	$P = 0.929$	$P = 0.328$
Manuka honey (n = 4)	170/165	0.70 (0.36, 1.35)	$P = 0.184$, $I^2 = 38.0\%$		Moderate	$P = 0.497$	$P = 0.394$
Local honey (n = 7)	180/174	0.44 (0.15, 1.30)	$P = 0.000$, $I^2 = 77.3\%$[b]		Low	$P = 0.133$	$P = 0.268$
Control arm							
Placebo (n = 9)	276/270	0.39 (0.14, 1.08)	$P = 0.000$, $I^2 = 82.0\%$[b]	$P = 0.219$	Moderate	$P = 0.048$	$P = 0.099$
Usual care (n = 12)	329/325	0.18 (0.09, 0.35)[a]	$P = 0.001$, $I^2 = 66.4\%$[b]		Moderate	$P = 0.411$	$P = 0.155$
Type of assessment scale							
RTOG scale (n = 6)	181/175	0.33 (0.10, 1.08)	$P = 0.001$, $I^2 = 76.7\%$[b]	$P = 0.586$	Moderate	$P = 0.348$	$P = 0.175$
WHO scale (n = 8)	215/216	0.12 (0.05, 0.29)[a]	$P = 0.011$, $I^2 = 61.8\%$[b]		Moderate	$P = 0.458$	$P = 0.349$
NCI-CTC scale (n = 4)	132/132	0.71 (0.34, 1.50)	$P = 0.133$, $I^2 = 46.4\%$		Moderate	$P = 0.308$	$P = 0.370$

T, treatment group; C, control group.
[a] Results with significant differences.
[b] Substantial heterogeneity.
[c] Factors could be an important source of heterogeneity.
[d] Publication bias.

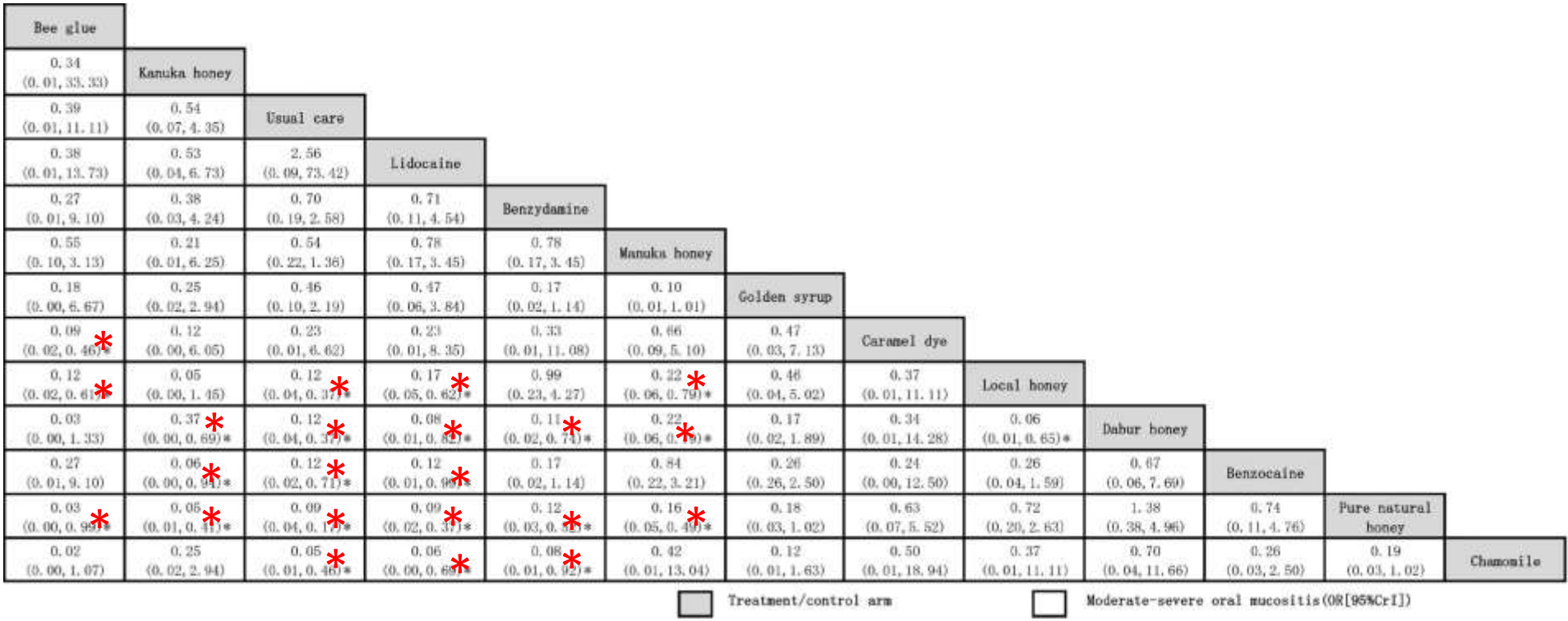


Fig. 3. Summary ORs and CrIs from network meta-analysis. Treatment are reported in order of incidence of moderate-severe oral mucositis ranking according to SUCRA. Comparisons between treatments should be read from left to right. For incidence of moderate-severe oral mucositis, OR < 1 suggests favors for the honey treatment arm than with the control arm.

Secondary efficacy outcomes between honey treatment arm vs. control arm.

honey not only did not increase the risk of adverse effects but but also reduced the onset time of oral mucositis (0.41, 0.08–0.73).
Moreover, the use of honey was effective and safe, with mostly moderate to high quality evidence according to GRADE assessment.

Table 3

Secondary efficacy outcomes between honey treatment arm vs. control arm.

Outcomes	Patients (T/C)	OR (95%CI)	Heterogeneity (P, I^2)	Quality of evidence
Treatment completed	5 (189/187)	0.91 (0.57,1.45)	$P = 0.370$, $I^2 = 6.4\%$	High
Onset time of mucositis	3 (76/76)	0.41 (0.08,0.73)[a]	$P = 0.363$, $I^2 = 1.3\%$	Moderate
Swallowing diary	3 (171/169)	0.98 (0.63,1.51)	$P = 0.571$, $I^2 = 0.0\%$	High
Fungal colonization	3 (104/103)	0.39 (0.11,1.35)	$P = 0.059$, $I^2 = 64.7\%$[b]	Moderate
Bacterial colonisation	2 (84/83)	0.35 (0.03.3.69)	$P = 0.006$, $I^2 = 86.8\%$[b]	Low
Antalgesic use	3 (171/169)	1.02 (0.64,1.65)	$P = 0.909$, $I^2 = 0.0\%$	High

T, treatment group; C, control group.

[a] Result with significant differences.

[b] Substantial heterogeneity.

蜂蜜並不會增加副作用，還可減緩發生口腔粘膜炎的機率。

步驟2:系統性文獻回顧的品質如何?(FAITH)

H-試驗結果是否相近-異質性?

- Although the overall sample and subgroups showed a significant effect favors for honey treatment arm, there was still substantial heterogeneity (P = 0.00, I^2 = 77.5%; Fig. 1, Table 2).
- Moderate evidence of bias could be found in Begg’ s test (P = 0.121) and Egger’ s test (P = 0.014), with moderate evidence according to the GRADE assessment.
- A meta-regression was used to assess the heterogeneity.
- mucositis cause and honey type were the main factors affecting heterogeneity.

Discussion-1

- The large differences in treatment arms (by meta-regression), according to network meta-analysis of therapy efficacy by treatment method, pure natural honey had superior efficacy in terms of treatment arms (Fig. 3).
- Overall, compared with non-honey control arm, honey was found to be both safe and efficacious in treatment for chemo/ radiotherapy-induced oral moderate-severe mucositis.
- Finally, honey not only did not increase the risk of adverse effects but also reduced the onset time of oral mucositis (Table 3).

Discussion-2

- A meta-regression was used to assess the heterogeneity.
- Over all, mucositis cause and honey type were the main factors affecting heterogeneity.
- we observed moderate evidence of publication bias by statistical assessment.

Discussion-3

- Although our group is very meticulous and detailed, but pure natural honey is intersecting, so the best choice is to use pure natural honey for treatment.
- Our results could be confirmed in many publication articles, Song’ s researched made a conclusion that overall relative risk of developing mucositis was almost 80% lower in the honey treatment group than in the control group (Song et al., 2012).
- Raeessi MA considered honey plus coffee regimen was the most effective modality for the treatment of oral mucositis, the results need further identification (Raeessi et al., 2014).

Discussion-4

- RCTs of honey should include larger samples and be robust and randomized to confirm the effects and toxicity of honey on patient-relevant or disease-specific outcomes, particularly in cancer patients undergoing chemo/radiotherapy-induced moderate-severe oral mucositis.
- Future studies should ensure that appropriate methods are used for randomization, blinding and intent to-treat. Furthermore, trials should assess outcomes using standardized or prescribed measures at similar time points. Analyses of individual data will be valuable for further exploration.
- More normative studies should be utilized in future network meta-analyses.

limitation

- First, in the GRADE framework, several comparisons were determined to be moderate or low-quality, which largely restricts the interpretation of the results.
- In addition, the network analysis contained some inconsistencies, which were mainly determined by the loop (Table 3).
- Moreover, thirteen arms in sixteen analyses were measured due to the small sample size.
- positive results are likely to be published, while negative results are not likely to be shared.
- An additional limitation of the standardized outcomes was the extensive heterogeneity (Fig. 1, Tables 2), which indicated substantial variability in the outcomes of the included studies, because there was no presence of heterogeneity in the baseline outcomes (Table 1).

結論

- The finding of this comprehensive network meta-analysis provides some evidence that honey might improve the therapy efficacy in patients with cancer undergoing chemo/radiotherapy-induced moderate-severe oral mucositis without increasing side effects.
- In the clinical therapy of patients with cancer undergoing chemo/radiotherapy- induced moderate-severe oral mucositis, honey can be invoked as a first-line adjuvant therapy agent.

Prophylactic and therapeutic effects of honey on radiochemotherapy-induced mucositis: a meta-analysis of randomized controlled trials

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Abstract

Purpose Oral mucositis is a common side effect of radiochemotherapy and may adversely affect the patients' quality of life (QoL). Honey application may reduce the mucositis grade in patients. Here, we conducted a meta-analysis of randomized controlled trials (RCTs) to evaluate the prophylactic and therapeutic effects of honey on radiochemotherapy-induced oral mucositis.

Methods Publications on RCTs were extracted from the PubMed, Embase, CINAHL, and Cochrane Library databases. The primary outcomes were mucositis grades and pain scores. Secondary outcomes were the recovery time and QoL. The study was registered with PROSPERO (number CRD42018108486).

Results Nineteen RCTs, involving 1276 patients, were reviewed. Honey considerably mitigated oral mucositis in both prophylactic and therapeutic phases. In the prophylactic phase, intolerable mucositis development was significantly prevented in the honey-treated group (RR = 0.18, 95% confidence interval [CI] = 0.09 to 0.41). Patients treated with honey showed significant decrease in pain scores in the first month of treatment (weighted mean difference [WMD] = − 3.25, 95% CI = − 4.41 to − 2.09) and at the end of the treatment (WMD = − 2.32, 95% CI = − 4.47 to − 0.18).

Conclusion Honey, which is relatively cheap and easily available, prevented mucositis and effectively mitigate mucositis in patients after radiochemotherapy. Moreover, it significantly reduced the mucositis grade and engendered a fast and painless healing process. Therefore, honey use during and after radiochemotherapy is recommended for mucositis prevention and treatment.

Keywords Honey · Mucositis · Radiotherapy · Chemotherapy · Meta-analysis

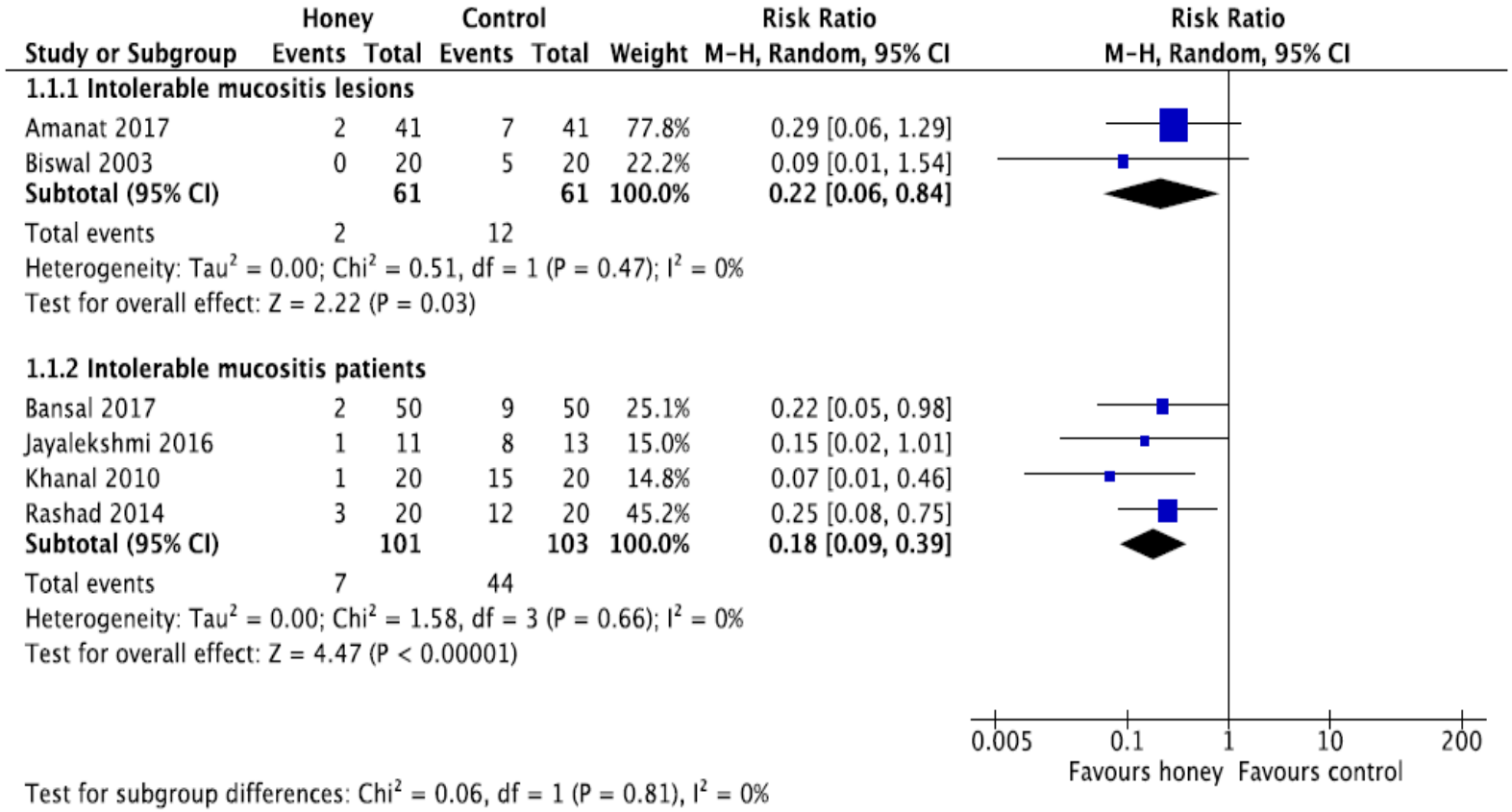

Fig. 2 Forest plot of honey-treated versus control group comparison in the therapeutic phase; outcome: number of intolerable mucositis lesions at weeks 6 and 4

Author [year]	Inclusion criteria	No. of patients (male, %)	Age, mean ± SD	Baseline of oral mucositis grade	Intervention
Prophylactic					
Al Jaouni [2017] [10]	Pediatric cancer patients who received radiochemotherapy; age > 1 year	H: 20 (55) C: 20 (50)	H:7.9 ± 4.1 C: 8.1 ± 4.9	H: 0‡ C: 0‡	H: Natural honey rinse 4–6 times/day C: Control
Amanat [2017] [11]	Adult patient with head and neck cancer planned for radiotherapy	H: 41 (65.8) C: 41 (80)	H: 49.9* C: 50.17*	H: 0 C: 0	H: 20 mL of natural honey rinse, 15 min before and after radiotherapy and before sleeping C: Saline rinse
Bansal [2017] [12]	Patients with oral cavity and oropharyngeal cancers planned for radiochemotherapy	H: 50 (94) C: 50 (94)	H: 50.82 ± 9.7 C: 49.36 ± 10.95	H: 0¥ C: 0¥	H: 1:1 glycerine:honey applied topically after meals, 3 times/day C: Anesthetic and antacid solution
Bardy [2012] [13]	Patients with oropharynx squamous cell carcinoma	H: 64 (82.8) C: 63 (73.0)	H: 59 (39–85) * C: 58 (38–83) *	H: 0 C: 0	H: 20 mL of Manuka honey rinse, 4 times/day (during 4 weeks of radiotherapy + 2 weeks after radiotherapy) C: 20 mL of golden syrup
Biswal [2003] [5]	Adult patient with head and neck cancer planned for radiotherapy; no history of radiochemotherapy	H: 20 (75) C: 20 (40)	H: 63 (19–89) * C: 54 (14–78) *	H: 0 C: 0	H: 20 mL of natural honey rinse, before and after radiotherapy and 6 h after every radiotherapy C: control

Author [year]	Inclusion criteria	No. of patients (male, %)	Age, mean ± SD	Baseline of oral mucositis grade	Intervention
Hawley [2014] [15]	Adult patient with head and neck cancer planned for radiotherapy	H: 54 (81) C: 52 (84)	H: 56.8 C: 59.5	H: 0 C: 0	H: 5 mL of Manuka honey gel rinse, 4 times/day throughout radiotherapy, plus 7 more days C: Sugar-free placebo gel looked and tasted like honey
Jayachandran [2012] [16]	Patients with oral malignancy; no history of radiochemotherapy	H: 20 (55) B: 20 (75) C: 20 (75)	H: 49.5 B: 54.0 C: 55.55	H: 0‡ B: 0‡ C: 0‡	H: 20 mL of natural honey rinse 15 min before and after radiotherapy and 6 h later B: 15 mL of 0.15% benzydamine hydrochloride rinse 15 min before and after radiotherapy and 6 h later C: 20 mL of 0.9% normal saline
Jayalekshmi [2016] [17]	Adult patient with head and neck cancer planned for radiotherapy	H: 14 C: 14	H: 59.71 ± 4.34 C: 52.28 ± 14.04	H: 0 C: 0	H: 15 mL of natural honey rinse 15 m before and after radiotherapy and 6 h later C: 15 mL of water
Khanal [2010] [18]	Adult patients with oral carcinoma planned for radiotherapy	H: 20 C: 20	Not provided	H: 0 C: 0	H: 20 mL of natural honey rinse 15 min before and after radiotherapy and before going to bed C: 20 mL of lignocaine gel
Khanjani pour-fard-pachekenari [2018] [19]	Adult patients with AML planned for 3 + 7 chemotherapy	H: 17 (70.6) O: 17 (64.7) C: 19 (63.2)	NA	H: 0‡ O: 0‡ C: 0‡	H: 5% natural honey rinsed 30 s after each meal and before going to bed O: Brush teeth twice/day, dental floss once/d, and 60 mL saline rinsed 3 times/day C: Control
Mishra [2017] [20]	Children patients planned for chemotherapy (5 Fluorouracil or methotrexate)	H: 20 C: 20	NA (5–19)*	H: 0‡ C: 0‡	H: Honey and Tulsi ice chips rinsed 5 min before chemotherapy and lasted 30 min C: Plain ice chips

Author [year]	Inclusion criteria	No. of patients (male, %)	Age, mean ± SD	Baseline of oral mucositis grade	Intervention
	ALL patients with grade 2 and 3 chemotherapy-related oral mucositis	M: 30 C: 30		M: 2–3 C: 2–3	H: 0.5 g of natural honey/kg (max 15 g) applied topically 3 times/day M: 0.25 g of HOPE/kg (max 5 g) applied topically 3 times/day C: Benzocaine 7.5% gel applied topically 3 times/day
Charalambous [2018] [14]	Head and neck cancer patients with grade 1 or above oral mucositis; age > 18 y	H: 43 (50) C: 43 (50)	Not provided	H: ≥1 C: ≥1	H: 20 mL of natural honey rinse 15 min before and after radiotherapy and 6 h later for 7 weeks C: Saline rinse
Raeessi [2014] [22]	Patients with chemotherapy-related oral mucositis; age 15–80 y	H: 23 (50) M: 23 (42.9) S: 23 (52.4)	H: 54.9 ± 11.6 M: 54.7 ± 15.4 S: 55.9 ± 12.7	H: 2.5‡ M: 2.67‡ S: 2.52‡	H: 10 mL of 50% natural honey rinse every 3 h × 1 week M: 10 mL of 50% natural honey + 3.3% coffee rinse every 3 h × 1 week S: 10 mL of diluted betamethasone every 3 h × 1 week
Samdariya [2015] [25]	Patients with head and neck cancer planned for radiochemotherapy; age 18–70 y	H: 40 (50) C: 38 (42)	H: 52.58 ± 12.21 C: 54.15 ± 7.92	NA	H: 20 mL of natural honey rinse 15 min before and after radiotherapy and 6 h later, with routine salt-soda + benzydamine every 3 h during radiotherapy and up to 3 m postradiotherapy C: Control
Singh [2018] [26]	Children with grade 1–2 oral mucositis	H: 50 C: 50	H: NA C: NA	H: 1–2‡ C: 1–2‡	H: 1–2 mL of natural honey 4 times/day with analgesic and antiseptic gel applied topically C: Control

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臨床運用

臨床運用

- 天然蜂蜜是否合適使用於化學/放射線治療之癌症病人口腔黏膜炎?

同意1 票

懷疑 35票

不同意3 票


THANK
YOU